



## Guest editorial: Agenda 21 as a guide for green chemistry research and a sustainable future†



Terry Collins asked in his recent editorial (*Green Chem.*, 2003, 5, G51) two important questions: 'How should education change to better promote a **sustainable future**?' and 'How should research change to better promote a **sustainable future**?' I can fully subscribe to the answers and the conclusions given by Terry, as I am sure will most readers of this journal. Then, rethinking the editorial, I thought that it would be useful to tackle these questions from another perspective. To give an answer, we must have a thorough and very precise understanding of what **sustainable development** may be, considering its ecological, economical and social dimensions. In principle, this is quite simple; in practice it is much more difficult.

Sustainable development is being understood as the implementation of the Rio Declaration and Agenda 21 including its ongoing advancement such as the Johannesburg Declaration and Plan of Implementation of the World Summit on Sustainable Development in 2002. Thus, chemistry will best promote sustainable

development by being devoted to the implementation of the Rio process. The 27 principles of the Rio Declaration were made concrete in Agenda 21, the comprehensive plan of action for the 21st century that was adopted by more than 170 governments in Rio. Agenda 21 'addresses the pressing problems of today and also aims at preparing the world for the challenges of the next century. It reflects a global consensus and political commitment at the highest level on development and environmental cooperation.' (Chapter 1.3). The 'pressing problems' were developed most precisely and flexibly in 40 chapters. 'The programme areas that constitute Agenda 21 are described in terms of the basis for action, objectives, activities and means of implementation. **Agenda 21 is a dynamic programme** ... It could evolve over time in the light of changing needs and circumstances.' (Chapter 1.6).

The fact that the Rio process marks the very beginning of a new global partnership for sustainable development is most important. In the 11 years since Rio we have all come to understand the fragility of this process on the one hand and the importance and the necessity of continuing it on the other. There is no alternative for mankind. The Rio process must become irreversible.

The 'Conservation and management of resources for development' constitutes the main focus of interest outlined in 14 chapters of Agenda 21. The sciences have to make considerable contributions if this aim is to be achieved. Chapter 35, 'Science for Sustainable Development', 'focuses on the role and the use of the sciences in supporting the prudent management of the environment and development for the daily survival and future development of humanity... The sciences should continue to play an increasing role in providing for an improvement in the efficiency of resource utilization and in finding new development practices, resources, and alternatives. There is a need for the sciences constantly to reassess and promote less intensive trends in resource utilization, including less intensive utilization of energy in industry, agriculture, and transportation. Thus, the sciences are increasingly being understood as an essential component in the search for

feasible pathways towards sustainable development.' If this statement is right—and I have no doubt that it is—then the sciences may have to change and focus on contributing to the solution of the pressing problems outlined. This, however, means nothing less than requesting scientists to develop their basic and applied research topics from the immense catalogue of unsolved problems that stand in the way of the sustainable development outlined in Agenda 21. This also applies to chemistry and chemical research topics thus developed. They clearly will be appropriately termed 'green chemistry' or 'sustainable chemistry' and should all become important topics of discussion in this journal.

As examples of what I mean, I will briefly outline several of these unsolved problems and the possible contribution of chemistry with respect to the important Chapter 4 'Changing Consumption Patterns'. This chapter focuses on 'unsustainable patterns of production and consumption' and 'national policies and strategies to encourage changes in unsustainable consumption patterns'.

The encouragement of the environmentally sound and sustainable use of natural resources is one aim of this chapter. At present, the proportion of renewable raw materials in the feedstock consumption of the chemical industry in the industrialized countries runs to less than 10%. It is assumed that this percentage will increase considerably. In 2020, 25% of the production of organic chemical products is expected to come from renewable feedstocks. In the long term, renewables are the only workable solution, and their processing by catalytic and other methods will make it possible to replace oil as civilization's basic feedstock. Here it should be pointed out that the selective catalytic transformation of the complex molecules of biomass presents a very great challenge to chemists. Most products obtained from renewable raw materials are at present not competitive with petrochemical products, a circumstance that will change rapidly when oil resources diminish and the oil price rises. Therefore, it is high time to expand basic research on the chemical transformation of renewable feedstocks to

†The opinions expressed in the following article are entirely those of the author and do not necessarily represent the views of either the Royal Society of Chemistry, the Editor or the Editorial Board of *Green Chemistry*.

achieve substitution processes and products as was pointed out by the German Chemical Society on the occasion of the world summit in Johannesburg (<http://www.gdch.de>). However, chemistry is changing very slowly. Obviously, chemical companies are comfortable with petrochemicals and are reluctant to process alternative renewable feedstocks such as plant oils and carbohydrates, which may not be suited to the usual petrochemical processing. This presents a serious general structural flaw in chemical education. Chemists learn from the very beginning to think in terms of petrochemical product lines. It is difficult for us to develop alternative thinking in terms of renewable feedstock product lines that have not been available up to now and have to be invented. While most chemists continue to prefer simple petrochemical molecules as feedstocks to develop catalysts and reactions, the growing trend among the newly forming green chemistry community to develop green catalysts, green solvents, and green reactions around renewable source materials is particularly important in the field. We need to a certain extent to substitute current curricular material that teaches today's students classical thinking in terms of petrochemical products with material that advances their ability to think about a future chemical industry based on renewable feedstocks. For the students, this will lessen the inevitable challenge of transforming their skills to suit the processing of feedstocks that will become more and more biomass-based. The classical approach that holds hegemony today is possibly not preparing them even remotely adequately for this challenge.

There is another problem tenuously connected with this old thinking. The competition between the cultivation of food and renewable raw materials for the limited available agricultural area could lead to problems, because food demand and consumption will also increase dramatically. The world population will rise from the present 6 billion people to about 9 billion by the year 2050. For that

reason, the United Nations programs to combat desertification (Agenda 21, Chapter 12; see also 'United Nations Convention to Combat Desertification') and deforestation (Agenda 21, Chapter 11, see also Statement of Principles for a Global Consensus on the Management, Conservation and Sustainable Development of all Types of Forests, Rio Conference, 1992) are most important. Unfortunately, the implementation of these programs has not advanced much, mainly because the industrialized countries have not been interested. Obviously, the implementation of these programs has to be greatly intensified, both to stop desertification and deforestation, and also to regenerate agricultural areas by 'combating land degradation through, *inter alia*, intensified soil conservation, afforestation and reforestation activities' (Agenda 21, Chapter 12.4b). The sciences and especially chemistry could make enormous contributions to these programs, which may also help to stabilize a favourable global climate. However, are the sciences, and in particular is chemistry, prepared to make the necessary contributions? We have already lost much time by not rising to the research challenges of sustainable development that have been available for study in the forty chapters of Agenda 21 for 11 years now, and we will lose much more if we continue to not refer to Agenda 21 in establishing our national and international research project priorities.

During the Christmas period, when I was writing this editorial, a European and an American mission arrived on the planet Mars, one most successfully, the other much less so. Obviously, it may be fascinating for some people, and, I confess, also for me, to know whether molecules of water or of any organic compound may be found on this planet. However, beside the fact that mankind will have available thousands of years to answer this interesting question, assuming that sustainable development of human civilization on this earth can be

established, it could be thought that this kind of research at this time is contra-sustainable. In other words, 2 billion euros—the approximate cost of these two missions to Mars—is now not available for sustainability-related research, *e.g.* to reverse desertification and deforestation, which is clearly an important step on the road to sustainable development.

Recently, energy ministers from around the world signed the first international framework for R&D on the capture and storage of CO<sub>2</sub> emissions (*Chem. Eng. News*, June 30, 2003, 19). Will that be a step towards sustainable development? Consulting Agenda 21 and also the documents of last year's world summit in Johannesburg reveals, remarkably, that CO<sub>2</sub> sequestration and R&D on this topic have not been on the agenda for sustainable development. One might think that this first international framework is just a program for the industrialized and some industrializing countries to continue their unsustainable practices, as strikingly characterized in chapter 4 of Agenda 21. Perhaps this framework could be oriented in the direction of sustainable development if it could be successfully coupled to the UN program to combat desertification and deforestation, because the most efficient system of CO<sub>2</sub> sequestration, validated over millions of years, is the terrestrial biosphere. However most probably these billions of dollars and euros spent on capturing and storing CO<sub>2</sub> will be wasted and will be lost to research contributing to sustainable development, as have been many more billions of dollars and euros in the years since Rio.

Terry Collins emphasized in his editorial that 'our responsibility translates into a duty to alert civilization to move away from the dependence that is undermining it.' There is no time like the present to be doing this!

Jurgen O. Metzger  
Oldenburg, January 2004



## Robin D. Rogers

A profile of Robin D. Rogers, Professor of Chemistry and Director of the Center for Green Manufacturing at The University of Alabama.

### Background

#### Timeline

1975–1978: The University of Alabama, Tuscaloosa, AL; Chemistry Honors student; B.S. Degree in Chemistry (ACS); Summa Cum Laude

1978–1982: The University of Alabama, Tuscaloosa, AL; Ph.D. in Inorganic Chemistry; Research Advisor: Professor Jerry L. Atwood

1982 (summer): Visiting Assistant Professor, The University of Alabama, Tuscaloosa, AL

1982–1996: Assistant, Associate, Full, Presidential Research Professor, Northern Illinois University, DeKalb, IL

1991–1998: Resident Associate Guest, Visiting Scientist, Faculty Appointee, Guest Appointee, Argonne National Laboratory, Argonne, IL

1996–: Professor, The University of Alabama, Tuscaloosa, AL

1998–: Director, The University of Alabama, Center for Green Manufacturing, Tuscaloosa, AL

2000: Visiting Professor, Université Louis Pasteur, Strasbourg, France



I was born in Ft. Lauderdale, Florida, USA on March 4, 1957, a few months before Sputnik was launched. When I was 2 years old my family moved to Athens, Alabama

where my father worked at Redstone Arsenal in Huntsville, AL. Growing up about 20 miles from Huntsville (and the Marshal Space Flight Center) during the 1960's space race, resulted in a deep appreciation for science and the desire to be a scientist. It was a time when science was revered and scientists were the good guys adding to the quality of life. Rather than a role model *per se*, it was the excitement around the field of science (generated by the space race) which attracted me to the field. I wanted to be a scientist so that I could be an astronaut. I felt that space travel would be common place within my lifetime.

In 1975, I entered The University of Alabama in Tuscaloosa, Alabama and chose Chemistry due to a fascinating Freshmen Chemistry Professor and the ability to conduct undergraduate research within that Professor's group. The first experiments I was given were synthetic in nature and blew up two ovens! After being assured that Dr. Jerry Atwood wasn't really trying to give me a subtle hint to give up Chemistry, I studied single crystal X-ray crystallography with minimal synthetic experiments!

I thoroughly enjoyed my undergraduate research and decided to stay for graduate school at Alabama. During my undergraduate and graduate school days, I learned a full appreciation for the totality of a University and, of course became immersed in 'Alabama Football.' I like to tell people that I played in two national championship football games with Coach Bear Bryant during my university time, but I do (usually) eventually tell them that I was a Tuba Player in the Million Dollar Marching Band! This love of the marching band led me to stay in a marching band (at NIU and Alabama) for 28 years; last year (2003) being the first year I have not played the tuba!

Growing up in Alabama and getting all my degrees from The University of Alabama, taught me valuable lessons about the comprehensive nature of a university, and the total impact it can have on one's life. In 1996, after 14 years as a faculty member at Northern Illinois University in DeKalb, Illinois, I was able to return to Alabama as a Full Professor. I feel exceptionally lucky to have this

opportunity to give something back to the university which gave me so much while I was growing up.

Tuscaloosa, itself is a town with a population of about 80,000 located in central/western Alabama, about an hour from the Mississippi border. The closest airport, which I seem to see a lot of these days, is an hour to the east in the State's largest city, Birmingham. It's hard to describe Tuscaloosa, so I will extend the invitation, Come see it for your self and enjoy some of our 'Southern Hospitality'!

### Green Chemistry and my research

During the 1980s as a faculty member at Northern Illinois University, I made an unexpected (to me!) discovery that polyethylene glycol can be salted out by simple inorganic salts while I was investigating the coordination chemistry of f-elements by crown ethers and polyethylene glycol. I was fascinated by the fact that when PEG is salted out like this, you form two immiscible phases, yet both are over 80% water on a molar basis.<sup>1</sup> The field had been around for 40 years or so, mainly being investigated by Chemical Engineers for gentle separations of proteins and cellular materials.

I thought, this is great!, you can partition ions and molecules between two phases which are both 80% water on a molar basis. Who needs VOCs! Even before 'Green Chemistry' was as widespread as it is now, it was obvious that more environmentally benign chemistry was needed and certainly 'volatile organic compounds' had achieved a very negative connotation in the general public. We have worked (and still do!) in this field for 15 years now and it was this research which led us to ionic liquids and ultimately Green Chemistry.

Although one could argue that Green Chemistry needs 'Research Money', every field could make the same claim. Certainly governments could hasten the progress of developing green technology, but this should not be only the governments' concern. Industry should be (and indeed some are) heavily investing in Green Chemistry.



There should not necessarily be legislative or regulatory barriers to Green Chemistry implementation. Any green technology which will eventually be successful, must not only be green, but also economically and socially acceptable. With such success, the technology will be adopted because it is good business, not because it's green.

Green Chemistry is by its very nature interdisciplinary. I have always enjoyed interdisciplinary projects which allow us to work in one area and learn from the top people focusing on that field and introduce our work to an entirely different community. I want to make connections between different aspects of science and engineering.

Our work with ionic liquids arose from such an experience. I met Ken Seddon at a Crystal Engineering Conference in Digby, Nova Scotia where we discussed hydrophobic ionic liquids. I wanted to do separations from water and ionic liquids sounded like another alternative to VOCs which would compliment our work with PEG aqueous biphasic systems.<sup>2</sup>

I really did not imagine that ionic liquids would take off quite as much as they did. I have felt my role in this field has been to help increase the awareness of the ionic liquid field, what ionic liquids can do, but also what they cannot do. I have tried to connect an underlying molecular level understanding between several apparently disparate areas which turn out to be similar.

Ionic liquids and Green Chemistry began to both pick up steam (and followers) about the same time. Neither idea was new, and a lot of really good work in both areas preceded the time of my entry, but once again, it was the possible connections between the two fields that interested me. Here was an opportunity to develop new chemistries and gain some understanding of new solvents and solvent behavior, while at the same time keeping in mind the goals of Green Chemistry.

Ken Seddon and I hosted a NATO Advanced Research Workshop to try and bring together the (at the time) limited ionic liquids community and set a research agenda for the field. Perhaps the two most important outcomes of that meeting included the following:<sup>3</sup>

Ionic Liquids are intrinsically interesting and worthy of study for advancing science (ionic vs. molecular solvents) with the expectation that something useful may be derived.

Combined with Green Chemistry, a new paradigm in thinking about synthesis in general, Ionic Liquids provide an opportunity for science/engineering/business to work together from the beginning of the field's

development.

Thus, from the beginning, it was intended that if we were going to be developing new chemistries that they be developed in a sustainable fashion. As the field has developed,<sup>4,5</sup> it has been obvious that sometimes we fall back on old habits, just to get to a specific goal rather than incorporating the bigger picture of sustainable development. We are starting to see a lot of work published in the ionic liquids field now, where it is obvious that 'ionic liquids research' has become the goal, rather than letting the goals of 'Green Chemistry' drive the development and utilization of ionic liquids.

My most important role now, may be to continue to highlight the good AND the bad in the ionic liquids/Green Chemistry relationship. Only through identification of the deficiencies and the recognition of Green Chemistry as the ultimate goal, will we be able to truly take advantage of the unique chemistries ionic liquids have to offer.

### Current responsibilities and Green Chemistry

As Professor of Chemistry and Director of the Center for Green Manufacturing,<sup>6</sup> I would like to influence Green Chemistry from several directions. First, we must educate our students, not only in the classroom, but in the laboratory as they develop their dissertation research projects, at meetings as they disseminate their research and learn from the world's experts, and during their career development. We can encourage and promote the ideals of Green Chemistry in everything we do for and with students and young professionals.

It is the responsibility of everyone in the field to explain their work to their colleagues and to the general public in a form which not only clearly delineates the chemistry, but also the motivation. There should be an honest assessment of the good and the bad. The work should be placed in proper context which not only delivers the message of Green Chemistry, but outlines how we may eventually achieve such technology.

I, of course, would also like to develop new knowledge and use that knowledge to develop new technologies that actually see industrial implementation. We are currently very excited about using ionic liquids as an enabling technology to dissolve cellulose and active ingredients which allow us to make new renewable advanced materials.<sup>7-10</sup> Hopefully, you will see more of this in the open literature soon!

Our goals of developing new green technology and transferring this to the business sector can be accomplished by strategic collaboration with academics,

industry, or national laboratories. To that end, The University of Alabama is rededicating its efforts to grow the Alabama Institute for Manufacturing Excellence,<sup>11</sup> under the helm of Dr. Robert L. Wells. We intend to make Green Chemistry a vital component of the AIME concept.

### Summary

The most difficult task we face is to continue the work of Green Chemistry without being able to give all the answers at once. As a Professor, my greatest impact will not be a single development which saves the world, it will be getting my students at all levels, and indeed anyone who hears one of my talks or lectures at meetings, to think about Green Chemistry and implement it in their own work.

What many do not realize when we are out discussing our work in the context of Green Chemistry, is that we are building a future where all the ramifications of the chemical profession are put out on the table and thought about up front. Most likely, none of us will immediately produce a process which will be a panacea to cure all the world's ills. We must be willing to take those small steps which lead to a brighter (greener!) future, and justify our work to critics that look at the short term rather than the long term goals. I should point out, that those critics are just as vital to this process as those working in the field! We need to be able to answer their questions and continue to work toward a common goal.

I enjoy (and use for motivation) a quote from Harry Emerson Fosdick, '*Always take a job that's too big for you, and then do your best.*' I see this attitude in the Green Chemistry community, and I believe it will serve us well to maintain it.

### Acknowledgements

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Melanie L. Moody, Megan B. Turner, Keith E. Gutowski, Nicholas J. Bridges, Violina A. Cocalia, Meghna Dilip, and Marcin Roman; and Undergraduate students, Jane Holly Poplin and J. Brett Wilson.

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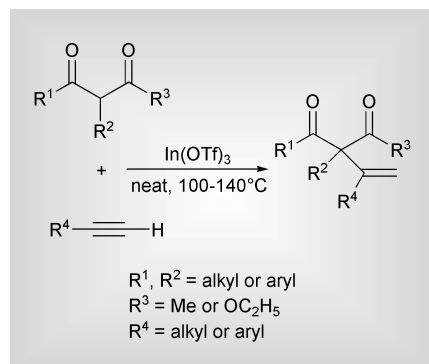


## Highlights

Markus Hölscher reviews some of the recent literature in green chemistry

### Solvent and waste free indium catalyzed enolate addition to alkynes

Addition of enolates to C–C multiple bonds proceeds in general only with activated alkenes and alkynes. While Nakamura's group has already shown that a variety of zinc enolates add to unactivated alkenes, they have now introduced solvent free indium catalyzed addition of enolates to unactivated alkynes (*J. Am. Chem. Soc.*, 2003, **125**, 13002). Indium triflate reacts with  $\beta$ -diketones or  $\beta$ -ketoesters to form an indium enolate, which adds across the triple bond of various alkynes with aliphatic and aromatic substituents.

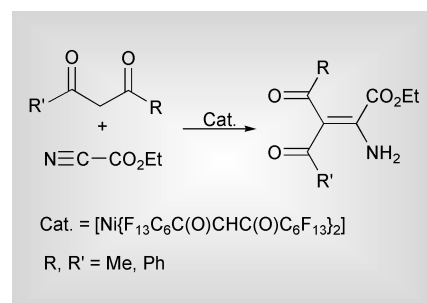


The reaction proceeds practically with 100% regioselectivity introducing the carbonyl compound to the substituted alkyne carbon atom. Also the yields were essentially quantitative for both the active methylene compound and for the alkyne. In the case of electron rich alkynes the yield is decreased due to formation of high molecular weight polymers. However, in most cases polymer formation could be reduced completely. Interestingly heating neat mixtures of the two reactants with catalytic amounts of  $\text{In}(\text{OTf})_3$  is more efficient than diluting the system with solvent. Since no further coactivators are needed and the reaction is atom efficient no waste is generated.

### Fluorous chemistry without fluorinated solvents

Biphasic systems consisting of an organic phase and a perfluorocarbon phase are

immiscible at low temperatures. Catalysts with perfluorinated ligands dissolved in the fluorinated phase consequently cannot transform substrates dissolved in the organic phase at reasonable rates, due to mass transfer problems. However, upon heating the two phases mix, the reaction can occur and after cooling, product/catalyst separation simply consists of phase separation. Though appealing this approach has suffered both from economical/ecological drawbacks (high cost and environmental persistence of perfluorocarbon solvents) and from leaching problems, which were not fully resolved. Stuart *et al.* from Leicester University describe an example of a modified procedure in which the catalyst with the perfluorinated ligand and the substrate are dissolved in dichloromethane (*Chem. Commun.*, 2003, 2430–2431). After the reaction (addition of ethyl cyanofornate to  $\beta$ -diketones) catalyst and product are separated by chromatography on fluorinated reverse phase silica gel.

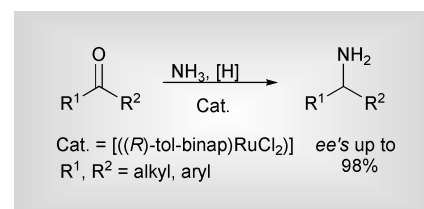


It was nicely shown that long and multiple perfluorinated groups are needed as ligand side chains to enable complete separation (the catalyst is recovered from the column by simply switching the solvent). Upon recycling multiple times the catalyst loses activity, which the authors ascribe to slow degradation. Obviously, the strategy would be even more attractive if no, or a more benign, solvent could be used during the reaction step.

### A green route to chiral amines

Optically active amines can be useful as building blocks for the synthesis of agrochemicals and pharmaceuticals.

Recently a new synthetic method, which can be considered as environmentally clean, was developed by Kadyrov and Riermeier (*Angew. Chem., Int. Ed.*, 2003, **42**, 5472–5474). They showed that chiral tol-binap type ligands such as (*R*)-2,2'-bis(di-*p*-tolylphosphanyl)-1,1'-binaphthyl furnish enantioselective ruthenium catalysts for the reductive amination of aromatic ketones.

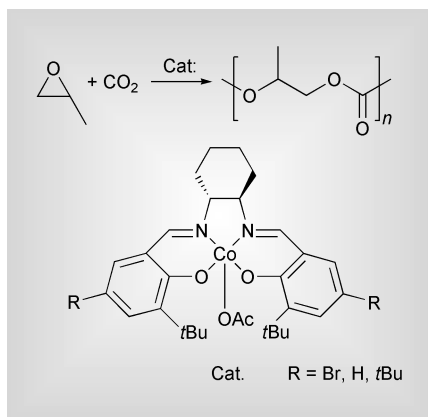


The catalysts tolerate quite a variety of substrates. The hydrogen source is ammonium formate and the reaction is run in methanol. Rhodium and iridium as catalyst metals were much less effective and enantioselective. Acids accelerate the reaction but diminish the enantioselectivity whereas addition of aqueous ammonia increased enantioselectivity, though raising the amount of alcohol produced as side product. Under optimized conditions alcohol formation can be reduced completely in many cases, with ee's and yields both reaching values between 90 and 95%.

### CO<sub>2</sub> as building block

As one of the major 'waste products' of human activities  $\text{CO}_2$  seems an attractive building block for chemical syntheses. Efficient and selective catalytic conversions of  $\text{CO}_2$  are therefore of great current interest. A new example was added by the group of Coates from Cornell University who succeeded in alternatingly polymerizing  $\text{CO}_2$  and propylene oxide for the first time without the concomitant production of cyclic carbonates (*Angew. Chem., Int. Ed.*, 2003, **42**, 5484–5487).

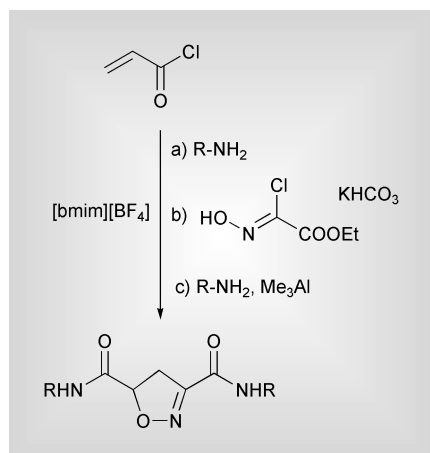
The secret is the catalyst:  $[\text{Co}(\text{sally})\text{OAc}]$ -complexes (sally = *N, N'*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine) yield effectively and selectively highly alternating polycarbonate polymers with narrow



polydispersities and molecular weights  $M_n$  between 3000 and 21 700 depending on reaction conditions. In contrast to similar Cr catalysts the Co complexes do not require any additives, and despite their lower activity they advantageously show a high selectivity for polymer formation and excellent regioselectivity.

### Multistep parallel synthesis of isoxazolines with ionic liquids as common phase

Though the use of ionic liquids has increased substantially in the past years, there has not been yet a trial employing these unique solvents as common phase for multistep parallel synthesis. The group of Taddei from the University of Siena took the first step in developing such a system (*Org. Lett.*, 2003, **5**, 4029–4031). They

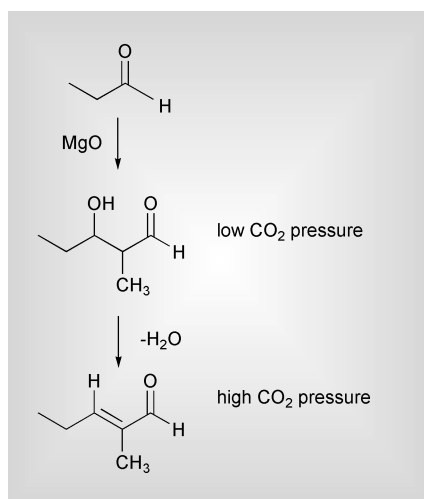


chose a three step sequence consisting of a Schotten–Baumann reaction, followed by 1,3-dipolar cycloaddition and a final ester amidation with  $\text{Me}_3\text{Al}$  to transform acryloyl chloride to isoxazoline.

At first all three steps were carried out individually to ensure that the reactions can be carried out in ionic liquids. Extraction of the reaction products with ether yielded the desired products in all cases. The ionic liquid  $[\text{bmim}][\text{BF}_4]$  serves just as well; when all three reaction steps are carried out without isolating the intermediates the overall yield for the test reaction was 43%. Subsequently the multistep reaction was carried out in a parallel synthesizer apparatus with 16 reaction tubes. The reactant chosen was acryloyl chloride and as amines the authors used cyclohexylamine, aniline, benzylamine and isobutylamine. Of the resulting 16 isoxazolines 14 were pure ( $^1\text{H-NMR}$ , 200 MHz), two needed to be purified chromatographically, with overall yields ranging between 38 and 51%.

### Selectivity control in aldol reactions in compressed $\text{CO}_2$ via pressure adjustment

The aldol reaction is a very important synthetic tool for the formation of C–C bonds. However, due to the high reactivity of the  $\beta$ -hydroxy aldehyde resulting in the first reaction step it is difficult to obtain



either the aldol or the enal product with satisfactory selectivities. Kawanami *et al.* from the Supercritical Fluid Research Centre in Miyagi reported a substantial improvement to overcome this problem in the self-aldol condensation of propionaldehyde (*Chem. Commun.*, 2003, 2502–2503).

Choosing MgO as the catalyst and compressed  $\text{CO}_2$  as the reaction medium, the authors showed, that at low  $\text{CO}_2$  pressures the  $\beta$ -hydroxy aldehyde is formed in high selectivity (93%), whereas the selectivity for enal only is 7%. Changing the pressure from 5 to 12 MPa results in a selectivity decrease for  $\beta$ -hydroxy aldehyde and an increase for enal (45 and 50%, respectively). Higher selectivity for enal could simply be achieved by adding water (94%).

### Predictions of air pollution and climate effects in a global hydrogen economy

The combustion of fossil fuels has influenced the chemical composition of the Earth's atmosphere with many consequences for air quality and global climate. Hydrogen seems to be a favorable replacement (*e.g.* for use in fuel cells); however its generalized use would most certainly alter atmosphere and climate as well. Schultz *et al.* from the Max-Planck-Institute for Meteorology, Hamburg, have simulated the impacts a switch to global hydrogen use would have (*Science*, 2003, **302**, 624–627). Prior to presenting their results, the authors emphasize the difficulties of such a quantitative prediction *via* simulation. Problems arise for example due to uncertainties in the estimation of hydrogen emission and hydrogen leakage present already or to be generated upon increasing hydrogen production. The study makes clear however that a large-scale transition from fossil fuel combustion to hydrogen fuel cell technology can lead to substantially improved air quality and reduced climate change, when care is taken that hydrogen production is not accompanied by additional emission of ozone precursors and greenhouse gases.





## Benign and sustainable chemical technologies—a UK perspective

Following the release, in January 2003, of the international assessment of university research in chemistry in the UK, 'Chemistry at the Centre', the RSC identified a number of projects to ensure that the major recommendations of the report were carried forward. One of these was to review the current state-of-the-art, and future prospects for, Green Chemical Technology. This was done through a wide-ranging workshop on 'Benign and Sustainable Chemical Technologies' held at King's Manor, York, 20–21 October 2003. This article summarises the outcomes of the workshop and highlights its main recommendations.

### Introduction

In 2002 the EPSRC commissioned the RSC to undertake an International Review of University Chemistry Research in the UK. This review was carried out by an international group of thirteen leading scientists and industrialists chaired by George Whitesides of Harvard University. The Panel's report *Chemistry at the Centre—An International Assessment of University Research in Chemistry in the UK* was published in December 2002<sup>1</sup>, followed by a public presentation in January 2003. Its release almost coincided with the DfEs White Paper on *The Future of Higher Education*<sup>2</sup> and with the appearance, a month earlier, of the report produced for the Science Minister, Lord Sainsbury, by the Chemicals Innovation and Growth Team on the Chemicals Industry in the UK<sup>3</sup>. The White Paper acknowledges that current strength in UK research cannot be maintained unless substantial changes are implemented; it also recognises the continued growth in competition from other countries. The CIGT report establishes that the UK chemical industry needs to (i) earn a better public reputation, (ii) respond to the challenges of sustainable development, (iii) increase innovation by improved use of science and technology, (iv) recruit a more diverse workforce to ensure availability of the right sets of skills and competences. These three reports convey a very similar message, though in different ways and with different emphasis. Together, they represent a clear wake-up call for the scientific community in general and for the chemistry community in particular.

Some of the major scientific concerns expressed in the *International Review Report* were:

- Creativity is perceived to be slipping: the quality of scholarship in chemistry in the UK is comparable with the world's best; levels of innovation, step changes in thinking and ground breaking discovery are declining.
- Financial/organisational structures favour conservative research. The system does not encourage revolutionary, multidisciplinary and

exploratory research. It does not facilitate the links with chemical engineering, physics, biology, medicine and materials science.

The report included key recommendations that were intended to address the perceived decline in creativity within academe. Undoubtedly, it is the community itself that should foster creativity by generating initiatives, and helping the research councils to focus their resources more effectively. The RSC sees itself as *facilitator* for such activities, providing the forum that makes possible effective dialogues between the interested parties and enabling constructive interactions between these groups.

A number of projects have been identified by the RSC with the aim of ensuring that the major recommendations of the International Review are carried forward. The first of these projects was the two-day Research Workshop in *Benign and Sustainable Chemical Technologies* that took place on 20/21 October 2003 at King's Manor, York. In this context, over the last five years the RSC has committed significant resources to this area, supporting the establishment of the Green Chemistry Network at York University as well as providing substantial effort towards the development of the Crystal Faraday Partnership where the RSC is one of three hub partners, along with the Chemical Industries Association and the Institution of Chemical Engineers (IChemE). The attitude of the RSC towards green chemical technology is therefore one of public commitment and active support. Correspondingly, the RSC has recently established the new Environment, Sustainability and Energy Forum (ESEF) to provide a platform to raise the profile of these subjects within the RSC and the wider community; it will also strategically address issues that span the interests of several RSC interest groups already active in these areas. In the *International Review* report particular note was made of the current state of green chemistry research, emphasising its importance and encouraging further development of these activities, thus: 'If the UK wishes, as a matter of public policy, seriously to

address environmental issues, it must engage some of the most able research groups in academic chemistry'. And more specifically: 'Multidisciplinary and collaborative research involving multiple departments and universities, and specifically including chemical engineering, are essential for significant progress'. Hence, in response to the 'Whitesides Review', the overall aims of the York workshop were to raise the national profile of the field within the academic and industrial communities and to sharpen the RSC's own related objectives.

During the 1990s, the US Environmental Protection Agency (EPA) developed a pioneering concept that became known as green chemistry. Green chemistry involves promoting the design of environmentally benign processes that minimise or eliminate the use of toxic substances (feedstocks, reagents, solvents) and maximise overall efficiency (reduction of unwanted by-products, especially toxic materials). The guiding principle is prevention rather than cure—it is far better to prevent toxic waste from being produced in the first place, rather than cleaning up after the fact. Green chemistry encompasses all aspects and all types of chemical processing—including synthesis, catalysis, reaction conditions, separations, monitoring and analysis—that reduce negative impacts on human health and the environment. The current challenge is to expand the concept of green chemistry to encompass a broader view of sustainable development. And this was one of the guiding principles of the workshop.

### Structure and content of the workshop

A panel of 31 UK chemists, engineers, agricultural chemists, biologists and biochemists, including representatives from both academe and industry, participated in the workshop. Representatives from the EPSRC and BBSRC were also present (see full report including complete list of attendees at [http://www.rsc.org/lap/polacts/benign\\_report.htm](http://www.rsc.org/lap/polacts/benign_report.htm)). The workshop participants



were selected after wide consultation within the RSC and with other organisations (Research Councils, IChemE, Green Chemistry Network and the Crystal Faraday Partnership). As the subject area is intrinsically multidisciplinary, the framework of the workshop extended beyond chemistry.

Biotechnology is becoming more important to the future of the chemical industry as biotechnological strategies become increasingly viable, both environmentally and economically. This is highlighted by the 2003 Presidential Green Chemistry Challenge Awards (Washington, USA), where three of the five winners were honoured for their bio-based developments in innovative syntheses, process improvements and new products that promote pollution prevention. One of the winners was DuPont who developed a commercially viable bioprocess for production of 1,3-propanediol from corn-derived glucose. In this context, it was therefore highly appropriate that Dr John Pierce, Director of Biochemical Sciences and Engineering Central Research, DuPont USA, opened the workshop with a superb presentation entitled 'Green and Sustainable—a Work in Progress'.

Day One began with a series of keynote lectures. These did not address the speakers' own research achievements but instead gave a broader view of the state of the art in the relevant area, facilitating the ensuing discussions. The speakers were: Professor Rodney Townsend, RSC Director of Science and Technology; Malcolm Wilkinson, Crystal Faraday Director; Dr Jeremy Tomkinson, CEO National Non-Food Crops Centre; Dr Cliff Burton, Viridian Envirosolutions Ltd.; Professor Keith Smith, Chemistry Department, Swansea University; Professor Andrew Livingston, Chemical Engineering Department, Imperial College of Science, Technology and Medicine; Dr Roshan Jachuck, Chemical Engineering Department, University of Newcastle upon Tyne; and Professor Martyn Poliakoff, School of Chemistry, Nottingham University.

The workshop emphasised discussion and brainstorming, partly through small multidisciplinary working groups. First, the panel divided into 5 groups structured so as to fully engage the participation of all concerned. These were:

- *Raw Materials, Agriculture and Chemistry*, chaired by Professor Colin Webb, Chemical Engineering Department, UMIST.
- *New Chemical Routes—Solvents and Chemicals*, chaired by Dr Gary Sheldrake, Chemistry Department, Queen Belfast University.
- *Catalysis, Biocatalysis and Materials*,

chaired by Professor Brian Hayden, Chemistry Department, Southampton University.

- *New Process and Process Strategies*, chaired by Dr Roshan Jachuck, Chemical Engineering Department, University of Newcastle upon Tyne.
- *Environmental Biotechnology*, chaired by Professor Neil Bruce, Biology Department, York University.

In each area, the discussion focussed on (i) recognising gaps, (ii) identifying potential advances and (iii) spotting key areas that should be promoted. The relative merits of single investigator grants *versus* collaborative projects were also considered.

Findings from these group sessions were discussed in a plenary session that served to define the issues to be addressed in a second set of three breakout sessions on Day Two: *Raw Materials*, chaired by Dr John Pierce, Dupont USA, *Products*, chaired by Dr Ian MacKinnon, Thomas Swan & Co. Ltd. and *Processes* chaired by Dr Adisa Azapagic, School of Engineering, Surrey University. The resulting conclusions were presented at a final plenary session where they formed the basis for a broad discussion.

The principal outcomes of the workshop are summarised below. Whilst these reflect on the wide range of experience of the participants, they are not intended to be exhaustive nor definitive. Rather they offer a basis for further discussion and debate.

## Principal findings and recommendations

(1) *The UK needs to attract more investigators from a range of disciplines into Benign and Sustainable Chemical Technology research.* Multidisciplinary teams will be very important drivers for developing new technologies within both academia and industry. Chemistry will play a vital role in formulating the new concepts necessary to understand and exploit highly complex systems—leading to revolutionary advances.

Petrochemical processes have provided low cost production routes for fuels, plastics and chemicals for well over 50 years but the escalating impact on the environment and the inevitable future depletion of fossil feedstocks make it essential that benign, sustainable, alternatives be developed commercially in the very near future. Progress in science and technology can address the challenges required to develop advanced technologies to overcome environmental burdens, improve the quality of life and create new business opportunities. But this can only happen with full co-operation between a wide range of currently disparate

disciplines. An effective way to replace many hazardous and noxious chemical processes may be through bioprocessing, yet the development of biotechnology has largely been limited to the production of high-value low-volume products because of relatively poor production economics. There is much to be gained by the synergistic combination of chemistry, biotechnology and process engineering in undertaking the difficult restructuring of the organic chemical industry for the production of commodities (fuels, chemicals and plastics) from alternative raw materials.

(2) *Chemical engineers and chemists should work together closely from the earliest stages of a project.* For instance, in the development of greener technologies, improved separation methods can have as much impact as synthetic strategies. Therefore one promising strategy is integrated design from the macroscopic scale down to the molecular scale—for example by combining reaction and separation. Clearly, such advances will depend critically on close collaboration.

Separations remain an important field in process design involving new reactor systems. One of the keys to success in this field lies in designing from the macroscopic scale (devices and systems) down to the molecular scale through self-organisation, catalyst selectivity to avoid the need for separation, specific interactions with solid phase reagents, and continuous flow separation processes. Here, effective communication between engineers and chemists will play a vital role.

In promoting new processes the following general principles and practices should be borne in mind:

- Chemists should think twice (or even more!) before using stirred tanks for their research—as it dictates the subsequent process development.
- Composition of the research team/consortium is critical—*Smaller multidisciplinary teams are often more productive.*
- Construction of a list of strategically important green chemical technologies and novel reactor/mixer/micro technologies backed with appropriate facilities to enable rapid development to large scale at low cost.
- Run process workshops in specific technology areas to identify strategically important areas of development.
- Effective management of intellectual property to attain industrial confidence.
- Availability of generic demonstration facilities. Easily accessible tool kit for chemists to explore intensified

modules.

- The role of technology developers should not be underestimated—hence involvement of the Faraday Partnerships should be encouraged.
- Bring together the RSC and IChemE to consolidate interactions between chemists and chemical engineers, particularly in the areas of curriculum development and accreditation.

(3) *Agricultural crops can provide a new range of platform chemicals that may be used as intermediates, hence there is a need to focus chemical research in this area.* To identify potential platform chemicals, research is required in both upstream and downstream directions (*i.e.* what intermediates can be produced from the raw materials? and what intermediates would be required to produce particular end products?). The former could involve, for example, bioconversion research, while the latter would benefit from retro-synthetic analysis. Once the platform chemicals are identified, new synthetic protocols and methodologies will be required to produce both traditional and new products. Plant breeding focussing on obtaining the optimum raw materials will be essential to improve the commercial viability of subsequent processing activities. Further development of fermentation and associated biotechnology, including modelling and control of bioprocesses and improved understanding of enzyme mediated biosynthesis, will also be required. Given that it may be necessary to carry out processing at source, research into process technology for appropriate scales of production would be beneficial.

A key point is that the whole crop should be used and this goal requires crop optimisation. To pump-prime this process it will be essential for governments to initiate relevant research and provide incentives for industry to change its reliance on petrochemical feedstocks. This has already happened to some extent, though not particularly in the UK, in creating the biofuel economy. Such developments will lead wholesale advances in fermentation technology, from which other bioconversions will benefit. There is a strong analogy here with the development of the petrochemicals industry, which was driven by advances in petroleum refining for fuels production. Once agricultural crops become competitive with non-renewable resources commercial activity will proliferate, hence the critical importance of government involvement.

(4) *The potential of catalysis and biocatalysis as tools for sustainable chemical technologies is very great.* Integration or combination of

bioconversion with chemical conversion offers exciting prospects and is an area that should be strongly encouraged: it is essential that chemists learn to regard enzymes as part of the standard tool kit for synthesis.

The genomic approach to access novel biocatalysts is becoming important because enabling technologies are now available that permit synthesis of ‘designer’ enzymes. Bioinformatics will facilitate the identification of gene sequences encoding potentially useful enzymes or binding domains. By exploiting this approach in combination with directed evolution methods it should be possible to invent stable biocatalysts with specific desired properties, optimised to perform under the required conditions (temperature, pH, solvent...). The performance of these systems at different scales of operation should also be carefully considered.

A potentially important opportunity is the development of non-aqueous enzyme chemistry, where the enzyme is stabilised by only a thin layer of water. This would open up alternatives to, for example, aqueous–organic systems. The integration or combination of bioconversion with chemical conversion offers therefore stimulating opportunities and should be encouraged.

The stable immobilisation of homogenous and enzymatic catalysts without loss of performance represents a major challenge. Fundamental issues and strategically important research themes include the following:

- Studying, understanding, controlling and optimising the catalyst/surface interaction.
- Creation of new high surface area support materials.
- Controlled sequential attachment of enzymes so as to achieve the desired overall conversion.
- The use of membranes for both support and separation.
- Identifying important target reactions for immobilised catalysts: *e.g.* enantioselective oxidations.

Progress towards the development of radically different catalysts, materials and processes requires a strategic approach. Pre-requisites include the supply of relevant information by industry to academia to answer questions such as: what is already possible but well worth improving? What is desirable but not yet possible? Ways should be devised for stimulating this exchange without compromising commercial needs. There can be little doubt that multidisciplinary should be an essential component of ambitious research programmes. Therefore, academic researchers should cultivate

critical awareness of key subjects that may be used to leverage the technological impact of their own specialisations. This will require a willingness and an ability to communicate across subject boundaries.

(5) *The creation of new material structures aimed at sustainability requires focussed and precise synthesis of building blocks using, for example, biological processes.* The workshop was unable to identify significant activity in this subject area in the UK.

(6) *A major barrier to implementation of new, greener solvents is the relative lack of data on fundamental physical properties and information about toxicity.* These gaps need to be addressed urgently. If benign and sustainable chemical technologies are to become a reality then dialogue between process engineers and chemists is essential. A major factor that impedes such dialogue is the imbalance between UK strength in synthetic organic chemistry and the low level of activity in physical organic chemistry. Therefore it is important to reinvigorate physical organic chemistry in UK universities, whilst maintaining strength in synthetic organic chemistry. An example of this is the pressing need for developing better predictive criteria for choosing solvents for industrial application from the vast array of new possibilities available. This requires a greater emphasis being placed on the gathering of fundamental physical data for new materials, which requires the specialist skills of the physical organic chemist. It should be kept in mind that physical organic chemistry is a very broad area whose potential impact on the chemical sciences is large. The mechanism of action of enzymes, the structure of signalling networks in cells, the mechanisms of environmental degradation of pesticides—all these are encompassed by physical organic chemistry.

(7) *Ways should be found to publicise within the industrial arena the economic benefits of new greener technology.* Among other things, this implies a clear role for the Faraday Partnerships.

## Conclusions and specific recommendations

The workshop was tremendously successful in bringing together a group of experts with disparate backgrounds but common interests. There was general recognition and agreement of the principle findings outlined above and, as a result, a number of specific actions have been recommended.

(1) *Stimulate the further development of Benign and Sustainable Chemical Technologies through focussed Research Workshops.*

- Act to bring more organic chemists into green chemistry research: *most industrial processes consist of organic chemical reactions but most organic chemists do not automatically think 'green'.*
- Organise meetings designed to bring together the distinct and currently separate catalytic communities (homogeneous, heterogeneous, biocatalysis, photocatalysis, electrocatalysis, bio-electrocatalysis) from both industry and academe. *This will be an important step towards fostering creativity.*
- Bring chemical engineers and chemists together at an early stage in the development of greener processes. *Both groups should play a key role in scaling-down and decentralising the production of chemicals—miniaturisation, intensification and the use of sophisticated technologies calls for an early dialogue and a common language.*
- Encourage further the involvement of chemists in environmental biotechnology research. *Bioremediation and marine biotechnology are important areas*

*that require chemical input. Understanding the concepts of bioavailability and bioaccumulation.*

**(2) Provide the right forum for chemists and engineers to begin a dialogue; recognise common aspirations and identify opportunities that can be exploited by collaboration.**

The IChemE and the RSC working together may have a role here, through the organisation and management of, for example:

- summer schools.
- focussed research workshops.
- training modules for chemists in, for example, process technology.
- continuing and expanding joint accreditation of courses.

**(3) Continue allocation of Research Councils' resources to 'Benign and Sustainable Chemical Technologies'.**

The use of such resources might be optimised by:

- facilitating collaborations across research council boundaries.

- attracting newcomers to the field by promoting increased awareness of the subject within the research community as a whole.

A final remark. We are indebted to the participants for generously giving their time, effort and energy, for their enthusiasm, and for their lively contributions to the discussions, formal and informal. One of the most encouraging aspects of organising and participating in this workshop has been the enthusiastic support received from the community before, during and after the event.

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## References

- 1 See Chemistry at the Centre at <http://www.rsc.org/lap/polacts/uniresearch.htm>.
- 2 See <http://www.dfes.gov.uk/highereducation/hestrategy/>.
- 3 See <http://www.dti.gov.uk/cigt/competitiveness.htm>.



# Novel solid networks containing Sn–H as a greener replacement for soluble alkyl Sn–H reagents in radical assisted organic synthesis†

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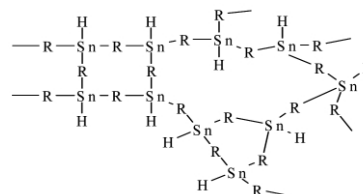
DiGrignard reagents of the form  $\text{XMg}(\text{CH}_2)_n\text{MgX}$ , where X = Br or I and  $n = 6, 8, 10$  or  $12$ , were allowed to react with  $\text{PhSnCl}_3$  to produce highly cross-linked Ph–Sn polymeric networks. The Sn–H moiety was incorporated into these insoluble network polymers by treatment with  $\text{Br}_2$  and  $\text{NaBH}_4$ . Excellent accessibility of the Sn–H was displayed by these solvent penetrable but insoluble networks, giving them higher Sn–H loadings than all previously reported supported reagents. These reagents were totally regenerable in  $\text{NaBH}_4$  for radical assisted organic synthesis and no detectable leaching of the Sn into solution was observed during these reactions.

Soluble forms of trialkyltin hydrides have been employed as reagents in the synthesis of fine chemicals for decades despite their associated problems (non-regenerable and toxic). Many radical assisted organic syntheses based on these reagents have been developed due to the Sn–H bond being homolytically very labile. Despite the fact that the toxicity of trialkyltin compounds is inversely related to the length (and nature) of the alkyl chains<sup>1</sup> ( $\text{Et}_3\text{SnCl}$ – 5 mg  $\text{kg}^{-1}$  LD<sub>50</sub> female rat;  $\text{Bu}_3\text{SnCl}$ – 129 mg  $\text{kg}^{-1}$  LD<sub>50</sub> rat;  $\text{Oct}_3\text{SnCl}$ – 10,000 mg  $\text{kg}^{-1}$  LD<sub>50</sub> male rat *etc.*), the possibility of contamination apparently hindered the introduction of tin hydride chemistry to the synthesis of pharmaceutical products destined for human consumption.<sup>2</sup> Many potential greener replacements have been investigated over the past two decades but only a few alternatives such as  $(\text{Me}_3\text{Si})_3\text{SiH}^3$  and  $\text{Bu}_3\text{GeH}$  display similar chemical properties to the trialkyltin hydrides.<sup>4,5</sup> Nevertheless, the superiority, versatility and selectivity at lower available costs still sustain trialkyltin hydrides as important industrial reagents.<sup>6</sup> We note the recent re-introduction of tributyltin hydride chemistry for drug synthesis highlighting the importance and unique synthetic roles of these reagents.<sup>7</sup>

For practicality, other studies have been focused on immobilised trialkyltin hydride analogues in order to combine the favourable reactivity associated with the tin and the separation capabilities of solid tethered reagents/catalysts. Most of the attention in this area has been focused on insoluble cross-linked polystyrene supports. These have proven to be more successful than most inorganic supports, although active tin hydride loadings struggle to reach values above about 1.4 mmol  $\text{g}^{-1}$  and leaching of tin into solution is still a problem.<sup>8,9</sup> Few tin hydrides immobilised onto non-styrenic polymer supports have been reported.<sup>10</sup> The key aspects concerning all previous support methods are that the tin centre is only bound by a single covalent Sn–C bond and that the loading has been low due to the use of bulk polymer. Cleavage of the single Sn–C linkage, by any given mechanism such as beta-elimination, will inevitably allow product contamination by soluble tin compounds.

† Electronic supplementary information (ESI) available: files describing synthesis and detailed characterisation using FTIR, <sup>1</sup>H NMR, SEM of typical network materials. See <http://www.rsc.org/suppdata/gc/b3/b313334f/>

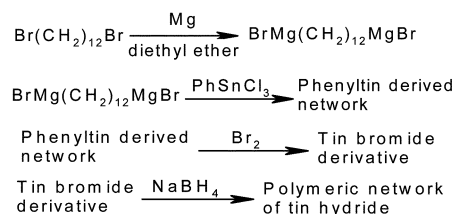
To eliminate or substantially reduce tin leaching and maximise active Sn–H contents (Sn–H loading per gram of material) we report, for the first time, a novel synthesis of polymeric networks containing tin hydride. These alkyltin hydride polymeric networks are designed to carry a high concentration of tin atoms in their 3-D backbones (exceptionally high Sn–H loading) allowing a firm anchorage of the tin into the solid (Scheme 1). The toxicity of the



**Scheme 1** An envisaged structure of 3-D alkyltin hydride networks R =  $-(\text{CH}_2)_n-$ ,  $n = 6, 8, 10$  or  $12$ .

corresponding trialkyltin is also minimised by the use of long chain hydrocarbons to cross-link these tin centres. In addition, we show that these polymeric networks containing Sn–H can be *ex situ* regenerated in  $\text{NaBH}_4$  rendering them as a genuine catalyst for radical assisted organic synthesis. Thus, Sn–H efficiency for chemical conversion is enhanced.

The polymeric networks were prepared by addition of a controlled excess of diGrignard reagent to  $\text{PhSnCl}_3$  (which has 3 replaceable Cl for the  $\text{MgBrCl}$  formation) hence generating a 3-D linkage of the tin-phenyl moieties. The subsequent bromination (controllable quantity as stated) and reduction of the tin bromide groups with excess  $\text{NaBH}_4$  selectively cleaved the phenyl from the tin yielding the polymeric network of tin hydride. This synthetic methodology is based on the higher labile nature of phenyltin over the alkyltin bond towards bromination, which is documented.<sup>11</sup> In particular the recent synthesis of fluorinated alkyltin hydride by Curran and Hoshino<sup>11</sup> based on this selectivity has been noted for our reaction profiles (Scheme 2). To rule out the possibility of Sn–



**Scheme 2** Reaction profiles.

H formation from the reduction of residual Sn–Cl or Sn–OH groups (from hydrolysis during workup) a control experiment for the direct reduction of the phenyltin chloride/hydroxyl groups to tin hydride was performed without the bromine treatment. No significant formation of a Sn–H bond was observed by FT-IR spectroscopy (see ESI†).

The insoluble networks that were obtained were easily filtered from solution. FTIR spectrum (see ESI†) showed a large and



distinctive tin hydride peak at  $\nu = 1806 \text{ cm}^{-1}$ . The presence of the Sn–H groups was also confirmed when a  $^1\text{H}$  NMR investigation (see ESI†) was made on a colloid containing the networks (5.23 ppm). With reference to the tentative structure in Scheme 1, 90–95% molar yields were generally derived when the precursors were reacted at high concentrations, followed by the phenyltin cleavage using  $\text{Br}_2/\text{Sn} = 1$  and reduction by treatment in excess  $\text{NaBH}_4$ . The networks were rubbery in texture and swelled well in most organic solvents indicating that the hydrocarbon inter-chains are likely to be structurally flexible in the presence of a solvating medium. The SEM micrograph clearly indicates the porous nature of the network (see ESI†). It is believed that this is an important property since the solvent swellable alkyl inter-linkers may have some implication in the Sn–H utilisation. The active hydride contents of these insoluble materials were assessed from the typical stoichiometric reductive dehalogenation reaction of 1-iodooctane to n-octane (exclusively formed) under free radical conditions. The reactions were performed in 1-butanol with AIBN as the initiator and the substrate and product were quantified and monitored until the reactions finished by GC with pre-calibrations. The hydrogen to tin ratios were calculated based on the active hydride contents measured above and by taking the mass balances into account for the tin components originally added (the total weight of networked Sn–H is used when loading is deduced). These values could reflect the accessibility or utilisation of the Sn atoms in the polymer networks (the maximum Sn–H ratio would be 1 if all the Sn atoms in the networks are in the form of active tin-hydride and are fully accessible). Typically, 0.3–0.4 hydrogen to tin ratios (see Table 1)

**Table 1** A study of regenerability of Sn–H content in the polymer networks ( $n = 12$ ,  $\text{Br}_2/\text{Sn}$  ratio added = 1, insoluble molar yield = 90–95%) upon subsequent reaction with iodooctane followed by  $\text{NaBH}_4$ .

Cycle	H : Sn ratio	Loading/mmol $\text{g}^{-1}$	Leaching/mol %
1	0.33	0.57	Nil
2	0.42	0.72	$1.56 \times 10^{-3a}$
3	0.42	0.71	Nil
4	0.44	0.75	Nil
5	0.36	0.61	Nil

<sup>a</sup> This fell just above the detection limit and was regarded as noise.

were obtained when the  $\text{Br}_2/\text{Sn}$  ratio was set at 1. Initially, the lower hydrogen to tin ratios appeared to indicate that there were severe accessibility problems however, it was later found that a significant loss of bromine during the synthesis was noted (as bromine fume). These Sn–H networks were repeatedly tested following the iteration order with iodooctane reaction, solid recovery,  $\text{NaBH}_4$  regeneration and extensive rinsing (no sign of B–H and solvent from the FTIR were ensured). Apart from the slightly lower hydrogen to tin ratio and loading value estimated for the 1<sup>st</sup> cycle (possibly from reduction of residual  $\text{Sn}(\text{CH}_2)_{12}\text{Br}$  remaining from incomplete diGrignard formation, *i.e.*  $\text{BrMg}(\text{CH}_2)_{12}\text{Br}$ ) the materials were recoverable and readily regenerated after treatment with  $\text{NaBH}_4$  in an *ex situ* manner as a genuine catalytic material with no loss of active tin hydride contents. Notice that the evaluation of soluble tin in solutions after each of the cycles by ICP showed that no tin was indeed lost from solid to solution during the testing, see Table 1. In contrast, the reported polymeric grafted reagents at similar loadings suffer a severe tin leaching under comparable conditions.<sup>10</sup>

As greater ratios of  $\text{Br}_2/\text{Sn}$  were used, the active hydrogen to tin ratios and tin hydride loadings were substantially increased. At high  $\text{Br}_2/\text{Sn}$  ratios the insoluble networks showed active hydrogen to tin ratios approaching 1.0. However, it was noted that a significant amount of the networks disappeared after the filtration (but could be retrieved in the filtrate by solvent evaporation) when  $\text{Br}_2/\text{Sn}$  values higher than 2.8 were used. It is thought that at these high  $\text{Br}_2/\text{Sn}$  values some degree of non-selective cleavage of alkyltin bonds

fragments the networks, see Table 2. Nevertheless, the use of  $\text{Br}_2/\text{Sn} \leq 2.2$  facilitates recovery for most of the materials with a 0.70 H/Sn ratio.

**Table 2** Effect of the  $\text{Br}_2/\text{Sn}$  ratio on the H–Sn/ loading content ( $n = 12$ )

$\text{Br}_2 : \text{Sn}$ ratio	H : Sn ratio	% molar yield of recoverable networks	Loading/mmol $\text{g}^{-1}$
1.1	0.36	93.07	0.61
1.7	0.45	91.08	0.77
2.2	0.70	89.16	1.25
2.8	0.88	85.10	1.60
3.3	0.80	79.54	1.44
4.1	0.95	36.59	1.75

As a result, the network materials with the alkyl chain length,  $n = 6, 8, 10$  and 12 were therefore prepared at  $\text{Br}_2/\text{Sn}$  ratios of 1.7–2.2 where ~90% molar yields (solid) and H/Sn ratios of ~0.7 were observed. It is very interesting to note that a higher loading of active (inorganic) tin hydride could be obtained on decreasing the chain length of the organic inter-linkers, see Table 3. (A

**Table 3** Effect of alkyl chain length on the Sn–H loading

$n$ ( $\text{Br}_2/\text{Sn}$ )	mmol $\text{g}^{-1}$	$n$ ( $\text{Br}_2/\text{Sn}$ )	mmol $\text{g}^{-1}$
6 (1.7)	3.07	10 (2.2)	1.35
8 (2.0)	1.79	12 (2.2)	1.25

preliminary study again indicated that little tin leaching is observed from these materials although a ten fold increase in tin contamination was observed when the  $\text{Br}_2:\text{Sn}$  ratio was raised from 1.1 to 4.1 with the contamination for  $\text{Br}_2 : \text{Sn}$  at 1.1 being  $1.84 \times 10^{-3}$  mol%). The reduction of typical model compounds has been studied over these novel polymer network tin hydrides with different inter-chain lengths and compared to soluble trialkyltin hydride reagents (see ESI†). The results clearly show that our solid regenerable Sn–H can be used to replace soluble trialkyl Sn–H reagents in reduction of fine chemicals/pharmaceutical chemicals. The selectivity of selected reactions depends on the chain length of the organic inter-linkers.

As discussed, a long-term greener approach for the important radical assisted syntheses may require the use of non-tin hydride alternatives, however no satisfactory candidate has yet been identified despite the research of the past 50 years.<sup>6</sup> Thus, the current solution involves the use of solid systems carrying tin reagents. It is therefore important that the solids carry a high tin hydride loading, a good Sn–H accessibility, resistance to tin leaching and be regenerable (rendering the reagents as catalysts for better tin utilisation). All previous work based on traditional immobilisation could not meet these criteria. A new hybrid class of tin hydride reagents containing hydrocarbon chains as interlinkers through a simple diGrignard preparation is now demonstrated, *for the first time*.<sup>12</sup> The solid materials are shown to display higher tin hydride loadings than all reported solid tin hydride reagents that primarily employed  $-\text{Bu}_2\text{SnH}$  grafting onto the pendant groups of existing rigid & bulky polymer/inorganic materials. Thus, the light hydrocarbon interlinkers used for the tin hydride in our case could give an extremely high Sn–H loading approaching that displayed by soluble tributyltin hydride ( $3.44 \text{ mmol g}^{-1}$ ) but in solid recoverable forms. The choice of hydrocarbon chain length may also diminish the risk of harmful effects resulting from tin remaining in reaction products. Regeneration of these solid hydrides in an *ex situ* manner has been clearly demonstrated, and the preliminary leaching evaluations gave a clear indication that the tin is firmly anchored within the solid networks. This fact is consistent with the stable tin environment against leaching envisaged for the 3-D networked alkyl-linkages to the Sn–H. A point to note is the solvent swellable

properties of these networks giving ease of access to the interconnected Sn–H sites by organic molecules therein, which are different from the typical active sites attached/anchored to a porous inorganic matrix where these sites are normally implanted deep inside the rigid porous structures. Although further work is needed to address diffusion problems, mechanical robustness, toxicity and leaching when subjected to more vigorous conditions, this preliminary account clearly shows that the new materials deliver an excellent tin hydride utilisation for organic synthesis. We demonstrate that the tin hydride content, accessibility, resistance to tin leaching and regeneration of the network materials can be tailored over these new polymeric networks through the control of the Br<sub>2</sub>/Sn ratio, hydrocarbon chain length and the use of other reductants.

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# “One pot” and selective synthesis of monoglycerides over homogeneous and heterogeneous guanidine catalysts

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The selective synthesis of monoglycerides was carried out in one step starting from an equimolar mixture of unprotected glycerol and fatty methyl esters. This reaction was catalyzed at low temperature by supported guanidine catalysts either in a solvent or without. Whereas most alkaline hydroxides or carbonate catalysts lead to monoglycerides in a limited purity and an excessive corrosive waste production, we showed that supported guanidine derivatives afforded monoglycerides in high yield according to an environmentally friendly process. Moreover, at the end of the reaction, the solid catalyst was easily recovered by filtration and reused several times without notable change of reactivity.

## Introduction

Agroresources are a huge renewable natural carbon source and are becoming an area of growing interest since scientists estimated to 50 years the remaining time of life of the last earth petroleum reserves.<sup>1</sup> Moreover the use of renewable raw materials is a tremendous industrial challenge to develop greener processes limiting the environmental impact of chemicals.<sup>2</sup> Glycerol is industrially available in large scale from the hydrolysis or methanolysis of vegetable oils.<sup>3</sup> Because of its biocompatibility, the glycerol transformation into monoglycerides has significant applications as safe and biodegradable emulsifiers in food, pharmaceutical, cosmetic, and detergent industries.<sup>4</sup>

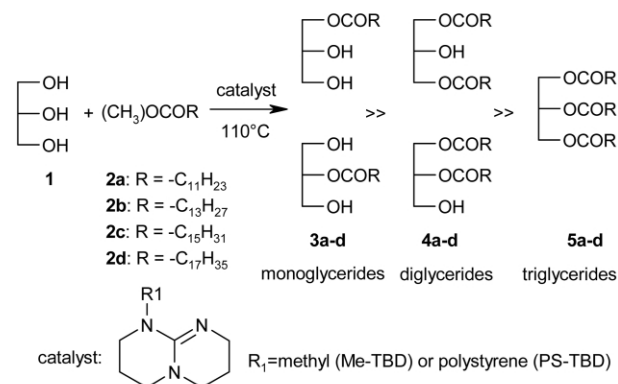
Synthesis of monoglycerides is commercially achieved either by glycerolysis of animal and vegetable fats and oils or by direct esterification of glycerol with fatty acids.<sup>5</sup> These catalytic processes require strong base catalysts such as KOH, NaOH or Ca(OH)<sub>2</sub> and lead to the formation of monoglycerides in a limited purity due to the side production of di-, triglycerides and soap. Recently, alternative methods involving immobilized enzymes were also reported and seem to be a viable process despite a relatively complex work up.<sup>6</sup>

Heterogeneous catalysts also offer many advantages like easy separation of the catalyst from the reaction products and recycling. Corma *et al.* reported that the glycerolysis of the 1,2,3-tri-(*cis*-9-octadecenoyl)glycerol (trioleine) and rapeseed oil can be performed over solid basic catalysts such as sepiolite-Na-Cs, Cs-exchanged MCM-41, MgO and hydrotalcites.<sup>7</sup> These heterogeneous catalytic routes afford glycerol esters with 90% yield and 75% selectivity to monoglycerides but require high temperature and a glycerol/triolein molar ratio of 12. Mesoporous silica functionalized either with acid or basic groups<sup>8</sup> or slightly basic Y-zeolites<sup>9</sup> led to more than 80% selectivity to monoglycerides starting from a glycerol/fatty acid molar ratio of 1. However these high selectivities were only obtained at 20% conversion and rapidly decreased to 40–50% at total conversion.

Recently, the glycerolysis of a 1,2,3-trioctadecanoylglycerol (tristearin) was carried out in the presence of alkyl guanidines, strong non-ionic bases, resulting in monoglycerides in more than 90% selectivity, but only at 50% conversion.<sup>10</sup>

We now report an environmentally friendly selective synthesis of monoglycerides with high yield starting from an equimolar mixture of fatty methyl esters and unprotected glycerol. This one pot transesterification reaction was catalysed at low temperature, either in DMSO or without solvent, by two guanidine derivatives: the

7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (Me-TBD) and the 1,5,7-triazabicyclo[4.4.0]dec-5-ene (2.5 mmol g<sup>-1</sup>) bound to a polystyrene network crosslinked with 2% of divinylbenzene (PS-TBD) (Scheme 1). To our knowledge, this is the first example of direct unprotected glycerol esterification over guanidine catalysts.



**Scheme 1** Catalytic esterification of unprotected glycerol over guanidine derivatives

## Results and discussion

Unprotected glycerol **1** (10 mmol) was stoichiometrically reacted with various fatty methyl esters **2a–d** at 110 °C in the presence of 1.25 mmol (12.5 mol %) of Me-TBD (Scheme 1). Whereas most of the hydroxide catalysts led to a limited yield in glycerol esters because of an important side production of soap, the Me-TBD catalyst afforded, in an environmentally friendly manner and in less than 3.5 h, glycerol esters with yield higher than 95% and more than 62% selectivity to monoglycerides (Table 1). As described in the literature, 1-monoglycerides were mainly produced against 2-monoglycerides in a ratio of 9:1.<sup>6</sup> These unprecedented results clearly evidenced the contribution of the guanidine derivatives for the environmentally friendly selective synthesis of monoglycerides in one step.

Based on these results, it occurred to us that heterogenized guanidine should be a versatile heterogeneous catalyst to develop greener monoglyceride synthesis processes. In the course of our work, studies were directed towards the use of a guanidine grafted

**Table 1** Catalytic activity of guanidine derivatives (glycerol/methyl ester molar ratio of 1, 110 °C, solvent free)

Methyl ester	Catalyst	Time/h	Yield (%) <sup>a</sup>	Mono-glycerides (%) <sup>b</sup>	Di-glycerides (%) <sup>b</sup>	Tri-glycerides (%) <sup>b</sup>
<b>2a</b>	Me-TBD	2	100	62	33	5
<b>2b</b>	Me-TBD	3	97	65	30	5
<b>2c</b>	Me-TBD	3.5	98	62	34	4
<b>2d</b>	Me-TBD	3.5	99	63	34	3
<b>2a</b>	PS-TBD	8	96	62	32	6
<b>2b</b>	PS-TBD	8	99	59	34	7
<b>2c</b>	PS-TBD	8	100	55	39	6
<b>2d</b>	PS-TBD	8	98	47	45	8

<sup>a</sup> Global yield in glycerol esters were determined by GC. <sup>b</sup> Selectivity.

on a Merrifield resin (PS-TBD). Schuchardt *et al.* reported the efficiency of the PS-TBD catalysts for the transesterification of soybean oil with methanol.<sup>10</sup> They clearly established that the grafting of the guanidine derivative on a polymer containing a high loading of chloromethyl groups (4 mmol g<sup>-1</sup>) led to an important deactivation of the catalyst due to the side reaction of the guanidine with two vicinal chloromethyl groups.<sup>10</sup>

To avoid this problem, the guanidine catalyst used in our study was functionalized with no more than 2.5 mmol of guanidine per gram. Titration of the catalyst with a solution of 0.1 M AgNO<sub>3</sub> in the presence of potassium chromate as indicator revealed the absence of chlorine indicating that all grafted guanidine are involved with only one chloromethyl group. Moreover titration of the catalyst with a solution of 0.1M HCl in the presence of phenolphthalein confirmed the presence of 2.5 mmol g<sup>-1</sup> of basic sites.

Using the same experimental conditions as described above for the homogeneous catalyst Me-TBD (glycerol/fatty methyl esters molar ratio of 1; guanidine content: 12.5 mol% *i.e.* 0.5 g of PS-TBD), the supported guanidine was tested as solid catalyst. Results are reported in Table 1.

In the case of the methyl dodecanoate **2a**, glycerol esters **3** were produced with 96% yield and 62% selectivity to **3a** (Table 1). However, as summarized in Table 1, the monoglyceride selectivity strongly depends on the fatty methyl esters used.

Contrary to what was observed with the homogeneous Me-TBD catalyst, an increase of the length of the fatty methyl esters hydrocarbon chain led to a significant change of the monoglyceride selectivities. Indeed, whereas **2a** afforded 62% selectivity to **3a**, methyl octadecanoate **2d** led to only 47% selectivity to **3d**. This selectivity change is due to the hydrophobic nature of the polystyrene used as solid support. Mono-octadecanoylglycerol **3d**, more hydrophobic than monododecanoylglycerol **3a**, stronger interacts with the solid catalyst leading to a higher production of diglycerides. However, if the selectivity was depending on the fatty methyl esters hydrophobicity, the reaction rate and yield always remained unchanged and glycerol esters were still produced with more than 96% yield and that whatever the fatty methyl esters used. At the end of the reaction, the solid catalyst was easily recovered by filtration and as expected no side products such as soap or polyglycerols were detected. Consequently, after removal of the catalyst, glycerol esters were directly recovered in high purity without a large excess of alcohol as it is the case for the methanolysis or glycerolysis of triglycerides affording a simpler purification work up and a greener process.

In order to increase the monoglyceride selectivities, the influence of solvent was also studied. Dimethylsulfoxide (DMSO) is one of the rare solvents authorized in the food and cosmetic industries and thus was chosen as solvent for the catalytic glycerol esterification. The reaction was carried out at 110 °C starting from an equimolar mixture of glycerol (10 mmol) and fatty methyl esters diluted in 5 mL of DMSO in the presence of 0.5 g (12.5 mol%) of supported guanidine. Results are reported in Table 2.

**Table 2** Influence of solvent (glycerol/methyl ester molar ratio of 1, 110 °C, 12.5 mol% of PS-TBD)

Methyl esters	Solvent	Time/h	Yield (%) <sup>a</sup>	Mono-glycerides (%) <sup>b</sup>
<b>2a</b>	DMSO	50	98	78
<b>2b</b>	DMSO	72	66	85
<b>2c</b>	DMSO	96	18	94
<b>2d</b>	DMSO	120	0	0
<b>2a</b>	MEE	11	98	71
<b>2a</b>	DMF	9	95	63
<b>2a<sup>c</sup></b>	DMSO	50	98	86
<b>2a<sup>d</sup></b>	DMSO	48	99	96

<sup>a</sup> Global yield in glycerol esters were determined by GC. <sup>b</sup> Selectivity. <sup>c</sup> Glycerol/methyl ester molar ratio of 1.5. <sup>d</sup> Glycerol/methyl ester molar ratio of 2.

The solvent considerably decreased the reaction rate. In the case of **2a**, the reaction was about 6 times slower than without solvent. However, after 50 h of reaction, glycerol esters were produced in more than 98% yield with a very high 78% selectivity to **3a**. Interestingly, the selectivity to **3a** remained higher than 92% up to 75% conversion. Compared to the other catalysts described in the literature this is the first example of a one pot glycerol ester synthesis with high yield and high monoglyceride selectivity starting only from a glycerol/methyl esters molar ratio of 1.

In order to gather information about the DMSO role, other solvents such as 2-ethoxyethylether (MEE) and dimethylformamide (DMF) were tested. Methyl dodecanoate **2a** is sparingly miscible with the DMSO. However, in MEE, **2a** is more miscible and the reaction, carried out in this solvent, proceeded 5 times faster leading to 98% conversion and a slight selectivity decrease of 7% (Table 2). When **2a** is totally miscible with the reaction solvent as in the case of DMF, the catalytic reaction led exactly to the same results as described above without any solvent. These experiments show that the selectivity improvement obtained in DMSO was mainly due to the slight miscibility of **2a** in the DMSO-glycerol phase. Consequently, at the beginning of the reaction the catalytic phase is *in situ* poorer of **2a** than of glycerol inducing an increase of the selectivity. However, after approximately 30% conversion, monoglycerides were in a sufficient quantity to act as emulsifiers and totally homogenized the mixture. When the hydrophobicity of the fatty methyl esters increased, their miscibility in the DMSO phase became lower and the reaction rate was rapidly decreased up to the extreme case of **2d** for which no reaction occurred after 5 days.

Using a slight excess of glycerol (glycerol/methyl dodecanoate molar ratio of 1.5 or 2), **3** were quantitatively produced with 96% selectivity to **3a** whereas most of the other catalysts required a much higher molar ratio (Table 2).

To ensure that no leaching of the guanidine occurred during the catalytic process, the catalyst was removed by filtration after only 30% conversion. The filtrate was then heated at 110 °C and no catalytic reaction took place. These results confirm that the reaction only occurred on the supported TBD active sites. The PS-TBD catalyst was also recycled four times and only a slight diminution of the catalytic activity was observed.<sup>10</sup>

The above results show an environmentally friendly catalytic process to obtain glycerol esters in high yield by direct and stoichiometric transesterification of fatty methyl esters with unprotected glycerol. This reaction can be performed without any solvent and, except methanol, no waste was produced as was generally observed with alkaline hydroxide or carbonate catalysts. Remarkably, the use of DMSO as solvent led to a tremendous improvement of the monoglyceride selectivities. However this solvent effect cannot be extended to all fatty methyl esters since the reaction rate was too long with highly hydrophobic esters. For this reason, future work will be directed towards the use of guanidine heterogenized on hydrophilic solid supports which should be able



to prevent the monoglycerides adsorption and consequently to increase the monoglyceride selectivities.

## Experimental

All solvents, reagents and catalysts were purchased from Sigma Aldrich and used as received without any further purification. PS-TBD solid catalyst was a polystyrene network crosslinked with 2% divinylbenzene and functionalized with 2.5 mmol g<sup>-1</sup> of benzylguanidine. In all experiments, glycerol (0.92 g, 10 mmol) was reacted in a narrow shlenk flask with fatty methyl esters (10 mmol) in the presence of 0.5 g (12.5 mol%) of PS-TBD catalyst either in 5 mL of solvent or without. The resulting mixture was stirred at 110 °C under a low nitrogen flow in order to remove the methanol produced and shift the equilibrium towards the glycerol esters formation. Contrary to what was observed starting from triglycerides,<sup>10</sup> at 110 °C the reaction mixture was here fluid enough to be stirred without any difficulty with a stirring bar. Moreover, the relatively high loading of the guanidine on the polymer allowed us to use a reasonable quantity of catalyst (12–16 weight%) without stirring perturbation. The reaction progress was monitored on a Varian 3300 GPC equipped with a BPX5 (SGE) column. Prior analysis, products were silylated according to the Sahasrabudhe method described in ref. 11. At the end of the reaction, the crude mixture was filtered at 110 °C and the glycerol esters solidified on cooling. The catalyst was then reused as collected without further purification.

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# Mannich reaction using acidic ionic liquids as catalysts and solvents†

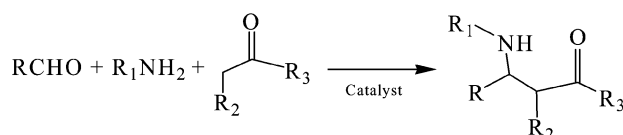
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Several Brønsted acidic ionic liquids were synthesized and successfully used as solvents and catalysts of three-component Mannich reactions of aldehydes, amines, and ketones at 25 °C. The used Brønsted acidic ionic liquids include 1-butyl-3-methylimidazolium hydrogen sulfate ([Bmim]<sup>+</sup>[HSO<sub>4</sub>]<sup>-</sup>), 1-butyl-3-methylimidazolium dihydrogen phosphate ([Bmim]<sup>+</sup>[H<sub>2</sub>PO<sub>4</sub>]<sup>-</sup>), 1-methylimidazolium *p*-toluenesulfonic acid ([Hmim]<sup>+</sup>Tsa<sup>-</sup>) and 1-methylimidazolium trifluoroacetic acid ([Hmim]<sup>+</sup>Tfa<sup>-</sup>). Higher yields were obtained in the presence of [Hmim]<sup>+</sup>Tfa<sup>-</sup> in comparison with other Brønsted acidic ionic liquids. The [Hmim]<sup>+</sup>Tfa<sup>-</sup> was reused four times without considerable loss of activity.

## Introduction

The synthesis of natural molecules, pharmaceuticals and other nitrogenous biologically active compounds has long been a significant branch of organic synthesis.<sup>1–3</sup> The Mannich reaction provides one of the most basic and useful methods for the synthesis of such compounds. In such a reaction, an amine, two carbonyl compounds and acid (or base) catalysts are used to produce beta-amino-carbonyl compounds (Scheme 1).



Scheme 1

The acid catalysts usually used involve organic and mineral acids, such as proline,<sup>1–3</sup> acetic acid,<sup>4</sup> *p*-dodecylbenzenesulfonic acid (DBSA),<sup>5,6</sup> or some Lewis acids<sup>7–9</sup> composed of transitional metal chloride salts. However, these conventional acid catalysts are often toxic, corrosive and difficult to separate and recover from products despite their high catalytic activity.<sup>10</sup> Utilization of solid acids may be a solution to the problem. But the shortcomings of rapid deactivation and decrease of activity site per area limit their application to some degree. To design a catalyst with high activity and selectivity, which is benign to the environment and easily recovered, is an interesting and rapidly developing area in chemistry. For acid catalyzed reactions, acidic ionic liquids are deemed as one of the most promising alternatives of conventional acid catalysts.<sup>11</sup>

Recently, ionic liquids (ILs), a kind of ion solvent, which combine the advantages of both traditional molecular solvents and melt salts, have been considered as promising new reaction media, and have found wide use in catalytic and non-catalytic reactions.<sup>11–14</sup> Not only can these useful materials dissolve many organic or inorganic substances, but they are also readily recycled. Moreover, their properties are tunable to satisfy specific chemical tasks. Among versatile ILs, acidic (basic) ILs are of special interest, which present dual solvent–catalyst function in some reactions. ILs that manifest innately Lewis-acidic character have been studied in the past decade by different authors.<sup>12,13</sup> And the ILs with latent acidity or superacidity can also be prepared by adding some weak base or mineral acid into acidic chloroaluminates, which broaden

the applications of ILs in many fields, such as acid–base catalyzed reactions, polymerizations, electrodeposits. However, chloroaluminates are sensitive to water, which can lead to undesired side reactions and causing considerable potential for corrosion (due to release of HCl). So the preparation and handling of such types of ILs often needs extreme operational conditions, which limits their applications. Hence, non-chloroaluminate ILs, which are air and moisture stable, have recently been developed and applied to acid catalyzed reactions.<sup>11–17</sup> For example, several research groups synthesized strong Brønsted acidic ILs and used them as dual solvent–catalyst for esterification, alcohol dehydro-dimerization and pinacol/benzopinacol rearrangement.<sup>11,15,16</sup> Compared with chloroaluminate ILs, the preparation procedures of these Brønsted acidic ILs are relatively simple, which can be accomplished by neutralization of acid and base.<sup>16</sup> Consequently, a series of Brønsted acidic ILs with different acidities can be synthesized by careful selection of the anions and cations.

In this work, we synthesized several acidic ILs and investigated their catalytic activity in Mannich reactions.

## Experiments

### Chemicals

1-Methylimidazole and trifluoroacetic acid were supplied by ACROS ORGANICS. All other chemicals (A.R. grade) were purchased from Beijing Chemical Reagent Factory and used as received unless stated. For Mannich reactions, the aldehydes used were benzaldehyde (**1a**), and 3-chloro-benzaldehyde (**1b**). The ketones were acetophenone (**2a**), cyclohexanone (**2b**), and the amines included aniline (**3a**), 4-bromoaniline (**3b**), sulfanilamide (**3c**), 3,4-xylydine (**3d**), *N*-methylaniline (**3e**), and 2-nitroaniline (**3f**). For the synthesis of ionic liquids, the solvents used involved

## Green Context

Beta-amino carbonyl compounds are very useful in pharmaceutical and other biologically related areas of chemistry. One of the many synthetic routes to these compounds is the Mannich reaction which brings together three compounds under appropriate catalytic conditions. Here the need for catalysts is avoided through the use of catalytically active ionic liquids as solvents. These simplified reaction systems fulfil several of the principles of green chemistry including the use of recyclable catalysts and reduced auxiliaries.

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† Electronic supplementary information (ESI) available: spectral data for the Mannich products, IR spectrum of the acidic ionic liquids. See <http://www.rsc.org/suppdata/gc/b3/b309700p/>

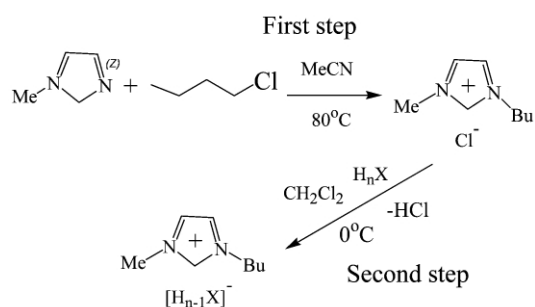
acetonitrile (distilled over phosphorus pentoxide (P<sub>2</sub>O<sub>5</sub>)), ethyl acetate and dichloromethane. 1-Methylimidazole was dried over potassium hydroxide (KOH) and distilled under vacuum. 1-Chlorobutane was used as received. The acids used to synthesize ionic liquids were concentrated sulfuric acid (98%), phosphoric acid (85%), trifluoroacetic acid (Tfa), and *p*-toluenesulfonic acid (Tsa).

### General procedures for the synthesis of ILs

In this study, several ILs were synthesized according to the procedures described in the literature.<sup>15,16,18</sup> These ILs included 1-butyl-3-methylimidazolium hydrogen sulfate ([Bmim]<sup>+</sup>[HSO<sub>4</sub>]<sup>-</sup>), 1-butyl-3-methylimidazolium dihydrogen phosphate ([Bmim]<sup>+</sup>[H<sub>2</sub>PO<sub>4</sub>]<sup>-</sup>), 1-methylimidazolium *p*-toluenesulfonic acid ([Hmim]<sup>+</sup>Tsa<sup>-</sup>), and 1-methylimidazolium trifluoroacetic acid ([Hmim]<sup>+</sup>Tfa<sup>-</sup>).

### Synthesis of [Bmim]<sup>+</sup>[H<sub>2</sub>PO<sub>4</sub>]<sup>-</sup> and [Bmim]<sup>+</sup>[HSO<sub>4</sub>]<sup>-</sup>

[Bmim]<sup>+</sup>[H<sub>2</sub>PO<sub>4</sub>]<sup>-</sup> and [Bmim]<sup>+</sup>[HSO<sub>4</sub>]<sup>-</sup> derived from chloride salts (Scheme 2) were obtained by a dropwise addition of one



**Scheme 2** Schematic illustration of the synthesis of [Bmim]<sup>+</sup>[HSO<sub>4</sub>]<sup>-</sup> and [Bmim]<sup>+</sup>[H<sub>2</sub>PO<sub>4</sub>]<sup>-</sup>: (i) 1-chlorobutane (1.3 equivalent), acetonitrile, reflux for 48 h; (ii) H<sub>n</sub>X represents H<sub>2</sub>SO<sub>4</sub> (98%, 1 equivalent) or H<sub>3</sub>PO<sub>4</sub> (85%, 1 equivalent), reflux for 48 h.

equivalent of concentrated sulfuric acid (98%) or phosphoric acid (85%) to a cooled solution of 1-butyl-3-methylimidazolium chloride in anhydrous dichloromethane.<sup>18</sup> The mixture was refluxed for 48 h and the by-product HCl formed in the reaction was carried out of the condenser under a stream of dry nitrogen and was dissolved in deionized water at 0 °C. When the formed HCl had been completely removed, CH<sub>2</sub>Cl<sub>2</sub> was evaporated with a rotary evaporator. The IL was dried under vacuum at 70 °C for 6 h and stored in a desiccator.

### Synthesis of [Hmim]<sup>+</sup>Tfa<sup>-</sup> and [Hmim]<sup>+</sup>Tsa<sup>-</sup>

We did not find the procedures for the synthesis of [Hmim]<sup>+</sup>Tfa<sup>-</sup> and [Hmim]<sup>+</sup>Tsa<sup>-</sup> in a literature survey. The two ILs were synthesized using similar procedures to those used to prepare [Hmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup>.<sup>16</sup> 1-Methylimidazole was placed in a two-necked flask, which was equipped with a magnetic stirrer and cooled in an ice-water bath. A small amount of water was added and then the acid (trifluoroacetic acid or *p*-toluenesulfonic acid, 1 equivalent) was added slowly with stirring. The reaction mixture was stirred for an additional period of 2 h. Then water in the crude product was evaporated with a rotary evaporator at 70 °C and thus a colorless liquid product was obtained. The obtained ILs were characterized using IR (Bruker Tensor 27).

### Procedures for Mannich reactions

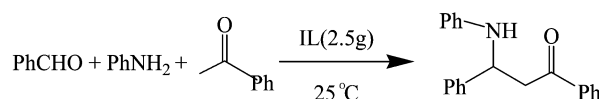
In a typical experiment, 10 mmol amine, 10 mmol aldehyde, 10 mmol ketone, and a certain amount of acidic IL were loaded into a magnetically stirred glass reactor in a constant temperature water bath at 25 °C. The reaction mixture turned turbid after a certain reaction time and at last became very viscous and close to solid. After reaction, the mixture was washed with distilled water (15 mL) and filtered. The solid product was re-crystallized using ethanol or

a mixture of ethanol and benzene and then dried at 50 °C under vacuum until constant weight. The filtrate (consisting of water, acidic ionic liquid and some other residual reactants or by-products) was extracted by ether and the aqueous solution was collected and dried at 70 °C using a rotary evaporator. Thus the acidic IL were recovered and can be used next time.

The products were characterized using IR spectra (Bruker Tensor 27), <sup>1</sup>H NMR (Bruker A.M. 300), EI-MS (Micromass TRIO 2000), and melting point measurement techniques.

## Results and discussion

Before reaction, we first investigated the miscibility of these ILs with other chemicals. All of them are miscible with water, ethanol, amines, ketones, and aldehydes, but are immiscible with ether. Then we chose a reaction of benzaldehyde, aniline, and acetophenone as a model reaction (Scheme 3) to test the catalytic



**Scheme 3**

activity of these acidic ILs and no other solvents were added as initial explorations. The results are shown in Table 1.

**Table 1** Three-component Mannich reaction catalyzed by acidic ILs at 25 °C (12 h)

Entry	Catalyst	Yield (%)
1	[Hmim] <sup>+</sup> Tfa <sup>-</sup>	83
2	[Hmim] <sup>+</sup> Tsa <sup>-</sup>	69
3	[Bmim] <sup>+</sup> [H <sub>2</sub> PO <sub>4</sub> ] <sup>-</sup>	67
4	[Bmim] <sup>+</sup> [HSO <sub>4</sub> ] <sup>-</sup>	No reaction

As shown in Table 1, the former three acidic ILs can catalyze the reaction efficiently (Entries 1–3) and [Hmim]<sup>+</sup>Tfa<sup>-</sup> shows the highest catalytic activity for the above reaction. However, [Bmim]<sup>+</sup>[HSO<sub>4</sub>]<sup>-</sup> reacts readily with amine due to its strong acidity and no Mannich base was produced (Entry 4).

On the basis of the results in Table 1, we focused our studies on the application of [Hmim]<sup>+</sup>Tfa<sup>-</sup> for different Mannich reactions. The results are given in Table 2.

**Table 2** Three-component Mannich reactions of aldehydes, amines, and ketones in the presence of [Hmim]<sup>+</sup>Tfa<sup>-</sup> at 25 °C

Entry	Aldehyde	Ketone	Amine	ILs/g	Time/h	Yield (%)
1	1a	2a	3a	3.11	12	85
2	1a	2a	3a	2.56	12	83
3	1a	2a	3a	1.4	12	71
4	1a	2a	3a	0.75	12	69
5	1a	2a	3a	0.37	12	68
6	1a	2a	3a	0.19	12	73
7	1a	2a	3a	3.11	8	80
8	1a	2a	3a	3.11	5	63
9	1b	2a	3a	1.4	24	35.7
10	1a	2b	3a	1.4	4	67
11	1a	2a	3b	1.4	12	66
12	1a	2a	3c	1.4	4	86.8
13	1a	2a	3d	1.4	2	97.7
15	1a	2a	3e	1.4	24	0
16	1a	2a	3f	1.4	24	0
17 <sup>a</sup>	1a	2a	3a	Tfa	12	68
18 <sup>b</sup>	1a	2a	3a	Tsa	12	67

<sup>a</sup> In ethanol (2.5 g); Tfa 3–4 drops. <sup>b</sup> In ethanol (2.5 g); Tsa 16 mol%

The amount of the IL affected the yield of product significantly. As shown by Entries 1–6, the yield of the product increased with the

increasing amount of the IL when there was not enough IL in the reactor, but did not change considerably as the amount of IL was more than 2.5 g. The main reason may be that the active sites increase with the addition of [Hmim]<sup>+</sup>Tfa<sup>-</sup>, which enhances the reaction rate. Moreover, pure [Hmim]<sup>+</sup>Tfa<sup>-</sup> was solid at room temperature. However, it melted when mixed with reactants and acted as solvent. Larger amounts of solvent added may also be favorable to increasing the yield. The data in Table 2 also demonstrates that the yield also increases with the reaction time (Entries 1, 7 and 8).

The substitutional group of the reactants is crucial to the yield of Mannich products, as can be known from Entries 9–16 in Table 2. The reaction activity of 3-chlorobenzaldehyde is lower than that of benzaldehyde (Entries 3 and 9). For the reaction of cyclohexanone, five equivalents of the ketones were added to avoid polyaminoalkylation (Entries 3 and 10). The reactivity order of amine components is 3,4-xylylidine > sulfanilamide > aniline > 4-bromoaniline (Entries 3 and 11–13). No reaction occurred when *N*-methylaniline (**3e**), or 2-nitroaniline (**3f**) were used (Entries 15 and 16), indicating that the space hindrance is also an important factor to determine the reactivity of amine.

The experiments that used ethanol as solvent and Tfa or Tsa as a catalyst were also carried out (Entries 17, 18) and the yield was 68% and 67%, respectively. Therefore, using the ILs as catalysts and solvents for the Mannich reactions can obtain higher yields than those used traditionally in the Mannich reaction system.

Mannich reactions of several aliphatic amines and carbonyl compounds were carried out in [Hmim]<sup>+</sup>Tfa<sup>-</sup> at 25 °C. Unfortunately, for each reaction several products were produced, and MS analysis indicated that the main products were not Mannich bases. So it can be concluded that the ionic liquids are not suitable for the Mannich reactions of aliphatic amines and carbonyl compounds.

Compared with traditional solvents and liquid acid catalysts, easy recycling is an attractive property of the acidic ionic liquids. Consequently, we investigated the catalytic activity of recycled [Hmim]<sup>+</sup>Tfa<sup>-</sup> in the reaction of benzaldehyde, aniline and acetophenone. As shown in Table 3, [Hmim]<sup>+</sup>Tfa<sup>-</sup> could be reused

**Table 3** Recycling of [Hmim]<sup>+</sup>Tfa<sup>-</sup> in the reaction of benzaldehyde, aniline and acetophenone (12 h, IL 3.11 g, 25 °C)

Cycle times	Yield%
1	85
2	83
3	87
4	80

at least four times without significant loss of activity. Our experiments exhibited that the IR spectrum of the used [Hmim]<sup>+</sup>Tfa<sup>-</sup> was consistent with that of the unused one.

## Conclusions

Several acidic ILs have been successfully used as catalysts and solvents for Mannich reactions using aldehydes, amines, and ketones. Utilization of acidic ILs as catalysts and solvents has several advantages: (1) high yield and high reaction rate can be achieved; (2) the preparation of acidic ILs is simple; (3) the ILs can be easily recycled and reused; (4) this protocol provides further examples of the capacity of ILs to be fashioned for specific chemical applications. The main contribution of this work is synthesizing [Hmim]<sup>+</sup>Tfa<sup>-</sup> successfully, which shows a balance between acidity and catalyst activity for the Mannich reaction.

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# Non-catalytic clean synthesis route using urea to cyclic urea and cyclic urethane compounds

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Clean synthesis to cyclic urea and cyclic urethane compounds using direct reaction of urea with diamine, amino alcohol or amino phenol has been achieved at 150 °C without any catalyst.

## Introduction

Cyclic ureas and urethanes find extensive applications as intermediates for fine chemicals, pharmaceuticals, cosmetics, pesticides *etc.* They are synthesized by reactions of diamines or amino alcohols with several different reagents such as phosgene,<sup>1</sup> dialkyl carbonates,<sup>2,3</sup> or a mixture of carbon monoxide and oxygen *via* oxidative carbonylation.<sup>4</sup> The dialkyl carbonates and oxidative carbonylation are currently in use. The use of phosgene and oxidative carbonylation is not eco-friendly due to risks associated with explosion hazards and poisonous phosgene or carbon monoxide. It should also be noted that dialkyl carbonates are currently produced *via* similar hazardous routes.<sup>5</sup> From an environmental viewpoint, the reaction of carbon dioxide with diamines or amino alcohols to produce cyclic ureas or cyclic urethanes was also studied.<sup>6–9</sup> In the absence of catalysts, yields of cyclic ureas from aliphatic diamines were high, but those of cyclic ureas from aromatic diamines and of cyclic urethanes from aliphatic or aromatic amino alcohols were low.<sup>9</sup> For the latter three reactions, high yields of the products can be achieved by employing homogeneous catalysts<sup>7</sup> or stoichiometrically consumed dehydration or deoxygenation reagents;<sup>8</sup> however, using such catalysts or reagents would cause problems associated with their separation and/or recycling and increase the cost of the reaction processes.

Urea can be used for the syntheses of cyclic ureas and urethanes from diamines and amino alcohols, respectively, in the absence of catalysts. These reactions are very attractive, since urea is an industrially synthesized cheap reagent. There are a few reports on these reactions.<sup>10–13</sup> Schweitzer<sup>10</sup> reported the ethyleneurea synthesis from urea and ethylenediamine and Butler and Hussain<sup>11</sup> studied the mechanism of this reaction. The reactions of urea and *o*-phenylene diamine<sup>12</sup> and of urea and  $\beta$ -amino alcohols were also reported.<sup>13</sup> In some of these studies using urea, the yields obtained were not satisfying and/or high reaction temperatures, which caused polyurea formation,<sup>14</sup> were required. Recently, the present authors carried out the reaction of urea and ethylene glycol to ethylene carbonate in the presence of zinc oxide and found that employing dynamic evacuation to remove the ammonia co-generated improves the reaction rate and the selectivity for ethylene carbonate.<sup>15</sup> Under these circumstances, we have decided to investigate the reactions of urea with a variety of diamine and amino alcohol substrates under dynamic evacuation.

## Results and discussion

Results obtained for the reaction between urea and various aliphatic diamines are presented in Table 1. For the reaction of 1,2-ethanediamine **1** and urea, imidazolidine-2-one **2** and 2-oxo-1-imidazoli-

**Table 1** Results of reactions of urea with aliphatic diamines using no solvent

Substrate	Product yield
<b>1</b>	<b>2</b> 65% <b>3</b> 21%
<b>4</b>	<b>5</b> 34% <b>6</b> 33% <b>6'</b> <sup>a</sup>
<b>7</b>	<b>8</b> 78%

Substrate, 165 mmol; urea: 165 mmol; pressure, 80 kPa; temperature, 150 °C; time, 3h.<sup>a</sup> Total yield of **6** and **6'**.

dinecarboxamide **3** are formed with yields of 65 and 21%, respectively. Similar to ethanediamine, the reaction of urea with 1,2-propanediamine **4** gives 4-methylimidazolidine-2-one **5** along with 4-methyl-2-oxo-1-imidazolidinecarboxamide **6** and 4-methyl-2-oxo-1-imidazolidinecarboxamide **6'**.<sup>†</sup> The selectivity of **5** is lower than that of **2** from **1** due to the formation of large amounts of the by-products. This may result from the effect of methyl group

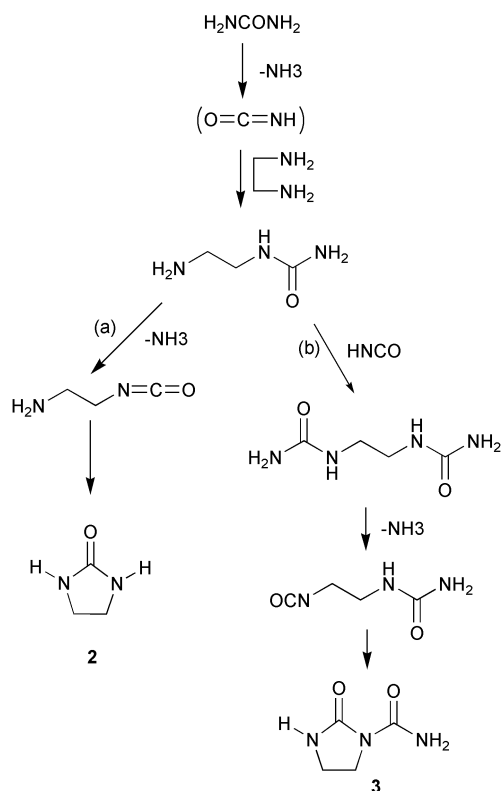
## Green Context

**Catalysis is one of the most important of the clean technologies that can often be used to “green” a chemical process. However, the use of catalysts can cause problems at the end of a process when they have to be separated and reused. It is reasonable to say “The best catalyst is no catalyst”. Here this is applied to the synthesis of useful cyclic ureas and urethanes *via* the direct thermal reaction of urea with different amino substrates. These simple reactions can be very efficient with only ammonia as a by-product. JHC**

<sup>†</sup> These two products showed different mass patterns but the mass numbers of the fragments were almost the same as each other. So, we were not able to identify the two products from GC-MS results and hence their total yield is given in Table 1.

in propanediamine. In contrast to the results obtained with the substrates **1** and **4**, 1,3-propanediamine **7** selectively gives tetrahydro-2-pyrimidinone **8** with a satisfying yield of 78%. For this reaction, no carboxamide compound was detected.

Butler and Hussain<sup>11</sup> carried out the reaction of urea and ethanediamine using <sup>15</sup>N labeled urea, *N*-methylated ureas and *N*-methylated diamines. They showed that all of the ammonia liberated comes from urea and proposed that an isocyanate intermediate ( $\text{H}_2\text{NC}_2\text{H}_4\text{N}=\text{C}=\text{O}$ ) is involved in the reaction. On the basis of their results, the reaction mechanism for the formation of the products **2** and **3** can be illustrated in Scheme 1. Probably, the



**Scheme 1** Reaction mechanism for the formation of products **2** and **3** (Table 1).

relative reaction rates of paths (a) and (b) should depend on the structure of substrates used, resulting in the difference in the selectivity for imidazolidinones between the substrates **1,4** and **7**.

Table 2 shows the results for the reactions of urea with aliphatic amino alcohols. The reactions of urea and the aliphatic amino

**Table 2** Results of reactions of urea with aliphatic amino alcohols using no solvent

Substrate	Product yield
<b>9</b>	<b>10</b> 91%
<b>11</b>	<b>12</b> 90%
<b>13</b>	<b>14</b> 79%
<b>15</b>	<b>16</b> 78%

Substrate, 165 mmol; urea: 165 mmol; pressure, 80 kPa; temperature 150 °C; time, 3 h.

alcohols selectively give the corresponding cyclic urethanes with excellent yields. The yields of oxazolidin-2-one **10** and 4-methylloxazolidin-2-one **12** from 2-aminoethanol **9** and 2-aminopropan-1-ol **11**, respectively, are almost the same, but that of 5-methylloxazolidin-2-one **14** from 1-aminopropan-2-ol **13** is slightly lower. These results suggest that a methyl group adjacent to an hydroxy group lowers the reactivity of the latter, while such an effect is absent between methyl and amino groups. The yield of 1,3-oxazin-2-one **16** from 3-aminopropan-1-ol **15** is lower than that of **10** from **9**.

In order to further widen the scope of the reaction, the reactions of urea with aromatic compounds have also been studied (Table 3)

**Table 3** Results of reactions of urea with aromatic compounds in DMF

Substrate	Product yield
<b>17</b>	<b>18</b> 98% (66%) <sup>a</sup>
<b>19</b>	<b>20</b> 96%
<b>21</b>	<b>22</b> 84%

Substrate, 50 mmol; urea, 75 mmol; DMF, 25 mL; pressure, 80 kPa; temperature, 150 °C; time, 3 h.<sup>a</sup> No solvent was used.

using DMF as a solvent. Benzene-1,2-diamine **17** gives almost quantitatively 1,3-dihydrobenzoimidazol-2-one **18**. However, when this reaction is conducted without solvent, the product yield appreciably decreases from 98% to 66%. In the absence of solvent, the solid product **18** made stirring the reaction mixture difficult, causing the lower yield. 2-Aminophenol **19** selectively gives 3*H*-2-benzoxazolone **20** with 96% yield. Similarly, (2-aminophenyl)methanol **21** selectively gives six-membered cyclic urethane of 1,4-dihydro-2*H*-3,1-benzoxazin-2-one **22** in a yield of 84%. Thus, urea is also applicable to the syntheses of cyclic urea and urethane from aromatic substrates.

In a previous study,<sup>9</sup> the authors carried out the reactions of condensed carbon dioxide with various diamines and amino alcohols without using any catalyst. With the reaction of carbon dioxide and aliphatic diamines, cyclic ureas were obtained selectively at high yields.<sup>9</sup> Hence, urea is not attractive for the preparation of aliphatic cyclic urea as compared with carbon dioxide, as seen in Table 1. However, this is not the case for the syntheses of cyclic urethane and aromatic cyclic urea, whose product yields and selectivities are high (Tables 2 and 3). For these reactions, carbon dioxide gave very poor yields for the desired products. Furthermore, in the case of the reaction of carbon dioxide and aminoalcohols, cyclic urethanes produced further reacted with the aminoalcohols, giving *N*-(hydroxyalkyl)imidazolidinones.<sup>9</sup> This reaction is absent in the present reaction system. Fu *et al.*<sup>3</sup> synthesized the products **20** and **22** from the substrates **19** and **21** using dimethyl carbonate in the presence of lead compounds as catalysts. However, higher reaction temperatures and an excess amount of dimethyl carbonate were required. Thus, urea is a useful reagent for the syntheses of cyclic urethane and aromatic cyclic urea.

In conclusion, aromatic cyclic ureas and cyclic urethanes can be obtained in high yields from the reaction of urea with aromatic diamines and amino alcohols without any catalysts under a reduced pressure. Ammonia generated can be used for ammonia-oriented products. Thus these routes are more green and eco-friendly. Aliphatic diamines also interact with urea, producing corresponding cyclic urea and substituted cyclic urea depending on the substrates used. Since urea is prepared industrially from ammonia

and carbon dioxide, the title reactions will be urea based carbon dioxide fixation to important chemicals.

## Experimental

The reactions were performed in a 100 mL glass reactor with a mechanical agitator and a water-cooled condenser attached. A water aspirator was attached above the condenser for creating suitable reduced pressure for removal of ammonia. After substrate (165 mmol) and urea (165 mmol) were charged into the reactor, the reactor was agitated under a reduced pressure of about 80 kPa. Then the reactor was heated to 150 °C and kept for 3 h. After the reaction, the reactor was cooled to room temperature. The reaction mixture was diluted with dimethyl formamide (DMF) to 50 mL and then analyzed on a gas chromatograph equipped with a flame ionization detector. The quantities of substrate consumed and products formed were determined from the results obtained from authentic standards. The structures of the compounds were confirmed by mass spectrometer. For aliphatic substrates (Tables 1 and 2) no solvent was used, while DMF was used for aromatic substrates (Table 3). For the latter, the amounts of substrate and urea were 50 mmol and 75 mmol, respectively, and 25 mL DMF was used. It should be noted that all components except for ammonia liquefied in the condenser and did not escape from the reaction mixture during the reaction.

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# Polymerisation of methyl methacrylate in supercritical difluoromethane

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The use of supercritical difluoromethane (scHFC 32) as a solvent is demonstrated for the polymerisation of methyl methacrylate. It is shown that appreciably higher molecular weight polymer can be obtained using scHFC 32 than scCO<sub>2</sub>, which is due to the higher solubility of the polymer in the more polar fluid. The solubility of various polymer standards is characterised at two pressures in scHFC 32 and is shown to be appreciable up to a molecular weight of 11 000 g mol<sup>-1</sup> whereas in scCO<sub>2</sub> the polymer of this mass is shown to be almost totally insoluble.

## Introduction

Carbon dioxide, principally in its supercritical (sc) state, has been widely heralded as an alternative to a wide range of organic solvents. It has been shown to be useful for extraction and synthesis and has been applied to tonne scale production in a variety of industries.<sup>1–3</sup> The use of sc fluids as relatively inert media for polymerisation reactions has received considerable recent attention, with most work being carried out in supercritical CO<sub>2</sub> (scCO<sub>2</sub>).<sup>4,5</sup> However, for large-scale commercial polymerisation processes this inevitably leads to the use of impractically large solvent volumes for the solubilisation of hydrocarbon monomer and macromolecules together with the added practical difficulties of using large volume, high-pressure plant. To surmount some of these difficulties, the addition of fluorinated polymeric surfactants or polar modifying fluids to scCO<sub>2</sub> has been reported. However, the use of additives adds an intrinsic cost and raises separation issues.<sup>6,7</sup> Notwithstanding, scCO<sub>2</sub> is currently being used by DuPont for the commercial synthesis of fluorinated polymers.

It has been highlighted that some hydrofluorocarbon (HFC) fluids such as difluoromethane (HFC 32) and 1,1,1,2 tetrafluoroethane (HFC 134a) are relatively polar solvents,<sup>8–10</sup> even in the sc state, and this allows them to be used as efficient extraction solvents either on their own or in conjunction with CO<sub>2</sub>.<sup>11,12</sup> Furthermore, these solvents are also readily available and non-toxic. They have easily accessible critical constants (HFC 134a  $T_c = 101.1$  °C;  $p_c = 40.6$  bar and HFC 32  $T_c = 78.1$  °C;  $p_c = 57.8$  bar) and gaseous dipole moments of about 2 D.<sup>10</sup>

HFCs have replaced a number of chlorofluorocarbons (CFCs) in the refrigeration and propellants industries<sup>13,14</sup> and, without justification, HFCs have also been associated with the same environmental problems as the CFCs. The environmental impact of these HFCs was the focus of intensive research in 1989 by the Alternative Fluorocarbons Environmental Acceptability Study (AFEAS). This research program concluded that HFCs do not contribute to ozone depletion as hydroxyl radicals break them down in the lower atmosphere to simple inorganic species that are already present in the atmosphere.<sup>15</sup> It is found, however, that a few HFCs may form trifluoroacetyl halides that will dissolve in water to give trifluoroacetate (TFA) salts.<sup>16</sup> These salts will then be present in rain and seawater at very low concentrations, but it is found that they can be degraded by microorganisms naturally present in soils and sediments. HFCs do not accumulate in the atmosphere to the same extent as CFCs so their contribution to the greenhouse effect is greatly reduced. Atmospheric decay rates of HFCs do vary, but the lifetimes are much less than those of carbon dioxide. For a relatively short lived gas like HFC 134a, the concentration and

hence contribution to global warming drops rapidly to zero after emission, but the contribution due to emission of a long lived gas like carbon dioxide persists for more than 500 years.

HFCs have been proposed as useful solvents for synthesis in the liquid state.<sup>17</sup> Cooper *et al.*<sup>18</sup> have recently shown that cross-linked polymers can be synthesised by dispersion polymerisation in liquified HFC 134a ( $T < 100$  °C,  $P < 50$  bar). Recent studies on scHFCs have suggested that they would be potential alternative media to CO<sub>2</sub> for a variety of reactions in the supercritical state.<sup>9,19</sup> Here, we contrast the use of scCO<sub>2</sub> and scHFC 32 for the preparation of poly(methyl methacrylate).

## Experimental

Methyl methacrylate (MMA) monomer (Aldrich 99%) and the heat-activated free radical initiator, azobisisobutyronitrile (AIBN) (Aldrich) were used as received. Fig. 1 shows a schematic diagram

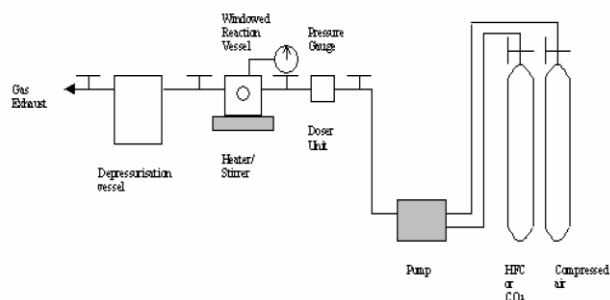


Fig. 1 High-pressure reaction apparatus.

of the high-pressure reaction apparatus utilised, consisting of a 30 ml heater/stirrer reaction vessel, a doser unit and a 50 ml depressurisation vessel. Pressure was applied using a model 10–600 pump (Hydraulic Engineering Corp., Los Angeles), driven by compressed air. The temperature of the cell was measured using an Fe/constantan thermocouple and retained at a given temperature ( $\pm 0.5$  °C) using a CAL 9900 heater. The pressure was monitored ( $\pm 2$  bar) using a UCC type PGE 1001.600 gauge. The solvent, HFC 32 (Ineos Fluor, 99.99%) was used as received. In all high-pressure reactions the system was purged with the solvent (HFC 32 or CO<sub>2</sub>), isolated and preheated to a temperature greater than the solvent critical temperature. The doser unit, being at room temperature, was loaded with the methyl methacrylate monomer and the AIBN radical initiator and sealed. The gas was then flushed through the doser and the reaction vessel was pressurised to above the critical pressure for the gas and the reaction was left for 6 hours. The toluene reaction was carried out *in vitro*, at 90 °C and atmospheric



pressure for 6 hours. Table 1 displays the reaction conditions used for all of the experiments.

The solubility of PMMA was determined using a standard gravimetric method.<sup>1</sup> The molecular weight distributions were determined using gel permeation chromatography with PLGel guard plus 2 × mixed bed-B columns, at a temperature of 30 °C using THF as the solvent and a refractive index detector. The PMMA standards ( $M_n/M_w < 1.1$ ) were used as received (Polymer Laboratories Ltd.). The solution relative permittivity was measured by the method previously reported.<sup>10,19</sup>

## Results and discussion

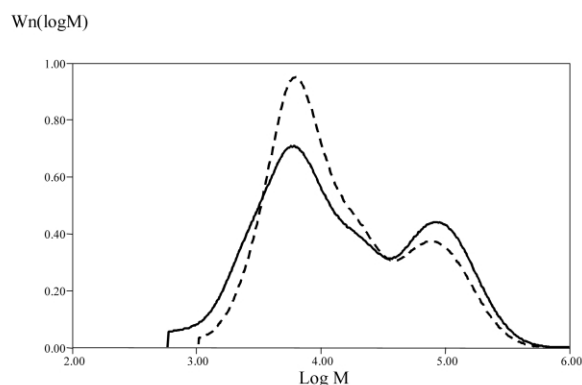
To determine whether homogeneous polymerisation of methyl methacrylate would be possible in HFC 32 the solubility of various PMMA standards was measured in scHFC 32 as a function of molecular mass at 120 and 200 bar. The solubility in scCO<sub>2</sub> was also measured as a comparison. Table 2 shows that at low molecular mass the polymer is extremely soluble in scHFC 32. As the molecular mass increases the solubility decreases and above a molecular mass of over *ca.* 20 000 g mol<sup>-1</sup> the polymer is almost totally insoluble at both pressures. In contrast, PMMA is totally insoluble in scCO<sub>2</sub> except at low molecular weight where it is three orders of magnitude less soluble than in HFC 32. DeSimone<sup>20,21</sup> studied the polymerisation of concentrated methyl methacrylate in scCO<sub>2</sub> solutions and suggested that homogeneous polymerisation occurred because the monomer acted as a polar modifying agent. The results in Table 2 show that PMMA has negligible solubility in pure scCO<sub>2</sub> and hence a high monomer concentration would be required to significantly increase the solution relative permittivity. The monomer concentrations reported<sup>21</sup> were very high with solvent : monomer ratios as low as 3 : 1 reported.

The data in Table 2 are also interesting because they suggest that significant differences in polymer solubility can be obtained in scHFC 32 with pressure. This suggests that scHFC 32 could be used for molecular weight fractionation or polymer purification. A sample of polydisperse poly(methyl methacrylate) was treated with scHFC 32 for 1 hour at 90 °C and 200 bar. The polymer swelled by approximately three times after treatment and changed its morphology from a dense solid to an open, soft amorphous structure. The molecular weight distribution was also affected with a significant proportion of the low molecular weight fraction being removed and deposited in the collection vessel. Fig. 2 shows the change in molecular weight distribution prior to and following extraction with scHFC 32. It can be seen that it is principally the polymer with molecular weight in the range 10<sup>3</sup>–10<sup>4</sup> g mol<sup>-1</sup> that is being removed, which ties in well with the solubility data listed in Table 2.

Free radical polymerisation of methyl methacrylate (MMA) was carried out in scHFC 32 using AIBN as the initiator. The high-pressure reactions were carried out in a stirred, windowed reactor in order to view the progress of the reaction and to ascertain any changes in phase behaviour. In scHFC 32, at reaction temperature and pressure, the supercritical solution of monomer and initiator

**Table 2** Solubility of PMMA in scHFC 32 and scCO<sub>2</sub> at 90 °C together with the relative permittivity of the solvents at the given conditions

$M_n/g\ mol^{-1}$	Solubility/mg ml <sup>-1</sup>		
	HFC 32 120 bar	HFC 32 200 bar	CO <sub>2</sub> 200 bar
24830	0	0	0
11100	0	0.10	0
5200	0.36	0.42	0
2220	0.79	3.49	0
1310	8.37	> 10.00	0.1
Relative permittivity	6.53	8.01	1.60



**Fig. 2** Distribution of molecular weights for PMMA sample before (dashed) and after (solid) extraction with scHFC 32.

exhibited a single-phase, which was milky in appearance (due to critical opalescence) showing that all of the monomer is soluble and polymerisation begins as a homogeneous process. As polymerisation proceeded, the solution darkened, eventually appearing black to transmitted light. As the reaction proceeded further, the solution became paler and, in most cases, was transparent after 30 minutes to 1 hour, the exact time being dependent upon the conditions employed. Attenuation of optical transmission with increasing solute concentrations is common for scHFCs, since colloidal light scattering is enhanced.<sup>18</sup>

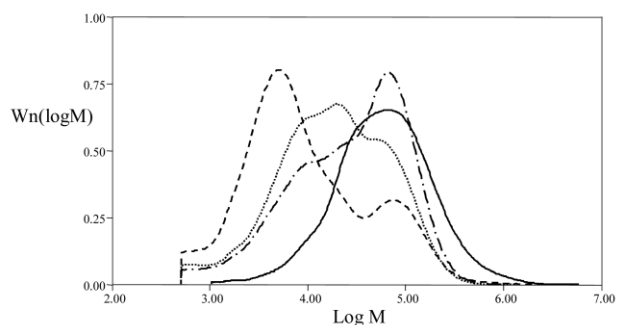
In scCO<sub>2</sub> the phase behaviour is somewhat different, in that the monomer is not totally soluble in the solvent under the reaction conditions<sup>20</sup> (two distinct phases are observable at all times) and the sc-phase does not darken as the reaction proceeds (consistent with no monomer dispersion/colloid formation). The polymerisation process can occur in either phase, but the lack of optical transmission attenuation suggests that the polymer does not grow to a significant molecular weight in the sc-phase before precipitation into the gas-expanded liquid phase. DeSimone *et al.*<sup>21</sup> reported the pulse laser polymerisation of MMA in liquid and scCO<sub>2</sub> and suggested that higher molecular weight polymer could be produced using high monomer concentration (6.2 mol L<sup>-1</sup>) such that the monomer itself acted as a polar modifier.

**Table 1** Polymerisation of methyl methacrylate in difluoromethane, CO<sub>2</sub> and toluene

Entry	Solvent	T/°C	P/bar	Relative permittivity <sup>a</sup>	MMA/mol l <sup>-1</sup>	MMA/AIBN	Conv(%)	<sup>a</sup> M <sub>n</sub> /g mol <sup>-1</sup>
1	Toluene	90	1	—	1.5	100	34	6 100
2	CO <sub>2</sub>	90	200	2.27	1.0	100	41	4 500
3	CO <sub>2</sub>	90	225	2.49	1.5	100	38	7 800
4	HFC 32	90	160	8.31	0.33	100	11	7 500
5	HFC 32	90	150	8.63	0.83	100	18	9 700
6	HFC 32	90	200	8.90	1.5	100	68	10 600
7	HFC 32	90	200	8.90	1.5	200	42	13 600
8	HFC 32	90	200	8.90	1.5	400	40	28 500
9	HFC 32	90	200	9.12	3.0	100	54	31 000

<sup>a</sup> Solution relative permittivity at the start of each reaction.

Table 1 shows that polymerisation in both toluene and scCO<sub>2</sub> yields a low molecular weight polymer (entries 1–3). It is interesting to note that as the monomer concentration is increased the molecular weight increases presumably because the solution relative permittivity is modified by the monomer allowing the formation of a higher molecular weight polymer in the solution phase before it precipitates in a similar way to that demonstrated by DeSimone (*cf.* Table 1 and 2). This also has a significant effect on the molecular weight distribution as can be seen from Fig. 3 (*cf.* entries 2 and 3) (note that the major contribution to the relative permittivity is the monomer concentration and not the pressure).



**Fig. 3** Distribution of molecular weights for entries 2 (---), 3 ( . . ), 6 (- - -) and 9 (—) in Table 1.

Reactions carried out in scHFC 32 formed significantly greater amounts of higher molecular weight fractions of PMMA compared to similar conditions in scCO<sub>2</sub>. Table 1 illustrates the effect of monomer concentration and the monomer/initiator ratio on the polymerisation process. Entries 5, 6 and 9 show that an increase in monomer concentration causes an increase in  $M_n$ . The increase in monomer/initiator ratio causes an increased degree of polymerisation (entries 6–8). This is in line with the expression that is known for solution free radical reactions:<sup>22</sup>

$$x_n \propto [M][I]^{-1/2}$$

where  $x_n$  is the number average degree of polymerisation,  $[M]$  and  $[I]$  are the concentrations of monomer and initiator, respectively.

Fig. 3 shows some representative molecular weight distributions selected from the data shown in Table 2. It is evident that multimodal distributions are obtained in both CO<sub>2</sub> and HFC 32. Clearly, scCO<sub>2</sub> and scHFC 32 support significantly different polymer growth mechanisms. Entry 2 shows that the majority of the polymer formed in scCO<sub>2</sub> at 200 bar has a molecular weight distributed around 5000 g mol<sup>-1</sup>. Since the relative permittivity of this solution is relatively low (Table 1), it is probable that the polymer phase separates at a low molecular weight. The proliferation of low molecular weight polymer suggests that phase separation may encourage chain termination. The smaller distribution around 10<sup>5</sup> g mol<sup>-1</sup> probably results from a second stage growth mechanism, *i.e.* once the polymer precipitates from the solution. This phase separation may have other ramifications as the monomer may also phase separate, being preferentially soluble in the PMMA rather than the CO<sub>2</sub> phase.

The relative permittivity of the HFC 32 solutions is considerably higher than that for the scCO<sub>2</sub> solutions permitting the polymer to

grow to higher molecular weights before precipitation (entries 6 and 9), something reflected by the narrower molecular weight distributions observed for entry 9 (Fig. 3). Here the monomer should reside predominantly in the scHFC 32 phase meaning that the growth rate may change significantly if the process is mass transport limited.

## Conclusion

For the first time scHFC 32 has been used as a polymerisation medium. This initial study has shown that the greater polarity of scHFC 32 over scCO<sub>2</sub> and toluene has allowed for the preparation of higher molecular mass PMMAs in the absence of any stabilisers. Given the large changes in solvent polarity around the critical temperature it is believed that the polarisability of certain monomers will allow greater control of polymer synthesis and, therefore, structure and properties than is currently available with scCO<sub>2</sub>.

## Acknowledgements

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# Chemical recycling of sulfur-cured natural rubber using supercritical carbon dioxide

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Sulfur-cured unfilled natural rubber (NR) was devulcanized in supercritical CO<sub>2</sub> (scCO<sub>2</sub>) by using diphenyl disulfide (DD) as a devulcanizing reagent. The product was fractionated into sol and gel components. The fraction of sol component that contains reusable linear polymer increased with the increase in CO<sub>2</sub> pressure, especially over the critical pressure. The molar mass of the resulting sol component was about tens of thousands and the crosslink density of the gel component decreased from the initial one.

## Introduction

Natural rubber (NR) that consists mainly of poly-*cis*-1,4-isoprene is a “green” polymer (an agricultural product) and the most widely used elastomer due in part to its unique properties. The demand for NR has gradually increased in recent years. The mass consumption of NR is thought to be favorable compared to that of synthetic rubber from the viewpoints of global concerns which include the saving of the limited petroleum resources. The production of NR contributes also to the immobilization of CO<sub>2</sub>. However, on the other hand, a large amount of used NR is being generated. Currently, most waste NR is burned as fuel, expiring CO<sub>2</sub> into the air. A recycling-oriented process for NR is desirable from the viewpoint of green sustainable development.

There is a problem associated with the recycling of NR. Raw NR has linear polymer chains and is processable into an arbitrary form. However, when NR is used as an industrial material, sulfur is added (vulcanized) to form 3-dimensional crosslinks. These crosslinks are essential for the rubber material to be retractable. On the other hand, once the NR is vulcanized, it is no longer processable; vulcanized NR is infusible and insoluble due to the crosslinks. In order to recycle the vulcanized NR as a processable material, the crosslinks should be severed selectively and the linear polymer chains must be recovered.

Various types of recycling process for the vulcanizates have been studied so far in order to improve the productivity and quality of the recycled raw rubber.<sup>1–7</sup> However, no recycling process with compatibility between productivity and quality has been established. One reason for the difficulty in recycling the vulcanized NR is that reagents for the process hardly diffuse into the bulk NR due to the network structure.

We propose a green process that utilizes supercritical CO<sub>2</sub> (scCO<sub>2</sub>) as devulcanization reaction media for the recycling of NR vulcanizate. (As a custom, the word “devulcanize” is used in this paper not only to remove sulfur but also to sever crosslinks in rubber.) Supercritical fluids (SCFs) show unique physicochemical properties: they are of low viscosity, high diffusivity and high thermal conductivity.<sup>8</sup> These properties can be varied by changing temperature and pressure.<sup>9,10</sup> The diffusion rates of some devulcanizing reagents into the rubber vulcanizates, which are 3-dimensional network polymer systems, are expected to be enhanced by using SCFs as reaction media. Among several SCFs, CO<sub>2</sub> is the most advantageous for the current purpose because it is chemically inactive, nontoxic, nonflammable, and inexpensive. Residual CO<sub>2</sub>

in the vulcanizate is easily and rapidly removed by releasing pressure. Furthermore, CO<sub>2</sub> has an easily accessible critical point (the critical temperature and the critical pressure are 31.1 °C and 7.38 MPa, respectively). Therefore, scCO<sub>2</sub> is expected to be applicable as devulcanization reaction media.

In our previous study,<sup>11</sup> the devulcanization of a model polymer network, *i.e.*, sulfur-cured unfilled synthetic polyisoprene rubber (IR; the main structure of NR) was carried out in scCO<sub>2</sub> and it was demonstrated that scCO<sub>2</sub> works very well in facilitating the penetration of the devulcanizing reagent into IR vulcanizate. Diphenyl disulfide (DD) was found to be one of the most effective devulcanizing reagents in scCO<sub>2</sub> among some reagents. (It has been known that DD is also an effective reagent for devulcanization of NR vulcanizate in some organic solvents.<sup>12,13</sup>) In this work, the devulcanization process using DD in scCO<sub>2</sub> is studied on unfilled NR vulcanizate. The optimum conditions for the devulcanization were investigated, and the structure and thermal properties of the devulcanized rubber were studied.

## Experimental

### Materials

RSS#3 (RSS is graded visually according to the international standards of quality) was used as NR. Sulfur including oil of 5% by weight was provided from Hosoi Chemical Co. and used for curing. *N*-cyclohexyl benzothiazyl sulfenamide (CBS), purchased from Sumitomo Chemical Co., and tetramethylthiuram disulfide (TMTD), purchased from Ouchishinko Chem. Ind. Co., were used as accelerating agents. DD (diphenyl disulfide, mp 58–60 °C) was purchased from Nacalai Tesque, Inc. and was used as the devulcanizing reagent. Solid carbon dioxide (dry ice) was used without further purification. Other chemicals not mentioned above were procured from indigenous sources and were used as such.

### General procedure

The whole experimental procedure is shown in Scheme 1. Unfilled rubber samples (vulcanizates) with different crosslink distributions were prepared by varying the cure time and kinds of curatives. These vulcanizates were characterized before the devulcanization. The devulcanization was performed under various conditions and the resulting products were characterized again.

The linear rubber molecules that are processable as recycled materials are contained in the sol component, and the polymer networks that still contain a certain degree of crosslinks remain as gel components. Therefore, a higher sol fraction indicates a more effective devulcanization.

<sup>†</sup> On leave from Toyo Tire & Rubber Co., Ltd.

Hereafter, the specimens described in the text will be indicated by the symbols s0, s1 *etc.*, in Scheme 1.

### Preparation of model NR vulcanizate

Model NR vulcanizates were made up of simple compositions without any fillers, antioxidants or oils in order to facilitate the analysis of the devulcanization reaction. Each compound was prepared by mixing NR with curatives in a Banbury mixer in accordance with the composition shown in Table 1. Gel permeation chromatography (GPC) measurement was made on the acetone-insoluble component of the compound (s1 in Scheme 1) and the results are shown in Table 2. Each compound was cured for a given temperature and time as shown in Table 3. The low molecular weight compounds of curing agents in each vulcanizate, such as free sulfur, parts of accelerators and stearic acid which had not reacted with polymer chains during the curing process, were removed by Soxhlet extraction using azeotropic acetone–chloroform (3 : 7 in volume, bp 64.4 °C) as solvent for 8 hours and the residue was dried *in vacuo*. The extracted vulcanizate (s2) was trimmed into several rectangular sheets (25 mm × 15 mm × 2.7 mm, 1.00 g). This sheet was subjected to the devulcanization reaction as a vulcanizate sample.

### Devulcanization reaction

Devulcanization reaction was carried out in an autoclave (inner volume: 62 ml) equipped with a thermocouple and a pressure gauge. A sheet of the vulcanizate sample (s2), a glass vessel containing DD (a devulcanizing reagent) and a prefixed weight of solid carbon dioxide were put into the autoclave as shown in Fig. 1. Then, the autoclave was immediately sealed off at room temperature and heated up to a prefixed temperature and maintained at that temperature without any mechanical stirring. The pressure was calculated and controlled only by the quantity of carbon dioxide in the autoclave. After the prefixed time, the system was cooled down to room temperature and depressurized. Then, the product (s3) was taken out of the autoclave.

### Separation of sol and gel components

After the devulcanization, each product (s3) was placed in acetone (20 ml, changed to a fresh solution every day) at room temperature

**Table 1** Formulation for model NR compounds

	A	B
NR <sup>a</sup>	100.0	100.0
Stearic acid	2.0	2.0
Zinc oxide	5.0	5.0
Sulfur	3.0	—
CBS <sup>b</sup>	1.0	—
TMTD <sup>c</sup>	—	6.0

The values are in parts per hundred rubber in weight (phr).<sup>a</sup> Natural rubber. <sup>b</sup> *N*-Cyclohexyl-2-benzothiazole sulfenamide. <sup>c</sup> Tetramethylthiuram disulfide.

**Table 2** Characterization of the model NR compounds

Compound	$M_n \times 10^{-4a/}$ g mol <sup>-1</sup>	$M_w/M_n^a$
A	26.1	2.15
B	22.2	1.88

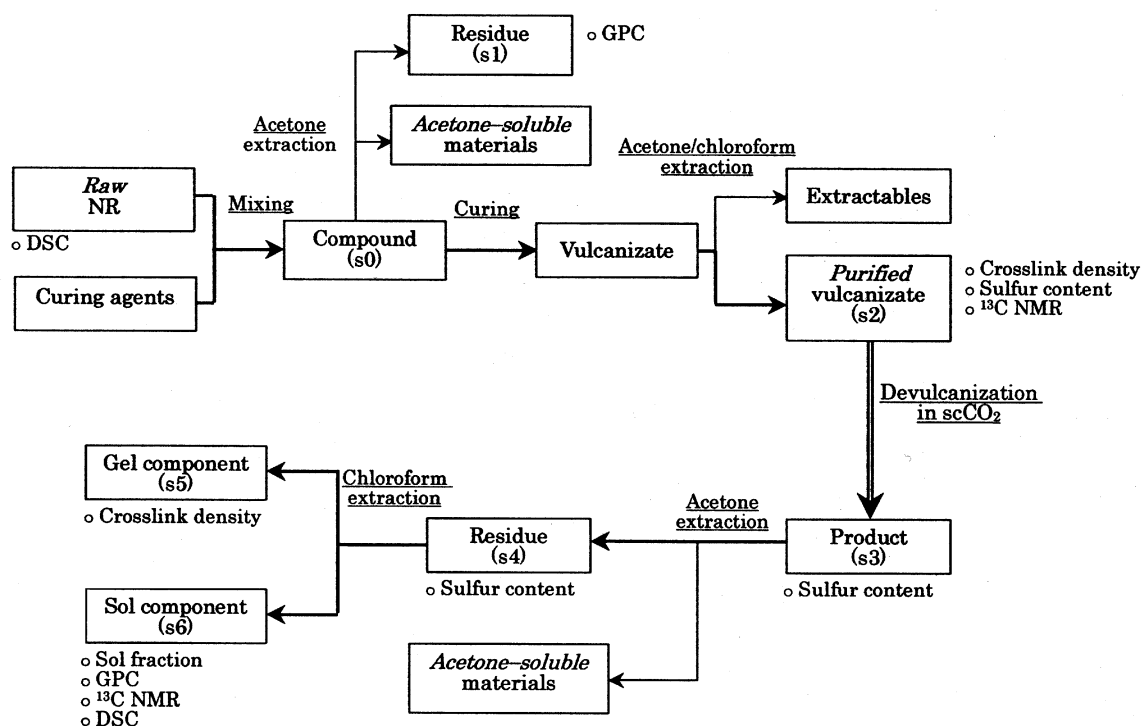
<sup>a</sup> By GPC using polystyrene standards.

**Table 3** Cure condition and curing data for the model NR vulcanizates with various crosslink distributions

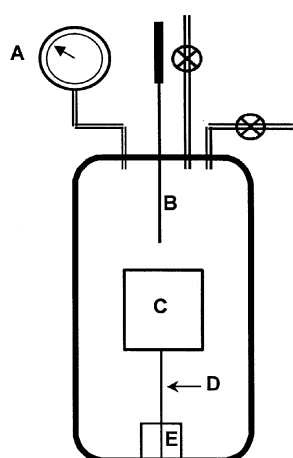
Compound	Vulcanizate	Cure temp./°C	Cure time/min	$t_{90}^a/$ min
A	A-30	141	30	23.90
A	A-45	141	45	
A	A-60	141	60	
A	A-120	141	120	
B	B-30	141	30	26.10

<sup>a</sup>  $t_{90}$  means the optimum cure time of the compound.

for 48 hours to remove the extractable constituents such as the devulcanizing reagents that had not reacted with the polymer chains. Then, the acetone-insoluble product (s4) was dried *in vacuo* at room temperature to constant weight. Subsequently, the product (s4) was placed in chloroform (50 ml, changed to fresh solvent every day) at room temperature for 72 hours. The chloroform solution containing the insoluble portion was filtered to separate the



**Scheme 1** Schematic diagram outlining the stages of the experiment.



A: Pressure gage  
 B: Thermocouple  
 C: Vulcanizate sample  
 (25 × 17 × 2.7 mm, 1.00 g)  
 D: Wire for holding the vulcanizate  
 E: Glass vessel containing  
 a devulcanizing reagent

Fig. 1 Apparatus for the devulcanization process.

sol (s6) and gel (s5) components. Both the sol and gel components were dried again *in vacuo* at room temperature to constant weight. The molecular weight of the sol component and crosslink density of the gel component were measured as below.

### Analysis

The optimum cure time ( $t_{90}$ ) was measured by Monsanto Rheometer MDR200 for the compound (s0). The crosslink densities of the vulcanizate (s2) and gel component (s5) were calculated by the swelling method using toluene as swelling solvent on the basis of the Flory–Rehner eqn. (1).<sup>14</sup>

$$\nu = \frac{-[\ln(1 - \nu_r) + \nu_r + \mu \nu_r^2]}{V_0[\nu_r^{1/3} - (\nu_r/2)]} \quad (1)$$

where

- $\nu$ : crosslink density
- $\nu_r$ : volume fraction of the rubber network in the swollen gel
- $V_0$ : molar volume of the swelling solvent
- $\mu$ : rubber–solvent interaction parameter.

In this calculation, a value of 0.393 was used as the rubber–solvent interaction parameter ( $\mu$ ).<sup>15</sup> The sulfur content in the samples (s2, s3, s4) was measured with a sulfur analyzer from LECO (model SC432) that detects the amount of SO<sub>2</sub> generated by complete combustion of the sample. The molecular weight (s1, s6) was measured by GPC (Shimadzu Co., LC10A, column; PLgel 10 $\mu$ , using tetrahydrofuran and polystyrene as solvent and an internal standard, respectively). The <sup>13</sup>C NMR spectrum was obtained by a Bruker DPX400S using deuterated chloroform as solvent for the structural analysis of the raw rubber, the rubber in uncured compound (s0), and the sol component (s6) extracted from the vulcanizates. The thermal properties of the sol component (s6) were determined by differential scanning calorimetry (DSC) at a scan rate of 20 °C min<sup>-1</sup> in nitrogen.

## Results and discussion

### Characterizations of raw rubber and model NR vulcanizate

The residue (s1) obtained from each compound (s0) after acetone extraction was subjected to GPC measurement. The results are shown in Table 2. Due to mechanical scission of the rubber main chain during Banbury mixing, the molecular mass of both uncured compounds A and B were considerably reduced when compared with that of the raw NR.

After the extraction by acetone–chloroform for purification of the vulcanizate, the crosslink density of each vulcanizate (s2) was measured, and the results are shown in Table 4. The crosslink

Table 4 Crosslink density of the model NR vulcanizates with various crosslink distributions

Vulcanizate	Crosslink density × 10 <sup>7</sup> /mol l <sup>-1</sup>
A-30	1.93
A-45	1.84
A-60	1.79
A-120	1.63
B-30	1.48

densities of the vulcanizates prepared from compound A decreased slightly with the increase in preceding cure time (Table 3). It is generally regarded that this phenomenon is reversion that occurs beyond the optimum cure time. However, the difference among the crosslink densities of these vulcanizates is not so large. Therefore, the effect of the degree of swelling on the devulcanization is supposed to be negligible among these vulcanizates (including B-30).

### Dependence of the devulcanization on amount of DD, pressure and time

The optimum amount of DD, pressure and time for the devulcanization were investigated using 1.00 g of A-30 (Tables 3, 4) as a standard NR vulcanizate.

Fig. 2 shows the effect of the amount of DD on the devulcanization (sol fraction, s6) at 180 °C, 10 MPa for 60 min. The

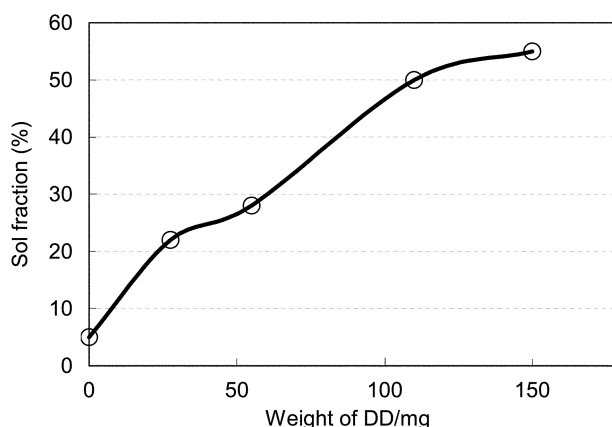
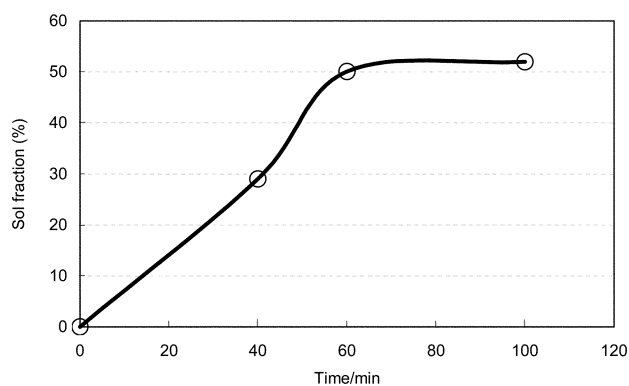


Fig. 2 Dependence of the sol fraction on the amount of DD using sample A-30 at 180 °C, 10 MPa for 60 min.

sol fraction was only 5% without DD. This result means that degradation of the NR vulcanizate will scarcely proceed without DD. The sol fraction increased with the increase in the amount of DD. Using 110 mg of DD against 1.00 g of A-30, a sol fraction of 50% was obtained. From the standpoint of practical use, the viscosity of this product was low enough to be used in a mixing process. The molar mass of the sol component (s6) was reduced to 1.45 × 10<sup>4</sup> (g mol<sup>-1</sup>) from 26.1 × 10<sup>4</sup> in compound A (s1, Table 2). It is obvious that the scission also occurred in the main chain, though we intended to break the crosslinks in the vulcanizate. Whether the scission occurred at the crosslink site or not will be discussed later. The number of molecules of DD in 110 mg (5.00 × 10<sup>-4</sup> mol) was 2.59 times larger than the estimated number of crosslinks contained in 1.00 g of A-30. Excess DD may have contributed to the main chain scission.

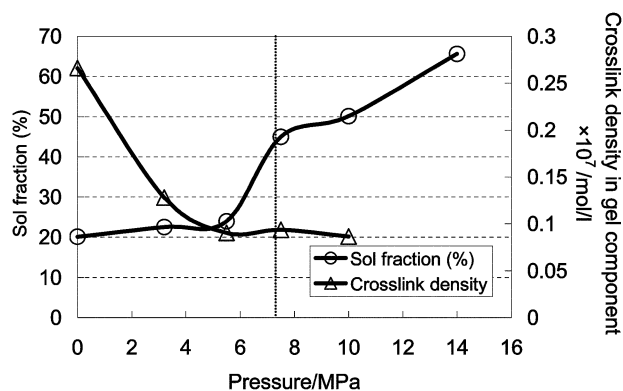
The reaction time dependence of the sol fraction (s6) is shown in Fig. 3 using 110 mg of DD under conditions of 180 °C and 10 MPa. The sol fraction increased in proportion to the reaction time until 60 min. It remained constant at approximately 50% after 60 min. A



**Fig. 3** Time dependence of the sol fraction using sample A-30 at 180 °C, 10 MPa.

reaction time of 60 min seems to be sufficient to attain a constant value of the sol fraction under these conditions.

The pressure dependence of the devulcanization of A-30 was investigated with 110 mg of DD at 180 °C for a reaction time of 60 min. The results are shown in Fig. 4. Even at 0.10 MPa, *i.e.* under



**Fig. 4** The dependence of the sol fraction and crosslink density in the gel component on the pressure of carbon dioxide using sample A-30 at 180 °C for 60 min. The vertical broken line indicates the critical pressure of carbon dioxide.

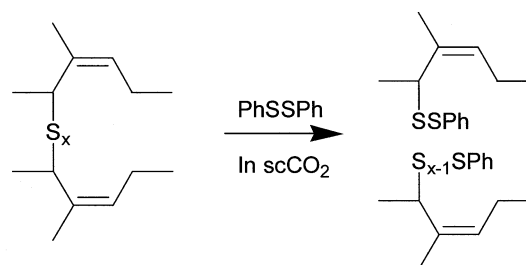
atmospheric pressure, the sol fraction (s6) was no less than 20%. Devulcanization at 0.10 MPa is due not only to DD but also to thermally-initiated radicals in the presence of oxygen in air. The latter may contribute to the degradation of the main chains and may not contribute much to that of crosslinks. The sol fraction increased with the increase in pressure, especially around and over the critical point (7.38 MPa). At 10 MPa, a sol fraction of 50% was attained. The crosslink densities of the gel components (s5) decreased with the increase in pressure up to 5.8 MPa and remained in the limited range from  $0.08 \times 10^{-1}$  to  $0.10 \times 10^{-1} \text{ mol l}^{-1}$  over 5.8 MPa. In other words, about 95% of the initial crosslink in the vulcanizate was broken in the gel components obtained over 5.8 MPa. The value of the crosslink density ( $0.10 \times 10^{-1} \text{ mol l}^{-1}$  or less) is assumed to be a critical one at which the residual network is separated as the gel component using chloroform as solvent.

Under conditions of 110 mg of DD against 1.00 g of the vulcanizate, a reaction time of 60 min and pressure of 10 MPa were regarded to be optimum and were used in the following part of this work. Under the optimum conditions, at least 50% of the initial sample (A-30) in the sol component can be recycled, and additionally, the residual gel component may also be used for compounding because the crosslink density is low enough. These results indicate that the recycling process using  $\text{scCO}_2$  is practical.

#### Plausible cleavage reaction of the devulcanization

The crosslink cleavage reaction of this devulcanization is presumed to be the one described below based on the analysis in the next

section. At first, some DD molecules should be dissolved in  $\text{scCO}_2$  and the DD molecules solvated by  $\text{scCO}_2$  will penetrate into the NR vulcanizate swollen in  $\text{scCO}_2$ . (We are now planning to investigate these phenomena separately.) Then, DD in the NR vulcanizate may attack the sulfur–sulfur bond of the crosslinks as shown in Scheme 2. This addition reaction will lead to the crosslink cleavage in the NR vulcanizate.



$x=1$ : monosulfidic crosslink  
 $x=2$ : disulfidic crosslink  
 $x \geq 3$ : polysulfidic crosslink

**Structure A**

**Structure B**

**Scheme 2** Plausible crosslink cleavage reaction in the NR vulcanizate using diphenyl disulfide.

#### Structure and thermal property of the devulcanized rubber

The structure and thermal properties of the devulcanized rubber obtained from A-30 after devulcanization under the optimum conditions were analyzed.

The sulfur contents of the product (see Scheme 1) before (s3) and after (s4) acetone extraction were analyzed as shown in Table 5.

**Table 5** Comparison of sulfur contents<sup>a</sup> of the vulcanizate and the product before and after the acetone extraction

Vulcanizate (A-30)	Product	
	before ac-ex <sup>b</sup>	after ac-ex <sup>b</sup>
2.88	4.91	3.14

<sup>a</sup> Weight%. <sup>b</sup> Acetone extraction.

The original vulcanizate (s2) contained 2.88% sulfur. The sulfur content of the product before acetone extraction (s3) increased to a large degree compared to that of the original vulcanizate, which implies that sulfur contained in the DD was transferred to the product during the devulcanization. The sulfur content of 4.91% implies that 62% of the DD in the glass vessel has been transferred into the product (s3). However, this amount includes the part that is not connected to the polymer chain. Therefore, acetone extraction was done on the product in order to exclude DD unreacted with polymer chain. The sulfur content of the product after the acetone extraction (s4) decreased to 3.14%. This value was still higher than that of the original vulcanizate. The difference in the sulfur content between specimens s2 and s4 corresponds to the amount of DD connected to the polymer chains during the devulcanization.

The  $^{13}\text{C}$  NMR spectrum of the sol component (s6) is shown in Fig. 5. The peaks of high intensity at 23.4, 26.4, 32.2, 125.1 and 135.2 ppm were attributed to poly-*cis*-1,4-isoprene. The peaks derived from the sulfide pendant produced by the addition of DD as shown in Structure B in Scheme 2 were detected at 127.0, 127.3, 129.1 and a region of 137–138 ppm. The other small peaks appearing at 16.0, 26.7, 40.1, 124.3 and 135.0 ppm were assigned to poly-*trans*-isoprene.<sup>16</sup> The vulcanizate before the devulcanization (s2) contained less than 2% of the *trans*-isomer, identified by solid  $^{13}\text{C}$  NMR. On the other hand, 7.1% *trans*-isomer was observed in the sol component (s6). It has been reported that *cis*-3-methylpent-2-ene was converted to the *trans*-isomer in 30% yield



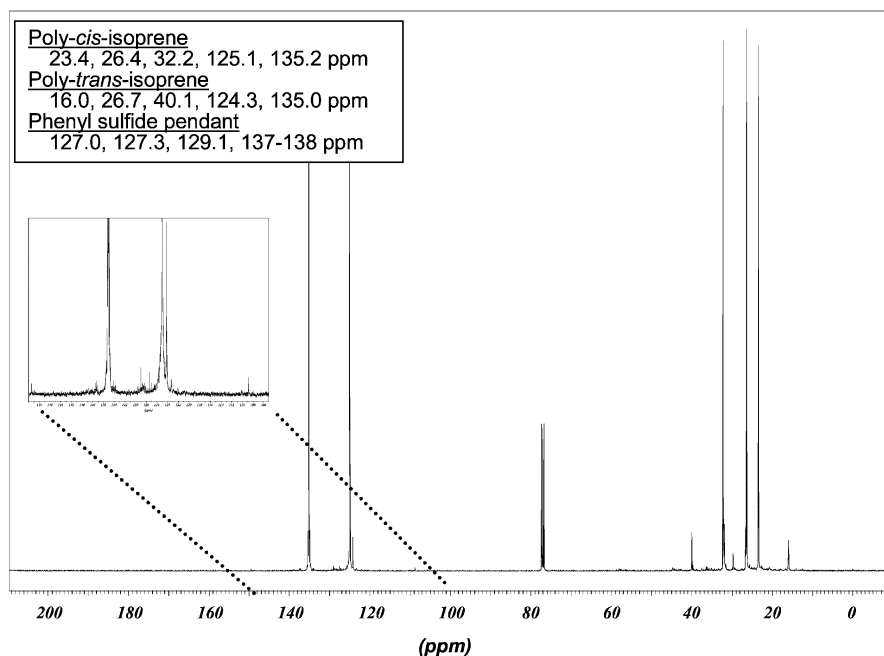


Fig. 5  $^{13}\text{C}$  NMR spectrum of the sol component obtained from sample A-30 devulcanized at 180 °C, 10 MPa for 60 min.

after treatment with DD at 140 °C for 6 hours.<sup>17</sup> In the same way, DD may have caused *cis*-to-*trans* isomerization in sulfur-cured NR during the present devulcanization.

The thermal properties of the sol component (s6) were analyzed by DSC and the results are shown in Fig. 6. The  $T_g$  of the sol

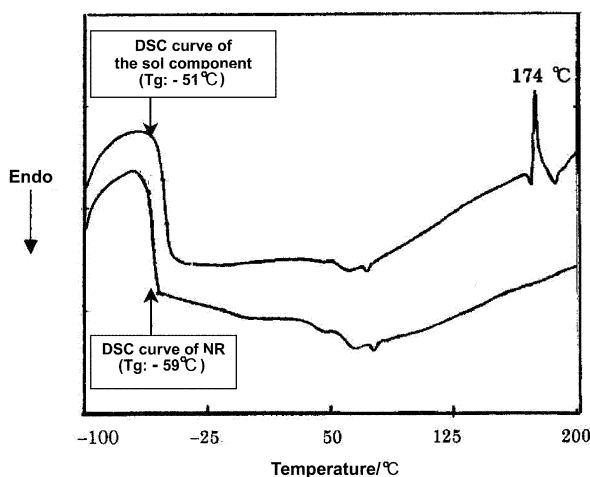


Fig. 6 DSC curves of NR and the sol component obtained from sample A-30 devulcanized at 180 °C, 10 MPa for 60 min.

component ( $-51$  °C) was at a slightly higher temperature than that of the raw NR ( $-59$  °C). It was reported that the  $T_g$  of poly-*trans*-isoprene ( $-69.8$  °C) is a little lower than that of the *cis*-isomer ( $-63.4$  °C).<sup>18</sup> The increase of  $T_g$  (8 °C) is, therefore, not ascribable to *cis*-*trans* isomerization during the devulcanization. It was supposed that the addition of DD onto polymer main chains during the devulcanization has resulted in a decrease of the molecular mobility, leading to the higher  $T_g$ . The adduction was observed by  $^{13}\text{C}$  NMR as aforementioned. A small peak observed at 174 °C was attributed to the exothermic cleavage reaction of residual sulfur-sulfur bonds.

#### Effect of the cure time and the vulcanization accelerator of the vulcanizate on the devulcanization

It is known that sulfur forms mono-, di-, and poly-sulfidic linkages as crosslinks in the vulcanizate as shown in Structure A in Scheme

2. The composition of these linkages in the vulcanizate is referred to as the “crosslink distribution”. The crosslink distribution in the vulcanizate can be controlled by the length of cure time and the kinds of vulcanization accelerator. Table 6 (for s5 and s6) shows the results indicating the effect of the cure time and the kinds of vulcanization accelerator of the vulcanizate on the devulcanization.

Table 6 Comparisons of sol fraction and crosslink density in the gel component obtained from the vulcanizate with different cure times and curatives

Sample	Sol fraction <sup>a</sup> (%)	Crosslink density in gel component $\times 10^7/\text{mol l}^{-1}$
A-30	50	0.0864 <sup>b</sup>
A-45	35	—
A-60	14	—
A-120	11	—
B-30	trace	0.785 <sup>c</sup>

<sup>a</sup> Soluble in chloroform. <sup>b</sup> Initial crosslink density is  $1.93 \times 10^7$  (mol l<sup>-1</sup>). <sup>c</sup> Initial crosslink density is  $1.48 \times 10^7$  (mol l<sup>-1</sup>).

The crosslink distributions as a function of cure time in sulfur-cured NR have been studied in several reports.<sup>19,20</sup> A longer cure time leads to less poly-sulfidic linkages in the vulcanizates. When samples prepared from compound A with different cure times were devulcanized under the optimum conditions, the sol fractions decreased with the increase of preceding cure time. It is presumed that this devulcanization tends to proceed more easily with the increase of poly-sulfidic linkages in the vulcanizate.

Sample B-30 was cured only with TMTD in order to prepare the vulcanizate with predominately mono-sulfidic linkages (corresponding to Structure A in the case of  $x = 1$  in Scheme 2).<sup>21,22</sup> This vulcanizate (B-30) was scarcely devulcanized to give little sol fraction under the optimum conditions. The NR vulcanizate with predominately mono-sulfidic linkages tends to resist the devulcanization.

The selectivity toward the crosslink distribution in the vulcanizate in the devulcanization proves that the scission occurs mainly at crosslinks, and partly at main chains. This tendency was also observed in the case of our investigation on the devulcanization of sulfur-cured IR using a combination of thiophenol and *n*-

butylamine as a devulcanizing reagent. Some devulcanizing reagents that can break the mono-sulfidic linkages in the vulcanizate are to be developed and are now under study.

## Conclusions

NR vulcanizates cured with shorter cure time were substantially devulcanized and converted into reusable materials using DD as a devulcanizing reagent in supercritical CO<sub>2</sub> at 180 °C, 10 MPa for 60 min. The devulcanized rubber showed a slightly higher  $T_g$  than that of raw NR. The obtained sol component has a main structure of poly-1,4-isoprene (including 7% *trans*-isomer).

## Acknowledgments

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## Solventless syntheses of pyrazole derivatives†

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Solventless condensation of a diketone and a hydrazine in the presence of a catalytic amount of sulfuric acid at room temperature afforded pyrazole derivatives **3a–3i** and **4g–4i** in high yields. The condensation of 2,4-pentanedione and hydrazides gave similar results, while the reaction between 1-phenylbutane-1,3-dione and hydrazides under the same conditions afforded 4,5-dihydro-5-hydroxypyrazole derivatives **6a** and **6b**, which can be transformed to **4i** (for **6b**) or a mixture of 1-acylpyrazole and **3i** (**4i**) (for **6a**) by thermolysis in the presence of a catalytic amount of sulfuric acid. Similar reaction of ethyl acetoacetate with phenylhydrazine or hydrazine formed 2-pyrazolin-5-one **8** and 3-pyrazolin-5-one **9**, respectively. Reactions of 2,4-dinitrophenylhydrazine with 2,4-pentanedione and ethyl acetoacetate yielded hydrazones **10** and **11**, respectively.

## Introduction

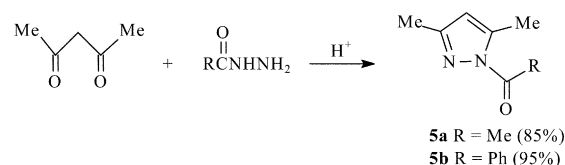
Pyrazole and its derivatives are shown to possess important biological and pharmaceutical activities<sup>1,2</sup> such as antimicrobial,<sup>3</sup> antiviral,<sup>4</sup> antitumor,<sup>5</sup> antiinflammatory,<sup>6</sup> antifungal<sup>7</sup> and antidepressant<sup>8</sup> activities. They are also useful intermediates for many industrial products.<sup>9,10</sup> A lot of syntheses of pyrazoles have been developed.<sup>11</sup> However, these syntheses are usually carried out in organic solvents. Recently, solventless organic reactions such as Michael additions,<sup>12</sup> aldol condensations,<sup>13</sup> Claisen condensation,<sup>14</sup> Stobbe condensation,<sup>15</sup> and Thorpe reaction<sup>16</sup> have been studied. Compared with the reactions in organic solvents, solventless reactions are often rapid, regio- or chemoselective, occur in high yields and have environmental and economic advantages.<sup>12</sup> For these reasons, we studied syntheses of pyrazole derivatives by the solventless reaction of 1,3-dicarbonyl compounds with hydrazines. Herein we report the results.

## Results and discussion

To an equivalent mixture of a diketone and a hydrazine in a mortar was added a drop of concentrated sulfuric acid. The mixture was ground at room temperature for 10 min. After leaving alone for 1 h, the mixture was washed with 10% Na<sub>2</sub>CO<sub>3</sub> solution and then water. The solid products were isolated by simple filtration. The liquid

products were obtained by extracting with diethyl ether. The yields are good to excellent (Table 1) and usually higher than those of the reactions carried out in organic solvents. In the case of the reaction between dipivaloylmethane (DPM) and PhNHNH<sub>2</sub>, the yield is relatively low (74%). This is ascribed to steric hindrance in DPM. When an unsymmetrical diketone was employed, two regioisomers were obtained (entries 7 and 8 in Table 1). The reaction of an unsymmetrical diketone with hydrazine hydrate gave single component (entry 6) or a mixture of tautomers (entry 9) depending on the diketones used.

Reaction of 2,4-pentanedione with hydrazides under the same conditions gave 1-acylpyrazole derivatives **5a** and **5b** (Scheme 1).



Scheme 1

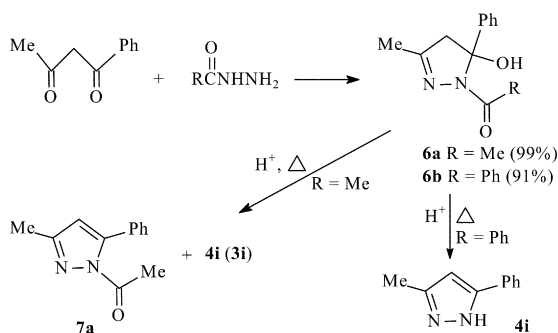
However, similar treatment of 1-phenylbutane-1,3-dione with the hydrazides afforded 4,5-dihydro-5-hydroxypyrazole derivatives **6a** and **6b** in excellent yields (Scheme 2). It is noteworthy that the condensation is highly regioselective.

This type of compounds have been reported in the literature and proved to be the intermediates of the condensation between 1,3-diketones and hydrazines.<sup>17,18</sup> We also found that both **6a** and

† Electronic supplementary information (ESI) available: analytical and spectroscopic data. See <http://www.rsc.org/suppdata/gc/b3/b312833d/>

Table 1 Condensation of a 1,3-diketone and a hydrazine

Entry	1		2	3a–3i		4g–4i	
	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Products (ratio)	Yield (%)	Mp/°C	
1	Me	Me	Ph	<b>3a</b>	86	Oil	
2	Me	Me	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	<b>3b</b>	86	Oil	
3	Me	Me	H	<b>3c</b>	96	107–109	
4	Bu <sup>t</sup>	Bu <sup>t</sup>	H	<b>3d</b>	92	191–193	
5	Bu <sup>t</sup>	Bu <sup>t</sup>	Ph	<b>3e</b>	74	106–108	
6	COOEt	Me	H	<b>3f</b>	90	80–82	
7	Me	COOEt	Ph	<b>3g+4g</b> (1 : 1)	91	Oil	
8	Me	Ph	Ph	<b>3h+4h</b> (1 : 13)	94	—	
9	Me	Ph	H	<b>3i+4i</b> (1 : 11)	96	—	



Scheme 2

**6b** could be dehydrated and deacylated thermally in the presence of a catalytic amount of sulfuric acid, the former giving a mixture of **7a** and **4i** (**3i**) and the latter giving **4i** (Scheme 2). Compounds **6a** and **6b** were identified by <sup>1</sup>H and <sup>13</sup>C NMR and IR spectroscopy, and the structure of **6a** was also determined by single crystal X-ray diffraction techniques (Fig. 1).<sup>‡</sup> The same structure has been reported in the literature.<sup>18c</sup>

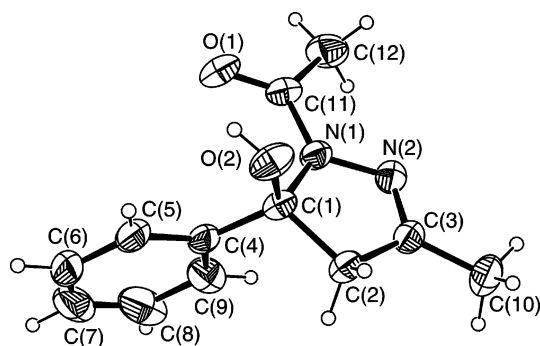


Fig. 1 ORTEP drawing of **6a**.

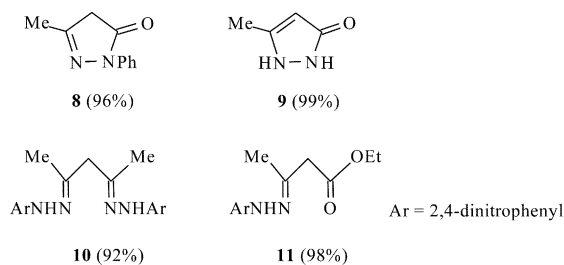
Ethyl acetoacetate reacted readily with phenylhydrazine or hydrazine hydrate under solventless conditions to form compounds **8** and **9**, respectively, in excellent yields. Each of compounds **8** and **9** exists in a keto-form identified by their respective NMR and IR spectra.<sup>19</sup> In addition, we also found that the reaction of 2,4-dinitrophenylhydrazine with 2,4-pentanedione afforded compound **10** and with ethyl acetoacetate afforded compound **11**. This is ascribed to lower reaction activity of 2,4-dinitrophenylhydrazine due to electron-withdrawing effect of the nitro groups.

## Conclusions

We report the reactions of hydrazines with 1,3-dicarbonyl compounds under solventless conditions. A range of pyrazole derivatives have been obtained in high yields. The reactions of hydrazides with 1,3-diketones were also studied and the products were dependent on the diketones used. The reaction with 2,4-pentanedione afforded 1-acylpyrazole derivatives, while the reaction with 1-phenylbutane-1,3-dione afforded 4,5-dihydro-5-hydroxypyra-

<sup>‡</sup> Crystal data for **6a**: C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>, *M* = 218.25, monoclinic, space group *C*2/*c*, *a* = 19.764(9), *b* = 8.877(4), *c* = 15.763(7) Å, β = 117.617(7)°, *V* = 2450.4(19) Å<sup>3</sup>, *F*(000) = 928, *Z* = 8, μ = 0.082 mm<sup>-1</sup>, 2529 independent reflections [*R*<sub>int</sub> = 0.0377] for 2.33 < θ < 26.50°, 1662 reflections with [*I* > 2σ(*I*)] and *R* indices: *R*1 = 0.0518, *wR*2 = 0.1276 [*I* > 2σ(*I*)] and *R*1 = 0.0844, *wR*2 = 0.1482 (all data).

Intensities were measured to θ<sub>max</sub> 26.50° on a Siemens CCD area-detector at 293(2) K with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The structure was solved by direct methods (SHELXS-97)<sup>20</sup> and refined against *F*<sup>2</sup> by full-matrix least-squares using SHELXL-97.<sup>21</sup> Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, CCDC reference number 222261. See <http://www.rsc.org/suppdata/gc/b3/b312833d/> for crystallographic data in .cif or other electronic format.



zole derivatives regioselectively. The reactions of 2,4-dinitrophenylhydrazine with 2,4-pentanedione or ethyl acetoacetate formed only hydrazones due to the electron-withdrawing effect of the nitro groups.

## Experimental

### General

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker av300 spectrometer and the chemical shifts are referenced to internal solvent resonances. IR spectra were recorded on a Bruker VECTOR-22 spectrometer. Elemental analyses were performed by the Analytical Centre of the University of Science and Technology of China. Melting points were uncorrected.

### Condensation of a dicarbonyl compound and a hydrazine

0.01 mol of 1,3-dicarbonyl compound and an equimolar amount of hydrazine were mixed in a mortar. To the mixture a drop of concentrated sulfuric acid was added. The mixture was ground for 10 min and left to stand for an hour. The solids or oil so obtained were washed successively with 10% of Na<sub>2</sub>CO<sub>3</sub> solution and water. The solid products were filtered and dried in air. The liquid products were extracted with Et<sub>2</sub>O. The extract was dried over MgSO<sub>4</sub> and the solvent removed under vacuum. The products so obtained were pure enough for most purposes as indicated by <sup>1</sup>H NMR spectra, but the samples for elemental analyses were recrystallised from appropriate solvents or purified by column chromatography.

**3a**: oil. Anal. Calc. for C<sub>11</sub>H<sub>12</sub>N<sub>2</sub>: C, 76.71, H, 7.02, N, 16.27. Found: C, 76.53, H, 7.13, N, 16.38%. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.20 (s, 3H, CH<sub>3</sub>), 2.21 (s, 3H, CH<sub>3</sub>), 5.90 (s, 1H, CH), 7.32–7.35 (m, 5H, Ph). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 12.17, 13.35, 106.82, 124.59, 127.05, 128.83, 139.20, 139.88, 148.75. IR (liquid film): ν(cm<sup>-1</sup>) 3062m, 2981m, 2959m, 2923m, 2866w, 1597vs, 1556vs, 1503vs, 1419vs, 1381vs, 1366vs, 1131m, 1072m, 1025s, 977m, 911m, 779vs, 755vs, 696vs, 678s, 661m, 640m.

**3b**: oil. Anal. Calc. for C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>: C, 77.38, H, 7.58, N, 15.04. Found: C, 77.12, H, 7.35, N, 14.97%. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.21 (s, 3H, CH<sub>3</sub>), 2.28 (s, 3H, CH<sub>3</sub>), 2.33 (s, 3H, CH<sub>3</sub>), 5.96 (s, 1H, CH), 7.17–7.24 (m, 4H, Ph). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 12.30, 13.24, 21.20, 106.91, 125.02, 129.82, 137.97, 140.33, 148.55. IR (liquid film): ν(cm<sup>-1</sup>) 3038w, 2981w, 2958w, 2922m, 2863w, 1613w, 1587w, 1555s, 1519vs, 1420s, 1383s, 1365m, 1261w, 1107m, 1039m, 1022m, 976w, 823s, 778m.

**3e**: mp 106–108 °C. Anal. Calc. for C<sub>17</sub>H<sub>24</sub>N<sub>2</sub>: C, 79.64, H, 9.44, N, 10.93. Found: C, 79.81, H, 9.39, N, 10.77%. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.16 (s, 9H, Bu<sup>t</sup>), 1.33 (s, 9H, Bu<sup>t</sup>), 6.01 (s, 1H, CH), 7.39–7.41 (m, 5H, Ph). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 30.75, 30.97, 32.01, 100.32, 128.61, 128.82, 129.15, 142.75, 153.20, 160.55. IR (KBr): ν(cm<sup>-1</sup>) 3051w, 2960vs, 2934m, 1598m, 1536s, 1501s, 1460m, 1364m, 1245m, 1203w, 1153m, 1111s, 1041s, 1007m, 791m, 772m, 753m, 696s, 621m.

**5a**: oil. Anal. Calc. for C<sub>7</sub>H<sub>10</sub>N<sub>2</sub>O: C, 60.85, H, 7.29, N, 20.27. Found: C, 61.02, H, 7.39, N, 20.09%. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.18 (s, 3H, CH<sub>3</sub>), 2.47 (s, 3H, CH<sub>3</sub>), 2.59 (s, 3H, CH<sub>3</sub>), 5.90 (s, 1H, CH), <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 13.53, 14.24, 23.22, 110.94, 143.71, 151.64, 171.18. IR (liquid film): ν(cm<sup>-1</sup>) 2987w, 2930w, 1732vs, 1583s, 1413s, 1379vs, 1335vs, 1275s, 1140w, 1084w, 1037w, 953s, 804m, 771w.

**5b**: mp 231–234 °C. Anal. Calc. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O: C, 71.98, H, 6.04, N, 13.99. Found: C, 71.71, H, 5.89, N, 13.87%. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.24 (s, 3H, CH<sub>3</sub>), 2.63 (s, 3H, CH<sub>3</sub>), 6.06 (s, 1H, CH), 7.43–7.56 (m, 3H, Ph), 7.98 (d, *J* = 7.4 Hz, 2H, Ph). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 13.94, 14.39, 111.18, 127.94, 131.47, 132.49, 133.52, 145.21, 152.21, 168.52. IR (KBr): ν(cm<sup>-1</sup>) 3056m, 2927s, 2857m, 1695vs, 1633w, 1603w, 1582m, 1526m, 1488w, 1448w, 1409w, 1375s, 1340vs, 1279w, 1151m, 1063s, 966w, 916m, 698m, 618m.

**6a**: mp 94–95 °C. Anal. Calc. for C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>: C, 66.04, H, 6.47, N, 12.84. Found: C, 65.97, H, 6.24, N, 13.01%. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.96 (s, 3H, CH<sub>3</sub>), 2.23 (s, 3H, CH<sub>3</sub>), 2.83 (d, *J* = 19.1 Hz, 1H, CH<sub>2</sub>), 3.19 (d, *J* = 18.9 Hz, 1H, CH<sub>2</sub>), 4.70–5.40 (b, 1H, OH), 7.19–7.28 (m, 5H, Ph). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 16.08, 22.32, 54.35, 93.43, 123.93, 128.03, 128.91, 143.84, 154.35, 170.35. IR (KBr): ν(cm<sup>-1</sup>) 3443b, 3068w, 3013s, 2924m, 2853w, 1651vs, 1449vs, 1418s, 1378s, 1351m, 1316s, 1258m, 1216s, 1167m, 1096m, 1071m, 1036m, 967w, 910w, 865w, 756vs, 700s, 666s.

**6b**: mp 118–119 °C. Anal. Calc. for C<sub>17</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>: C, 72.84, H, 5.75, N, 9.99. Found: C, 72.88, H, 5.66, N, 9.64%. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.99 (s, 3H, CH<sub>3</sub>), 2.91 (d, *J* = 18.5 Hz, 1H, CH<sub>2</sub>), 3.22 (d, *J* = 18.5 Hz, 1H, CH<sub>2</sub>), 5.36 (s, 1H, OH), 7.17–7.42 (m, 8H, Ph), 7.84–7.87 (m, 2H, Ph). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 16.32, 53.76, 94.67, 124.13, 127.93, 128.17, 128.85, 130.16, 131.71, 133.82, 143.80, 155.12, 168.28. IR (KBr): ν(cm<sup>-1</sup>) 3358vs, 3054w, 3024w, 2919w, 1620vs, 1574s, 1493w, 1452s, 1435s, 1376m, 1319s, 1287w, 1229m, 1187w, 1115w, 1072w, 1027w, 981w, 843m, 792w, 786m, 735m, 703s, 690m, 671w, 611m.

**10**: 92% yield based on 2,4-dinitrophenylhydrazine, mp 179–180 °C. Anal. Calc. for C<sub>17</sub>H<sub>16</sub>N<sub>8</sub>O<sub>8</sub>: C, 44.35, H, 3.50, N, 24.34%. Found: C, 44.28, H, 3.65, N, 23.97. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.17 (s, 6H, CH<sub>3</sub>), 3.57 (s, 2H, CH<sub>2</sub>), 7.93 (d, *J* = 9.5 Hz, 2H, Ar), 8.34 (dd, *J* = 9.5, 2.0 Hz, 2H, Ar), 9.14 (d, *J* = 2.0 Hz, 2H, Ar), 11.14 (s, 2H, NH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 16.27, 48.54, 116.58, 123.71, 129.86, 130.44, 138.25, 145.22, 153.07. IR (KBr): ν(cm<sup>-1</sup>) 3313s, 3102m, 2985m, 1615vs, 1591vs, 1539m, 1498s, 1422s, 1332vs, 1312vs, 1219m, 1133m, 1093s, 1061m, 924w, 829m, 742m, 726w, 669vw.

**11**: mp 88–90 °C. Anal. Calc. for C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>6</sub>: C, 46.45, H, 4.55, N, 18.06. Found: C, 46.36, H, 4.63, N, 17.99%. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.31 (t, *J* = 7.1 Hz, 3H, C<sub>2</sub>H<sub>5</sub>), 2.17 (s, 3H, CH<sub>3</sub>), 3.48 (s, 2H, CH<sub>2</sub>), 4.24 (q, *J* = 7.1 Hz, 2H, C<sub>2</sub>H<sub>5</sub>), 7.95 (d, *J* = 9.6 Hz, 1H, Ar), 8.31 (dd, *J* = 9.6, 2.3 Hz, 1H, Ar), 9.13 (d, *J* = 2.5 Hz, 1H, Ar), 11.09 (s, 1H, NH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.26, 16.21, 44.58, 61.48, 116.66, 123.37, 129.61, 130.05, 138.33, 145.10, 151.03, 169.27. IR (KBr): ν(cm<sup>-1</sup>) 3312m, 3105w, 2981w, 1727vs, 1620vs, 1596s, 1517s, 1425w, 1368m, 1341s, 1313s, 1287s, 1255m, 1207s, 1184m, 1136m, 1086m, 1059w, 1026w, 920w, 837w, 743w, 719vw, 655vw, 611w.

The other compounds prepared have been reported in the literature, and their analytical and spectroscopic data are provided as ESI.†

### Thermolyses of compounds 6a and 6b

0.51 g of **6a** was mixed with a drop of H<sub>2</sub>SO<sub>4</sub> and then the mixture was heated at 120 °C (bath temperature) for 4 h. The resultant substance was washed with 10% Na<sub>2</sub>CO<sub>3</sub> solution and then water.

The solid was filtered and dried in the air to give a mixture of **7a** and **3i** (**4i**) (0.31 g, 1 : 1 : 4.3 ratio based on its <sup>1</sup>H NMR spectrum).

Thermolysis of **6b** is similar. 0.50 g of **6b** was mixed with a drop of H<sub>2</sub>SO<sub>4</sub> and then the mixture was heated at 100 °C (bath temperature) for 4 h. After similar work up, compound **4i** (0.27 g, 96%) was obtained, mp 98–100 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.34 (s, 3H, CH<sub>3</sub>), 6.36 (s, 1H, CH), 7.32 (d, *J* = 7.1 Hz, 2H, Ph), 7.37 (t, *J* = 7.0 Hz, 2H, Ph), 7.71 (d, *J* = 7.1 Hz, 2H, Ph).

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# Comparison of the immobilization of chiral bis(oxazoline)–copper complexes onto anionic solids and in ionic liquids

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Chiral bis(oxazoline)–copper complexes can be easily immobilized onto anionic solids or in ionic liquids and used as catalysts in cyclopropanation reactions. The efficiency and recovery of the catalysts are strongly dependent on the stability of the complex. In the case of a highly stable bis(oxazoline)–copper complex, both solid supports and ionic liquids allow efficient recovery of the catalyst with results quite similar to those obtained in molecular solvents. However, ionic liquids are clearly better when the complex is not so stable. In this case, the nature of both the anion and cation, the presence of water and the method used to synthesize the ionic liquid have a noticeable influence on both catalytic performance and catalyst recovery. Enantioselectivity is also influenced by the ionic liquid/catalyst molar ratio.

## Introduction

Enantioselective reactions promoted by chiral catalysts constitute a field of great importance in organic synthesis.<sup>1</sup> A controversial point in this field is the choice between homogeneous and heterogeneous catalysis—a choice influenced by the advantages and disadvantages of the two systems. In the homogeneous phase the catalytic centers are usually well defined. This situation makes the interpretation and optimization of the results easier. Furthermore, all the catalytic centers are accessible to the reagents. However, from a practical point of view, separation of the homogeneous catalysts from the reaction products is often difficult and this reduces their applicability. In contrast, heterogeneous chiral catalysts are easily separated by filtration and, in some cases, can be reused. However, the activity of heterogeneous systems is frequently reduced due to diffusion limitations. In most cases chiral heterogeneous catalysts are obtained by immobilization of homogeneous systems and the effect of immobilization on the enantioselectivity is difficult to predict.<sup>2</sup>

Ionic liquids offer the possibility of combining the advantages of both homogeneous and heterogeneous catalysts. The reaction in the ionic liquid takes place in a homogeneous phase and the catalyst can be separated by extraction of the products with an immiscible solvent. Ionic liquids have proven useful in many reactions catalyzed by transition metal complexes and, in some cases, the catalyst can be recovered and reused.<sup>3</sup> Despite this promise, however, there are comparatively few examples concerning enantioselective catalysts. Most of the systems that have been described relate to hydrogenation<sup>4</sup> and oxidation<sup>5</sup> reactions. One paper is devoted to the enantioselective opening of epoxides with azides<sup>6</sup> and several others describe C–C bond forming reactions.<sup>7,8</sup> As stated above, the use of ionic liquids in enantioselective catalysis appears to be a viable alternative to immobilization onto insoluble supports and, as such, it is interesting to compare the scope and limitations of these two strategies.

In recent years we and others have studied the immobilization of bis(oxazoline)-based catalysts by covalent bonding to organic<sup>9,10</sup> and inorganic supports.<sup>10,11</sup> In most cases this type of immobilization modifies the catalytic performance and, in particular, the enantioselectivity. Modification of the chiral ligand with a large

substituent, formed by the linker plus the solid support, is considered to be responsible for this change in enantioselectivity.

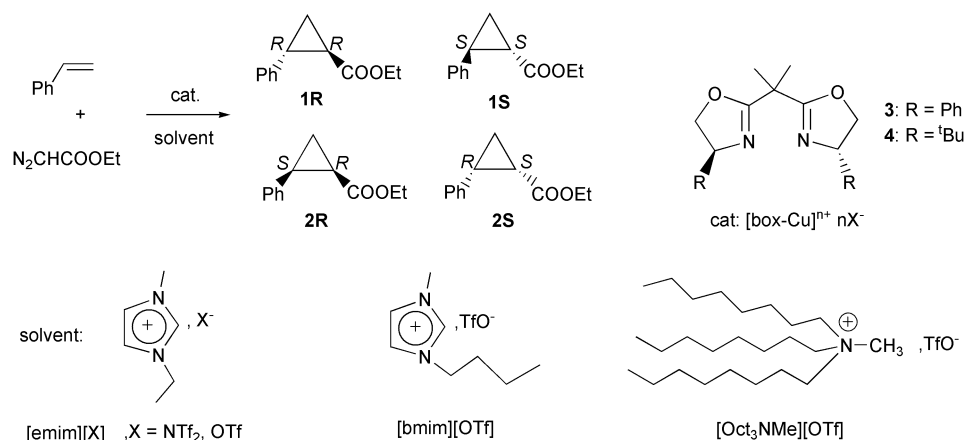
An alternative approach involves immobilization by ion-pairing of cationic bis(oxazoline)–metal complexes on anionic supports,<sup>12,13</sup> a change that does not require modification of the chiral ligand. In this regard, electrostatic immobilization is closely related to the use of ionic liquids as catalyst reservoirs. In this paper we compare both strategies in the enantioselective benchmark cyclopropanation reaction of styrene with ethyl diazoacetate promoted by bis(oxazoline)–copper complexes (Scheme 1), a reaction that has given excellent results in dichloromethane.<sup>14,15</sup>

## Results and discussion

### Comparison between homogeneous and heterogeneous methods

First of all, the results obtained with copper(II) complexes of 2,2'-isopropylidenebis[(4*S*)-4-phenyloxazoline] (**3**) under different conditions were compared (Table 1). In dichloromethane the nature of the copper counter-ion strongly influences the results of the cyclopropanation reaction. For example, the use of chloride (entry 2) leads to poor results both in terms of yield and selectivity. When the copper complex was exchanged on an anionic solid, the nature of the solid counter-ion was again important. In the case of the synthetic clay laponite, its lamellar structure leads to surface–complex interactions that modify the stereochemical course of the reaction. This effect is more significant in the *cis* cyclopropanes (**2**) (entry 3) and it is increased by the use of less polar reaction solvents.<sup>13</sup> Better results were obtained with SAC-13 (entry 5), a Nafion–silica nanocomposite with perfluoroalkylsulfonic acid groups. The results obtained with this support are comparable to those obtained with triflate in dichloromethane and, furthermore, only a very small amount of catalyst is employed, which can be recovered and reused (entry 6). Similar results were also obtained with the complex with copper(II) chloride in the ionic liquid [emim][NTf<sub>2</sub>] (entry 7), showing that chloride has been replaced by NTf<sub>2</sub> in the immediate environment of copper. This type of anion replacement has also been observed in other cases.<sup>16</sup> Reaction products were extracted with hexane and the catalyst remained in the ionic liquid phase, a situation that allows the catalyst to be





**Scheme 1** Cyclopropanation reaction between styrene and ethyl diazoacetate catalyzed by bis(oxazoline)-copper complexes in ionic liquids.

**Table 1** Results obtained from the cyclopropanation reaction between styrene and ethyl diazoacetate catalyzed by **3**-Cu(II) complexes.<sup>a</sup>

Entry	Counter-ion	Solvent	% catalyst	Run	Yield (%) <sup>b</sup>	<i>trans</i> : <i>cis</i> <sup>b</sup>	Ee (%) <sup>c</sup>	
							<i>trans</i> <sup>d</sup>	<i>cis</i> <sup>e</sup>
1	OTf	CH <sub>2</sub> Cl <sub>2</sub>	10	1	33	68 : 32	60	51
2	Cl	CH <sub>2</sub> Cl <sub>2</sub>	10	1	19	67 : 33	17	13
3	Laponite	CH <sub>2</sub> Cl <sub>2</sub>	0.9	1	30	62 : 38	49	24
4				2	28	58 : 42	43	19
5	SAC-13	CH <sub>2</sub> Cl <sub>2</sub>	0.3	1	27	66 : 34	57	46
6				2	27	66 : 34	56	45
7	Cl	[emim][NTf <sub>2</sub> ]	1	1	34	67 : 33	55	47
8				2	32	66 : 34	53	45
9				3	33	66 : 34	53	45

<sup>a</sup> Using equimolecular amounts of styrene and ethyl diazoacetate at room temperature. <sup>b</sup> Determined by GC. Total conversion of ethyl diazoacetate. <sup>c</sup> Determined by GC with a Cyclodex-B column. <sup>d</sup> *1R* is the major isomer. <sup>e</sup> *2R* is the major isomer.

reused with the same performance (entries 8–9). As can be seen, the use of an anionic solid support or an ionic liquid does not give rise to any clear difference in catalytic performance when bis(oxazoline) **3** is used as a ligand.

The use of 2,2'-isopropylidenebis[(4*S*)-4-*tert*-butyloxazoline] (**4**) as the chiral ligand leads to significant differences between the homogeneous reaction in dichloromethane, the use of heterogeneous catalysts and the reaction in an ionic liquid (Table 2). In dichloromethane the effect of the counter-ion is even more marked than in the case of bis(oxazoline) **3**. However, with catalysts immobilized onto anionic solids the results were worse than expected. In fact, the effect of the solid counter-ion does not show the same trend as observed for ligand **3**. Laponite (entry 3) leads to better enantioselectivities than Nafion-silica (entry 5), although in

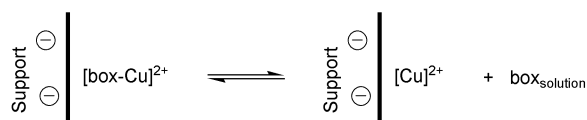
both cases the enantiomeric excesses are not comparable to those obtained in the homogeneous reaction. These selectivities are even lower upon recovery. The reason for this behavior is the existence of an equilibrium between free and complexed copper, which leads to the formation of non-chiral catalytic centers (Scheme 2). In fact, the addition of an excess of bis(oxazoline) **4** to the reaction mixture, with the subsequent shift to the complexed form, increases the enantioselectivities (entry 7) to values similar to those obtained in solution.

When the reaction was carried out in [emim][NTf<sub>2</sub>] (entry 8) the enantioselectivities obtained were not far from those obtained in dichloromethane. When one considers the difference between a solid anion and an ionic liquid, it can be speculated that steric interactions between the solid support and the chiral catalyst, which

**Table 2** Results obtained from the cyclopropanation reaction between styrene and ethyl diazoacetate catalyzed by **4**-Cu(II) complexes.<sup>a</sup>

Entry	Counter-ion	Solvent	% catalyst	Run	Yield (%) <sup>b</sup>	<i>trans</i> : <i>cis</i> <sup>b</sup>	Ee (%) <sup>c</sup>	
							<i>trans</i> <sup>d</sup>	<i>cis</i> <sup>e</sup>
1	OTf	CH <sub>2</sub> Cl <sub>2</sub>	10	1	72	71 : 29	94	91
2	Cl	CH <sub>2</sub> Cl <sub>2</sub>	10	1	24	70 : 30	2	7
3	Laponite	CH <sub>2</sub> Cl <sub>2</sub>	0.33	1	39	66 : 34	69	64
4				2	26	58 : 42	43	37
5	SAC-13	CH <sub>2</sub> Cl <sub>2</sub>	0.42	1	28	62 : 38	23	19
6				2	30	60 : 40	14	14
7	SAC-13	CH <sub>2</sub> Cl <sub>2</sub>	0.42 <sup>f</sup>	1	20	66 : 34	91	88
8	Cl	[emim][NTf <sub>2</sub> ]	1	1	50	62 : 38	86	85
9				2	42	60 : 40	55	56
10	Cl <sup>g</sup>	[emim][NTf <sub>2</sub> ]	1 <sup>h</sup>	1	35	63 : 37	80	77
11				2	35	63 : 37	65	63
12				3	42	62 : 38	44	44

<sup>a</sup> Using equimolecular amounts of styrene and ethyl diazoacetate at room temperature. <sup>b</sup> Determined by GC. Total conversion of ethyl diazoacetate. <sup>c</sup> Determined by GC with a Cyclodex-B column. <sup>d</sup> *1R* is the major isomer. <sup>e</sup> *2R* is the major isomer. <sup>f</sup> Addition of chiral bis(oxazoline) to the reaction medium. Bis(oxazoline)/copper = 10. <sup>g</sup> Copper(I) chloride. <sup>h</sup> Bis(oxazoline)/CuCl = 2.



**Scheme 2** Equilibrium between free and complexed copper on solid supports.

are not present in the ionic liquid, might favor a shift in the equilibrium to the non-complexed copper centers. Unfortunately, the catalyst dissolved in the ionic liquid does not perform as well after recovery (entry 9) as the freshly prepared material. In an attempt to improve the results, CuCl was used as the copper precursor on the basis that Cu(I) is the active species.<sup>17</sup> Furthermore, the possible equilibrium between free and complexed copper was prevented by the addition of a twofold excess of chiral ligand. Despite these changes a clear positive effect was not observed and only a slight improvement in the recovery of the catalyst resulted (entry 11).

### Parameters affecting the enantioselective cyclopropanation in ionic liquids

From the results described above it is clear that the role of the counter-ion is critical for the catalytic performance. On the other hand, ionic liquids allow the use of copper chloride as the precursor because this anion is exchanged by that of the ionic liquid. Taking into account that triflate is an excellent counter-ion in dichloromethane, we tested several ionic liquids containing this anion. Ligand **3** did not present any particular problem in terms of immobilization and so this study was focused on bis(oxazoline) **4** (Table 3), which contains the ligand that led to the best results in dichloromethane.

The first results in [emim][OTf] using both CuCl<sub>2</sub> and CuCl (entries 1 and 3) show lower enantioselectivities than those obtained with [emim][NTf<sub>2</sub>]. It is known that ionic liquids are quite hygroscopic and significant amounts of water can be present even in the most hydrophobic systems.<sup>18</sup> In cases where the amount of water present is comparable to or higher than the amount of ligand, it is feasible that water could replace the chiral ligand in the immediate copper environment and lead to non-chiral catalytic sites. When the ionic liquid was dried under vacuum in the presence of phosphorus pentoxide, the catalytic performance was clearly improved and the reaction gave higher yields and enantioselectivities (entry 5)—not far from those obtained in dichloromethane. Furthermore, catalyst recovery in [emim][OTf] (entries 6–8) is much more efficient than in [emim][NTf<sub>2</sub>]. In spite of this higher efficiency, enantioselectivities decay after the second recycle. One possible explanation is the gradual loss of bis(oxazoline) by extraction of the free ligand into the hexane phase. This process would be associated with a subsequent shift of the equilibrium to the free form of copper. The addition of a supplementary amount of bis(oxazoline) (0.5 equivalents with respect to copper) in the fifth run restores the enantioselectivities (entry 9) to the values obtained in the first run. This result, together with the influence of water, shows the importance of the binding constant of the copper complex.

The reactions take place with total conversion of ethyl diazoacetate and so chemical yield is indicative of the chemoselectivity between cyclopropanation and side reactions such as carbene dimerization, which leads to diethyl maleate and fumarate, and oligomerization of these side products. In an attempt to increase the chemoselectivity, an excess of styrene was used (entry 10). A slight increase in the yield was obtained but this was accompanied by significantly lower enantioselectivities and the catalyst proved

**Table 3** Results obtained from the cyclopropanation reaction between styrene and ethyl diazoacetate catalyzed by **4**-Cu complexes in ionic liquids.<sup>a</sup>

Entry	Copper precursor	Solvent	Run	Yield (%) <sup>b</sup>	<i>trans</i> : <i>cis</i> <sup>b</sup>	Ee (%) <sup>c</sup>	
						<i>trans</i> <sup>d</sup>	<i>cis</i> <sup>e</sup>
1	CuCl <sub>2</sub>	[emim][OTf]	1	24	71 : 29	46	40
2			2	12	68 : 32	15	12
3	CuCl	[emim][OTf]	1	24	69 : 31	28	22
4			2	18	69 : 31	20	17
5	CuCl	[emim][OTf] <sup>f</sup>	1	38	72 : 28	85	73
6			2	40	70 : 30	85	73
7			3	38	69 : 31	77	64
8			4	20	67 : 33	58	45
9			5 <sup>g</sup>	24	71 : 29	83	72
10	CuCl	[emim][OTf] <sup>f</sup>	1 <sup>h</sup>	45	70 : 30	74	64
11			2 <sup>h</sup>	27	65 : 35	5	5
12	CuCl	[emim][OTf] <sup>f,i</sup>	1	51	73 : 27	85	78
13			2	56	70 : 30	85	78
14			3	45	69 : 31	77	71
15			4	51	68 : 32	71	63
16			5	42	67 : 33	63	55
17			6 <sup>g</sup>	39	70 : 30	85	78
18	CuCl	[emim][OTf] <sup>f,i</sup>	1 <sup>k</sup>	32	70 : 30	85	79
19	CuCl	[bmim][OTf] <sup>f,i</sup>	1	38	70 : 30	79	71
20			2	37	70 : 30	79	71
21			3	40	68 : 32	69	60
22			4	43	67 : 33	64	55
23			5	43	67 : 33	61	52
24			6 <sup>g</sup>	38	70 : 30	86	79
25	CuCl	[bmim][OTf] <sup>f,i</sup>	1 <sup>k</sup>	33	70 : 30	76	67
26	CuCl	[Oct <sub>3</sub> NMe][OTf] <sup>f,i</sup>	1	15	70 : 30	64	54
27 <sup>l</sup>	CuCl	[emim][OTf] <sup>f,i</sup>	1	34	72 : 28	92	88
28 <sup>l</sup>			2	37	71 : 29	90	84
29 <sup>l</sup>			3	39	70 : 30	87	79

<sup>a</sup> Using equimolecular amounts of styrene and ethyl diazoacetate with 1% catalyst at room temperature. Concentration of catalyst in the ionic liquid:  $\approx$  76 mM. <sup>b</sup> Determined by GC. Total conversion of ethyl diazoacetate. <sup>c</sup> Determined by GC with a Cyclodex-B column. <sup>d</sup> 1*R* is the major isomer. <sup>e</sup> 2*R* is the major isomer. <sup>f</sup> Ionic liquid dried under vacuum in the presence of P<sub>2</sub>O<sub>5</sub>. <sup>g</sup> Addition of bis(oxazoline), 0.5 eq. with regard to copper. <sup>h</sup> Reactions carried out with 3 eq. of styrene. <sup>i</sup> Ionic liquid prepared by direct alkylation of *N*-butylimidazole and *N*-ethylimidazole with methyl triflate (see Experimental section). <sup>j</sup> Ionic liquid prepared by chloride exchange with Ba(OTf)<sub>2</sub> (see Experimental section). <sup>k</sup> Bis(oxazoline)/copper = 2. <sup>l</sup> Concentration of catalyst in the ionic liquid:  $\approx$  25 mM.

impossible to recycle (entry 11). The excess styrene may induce a phase segregation, with a proportion of the cyclopropanation taking place in each phase and a more efficient extraction of the chiral ligand into the hexane–styrene mixture.

Ionic liquids are difficult to purify and this factor represents another concern in this application. The ionic solvents used throughout this work were prepared by the exchange method from [emim][Br]<sup>8</sup> and this may lead to the possible presence of unreacted [emim][Br] or traces of NaBr. With the aim of preventing this problem, [emim][OTf] was prepared using an alternative method; namely the direct quaternization of ethylimidazole with methyl triflate. Although the enantioselectivities were not modified, the use of this solvent improves the chemical yield (entry 12) and the catalyst recovery (entries 13–17). A better comparison can be made by considering the turnover number (molecules of new product per catalytic center), which increases from 136 in four runs with the first solvent to 203 with that prepared using the new synthetic method. The decay in enantioselectivity after four runs is again due to the gradual extraction of the free chiral bis(oxazoline) to the hexane phase, as demonstrated by the recovery of the enantioselectivity level after the addition of ligand to the ionic liquid solution (entry 17).

Although a high enantioselectivity (85% ee) is obtained in [emim][OTf], the result is still slightly lower than that obtained in dichloromethane. This situation may be due to the effect of solvent on the complexation equilibrium, with the presence of free copper in solution from the outset of the reaction. In an attempt to prevent this problem the complex was prepared with a two-fold excess of chiral bis(oxazoline) (entry 18) in order to shift the equilibrium to the complexed form. These conditions are detrimental for the catalytic activity, with the decrease in chemical yield probably a consequence of the formation of a significant amount of unreactive 2 : 1 complexes. Furthermore, the enantioselectivity was not improved, showing that the lower enantioselectivity must be an effect of solvent properties such as polarity or solvophobicity.

The properties described above can be tuned by modification of the cation in the ionic liquid<sup>19</sup> and two more solvents were tested. The introduction of a longer aliphatic chain, such as a butyl group, on the imidazolium would reduce the polarity of the ionic liquid. The catalyst showed lower activity and selectivity in [bmim][OTf] (entries 19–24), although the recoverability was good and the enantioselectivity after addition of supplementary bis(oxazoline) was as good as in the case of [emim][OTf]. This result seems to indicate that the reduction in polarity shifts the equilibrium to the free form of copper. The reduction in activity and enantioselectivity was more pronounced in [Oct<sub>3</sub>NMe][OTf] (entry 26), thus confirming the effect of the polarity.<sup>20</sup>

As one of the referees suggested, the enantioselectivity may be also affected by the ionic liquid/copper salt molar ratio. Thus the best ionic liquid solvent, [emim][OTf], was used in a larger excess over the copper salt, leading to a 3-times lower catalyst concentration (entry 27). As can be seen, the enantioselectivity obtained under these new conditions is significantly better, 92% ee for the *trans* cyclopropanes, than that obtained with a more concentrated catalyst solution. The most plausible explanation would consider the equilibrium between the chloride and triflate forms of the chiral complex. As the chloride species is much less enantioselective,<sup>20</sup> the presence of a residual amount of this complex would lead to a decrease in the enantioselectivity. A higher amount of ionic liquid will shift the equilibrium to the more enantioselective triflate form, as happens in the experiment. However, we cannot ignore the presence of residual amounts of copper species free of chiral ligand, which might be responsible for this slight decrease in enantioselectivity. This amount would be modified by the concentration of the ionic liquid solution, the type of anion and even the type of bis(oxazoline) ligand. Also higher enantioselectivity is observed along the recycling experiments (entries 28–29), although the tendency of slow decrease of enantioselectivity detected in the more concentrated solution is again present. As pointed above, the

gradual loss of chiral ligand accounts for this behaviour, which would be made slower due to the larger amount of ionic liquid solvent.

## Conclusions

Ionic liquids and anionic solids can be used to obtain recoverable catalysts for reactions promoted by cationic chiral complexes. When the complex is very stable, catalyst recovery is efficient in both cases but solid catalysts have the advantage of easier handling. When the complex is not so stable, the equilibrium between the complexed and free form of the metal may lead to the presence of non-chiral sites, with the consequent reduction in enantioselectivity. In this case the use of ionic liquids is advantageous because it avoids steric interactions between the chiral ligand and the support, which may shift the equilibrium to the non-complexed form. In the case of the cyclopropanation reaction catalyzed by bis(oxazoline)–copper complexes in ionic liquids, several factors were found to play a crucial role. The nature of the anion is very important as it replaces chloride in copper complexation, and in this regard the ionic liquid/copper salt molar ratio influences the enantioselectivity. The solvent must be dried because the presence of water decreases both catalytic activity and enantioselectivity. The synthetic method used for the preparation of the ionic liquid is also important, probably due to a question of purity. Finally, the cation is responsible for the solvent polarity and better results are obtained with more polar solvents.

## Experimental

<sup>1</sup>H-, <sup>13</sup>C- and <sup>19</sup>F-NMR spectra were recorded at 300.13, 75 and 282 MHz respectively. High resolution mass spectra measurements were performed using a TOF instrument with EBE TOF geometry LSIMS (Liquid Secondary Ion Mass Spectrometry) at 8 kV with Cs<sup>+</sup> in *m*-nitrobenzyl alcohol (mNBA). Gas chromatography was carried out with He as carrier gas (20 psi); injector temperature: 230 °C; FID detector temperature: 250 °C. Columns: cross-linked methyl silicone (25 m × 0.2 mm × 0.33 μm) and Cyclodex B (30 m × 0.25 mm × 0.25 μm).

### Synthesis of ionic liquids

**1-Ethyl-3-methylimidazolium trifluoromethanesulfonate: [emim][TfO].** The entire process was carried out under argon. Freshly distilled methyl triflate (25.43 g, 0.155 mol) was added dropwise over 1 h to a vigorously stirred solution of 1-ethylimidazole (9.62 g, 0.10 mol) in acetonitrile (200 mL) at 0 °C. The mixture was stirred for 12 h at room temperature. The acetonitrile was evaporated and the ionic liquid was washed twice with diethyl ether (100 mL) and dried in a Kugelrohr for 1 h at 40 °C at a pressure of 0.1 mbar. The product [emim][OTf] (yield = 32.24 g, 92%) was obtained as a pale yellow mobile liquid. Anal. Calcd. for C<sub>7</sub>H<sub>11</sub>N<sub>2</sub>O<sub>3</sub>F<sub>3</sub>S: C, 32.31; H, 4.26; N, 10.76; O, 18.44; F, 21.90; S, 12.32. Found: C, 32.08; H, 4.37; N, 10.44; S, 12.04%. <sup>1</sup>H-NMR (Acetone-d<sub>6</sub>, δ/ppm relative to TMS): 1.56 (t, 3H, *J* = 7.4 Hz), 4.04 (s, 3H), 4.40 (q, 2H, *J* = 7.4 Hz), 7.71–7.79 (m, 2H), 9.09 (s, 1H). <sup>13</sup>C-NMR (Acetone-d<sub>6</sub>, δ/ppm relative to TMS): 14.68, 35.62, 44.71, 121.00 (q, *J*<sub>C-F</sub> = 318 Hz), 122.10, 123.72, 136.43. <sup>19</sup>F-NMR (Acetone-d<sub>6</sub>, δ/ppm relative to CFCl<sub>3</sub>): –79.58.

**1-Butyl-3-methylimidazolium trifluoromethanesulfonate: [bmim][TfO].** The same procedure as for [emim][TfO] was used starting with methyl triflate (25.43 g, 0.155 mol) and redistilled 1-butylimidazole (18.63 g, 0.150 mol). The product [bmim][TfO] (42.74 g, 97%) was obtained as a clear pale-yellow mobile liquid. Anal. Calcd. for C<sub>9</sub>H<sub>15</sub>N<sub>2</sub>O<sub>3</sub>F<sub>3</sub>S: C, 37.50; H, 5.24; N, 9.72; O, 16.65; F, 19.77; S, 11.12. Found: C, 37.94; H, 5.13; N, 9.92; S, 10.94%. HRMS (FAB) calcd. for C<sub>17</sub>H<sub>30</sub>N<sub>4</sub>O<sub>3</sub>F<sub>3</sub>S, [2C<sup>+</sup>, TfO<sup>-</sup>]: 427.1990. Found: 427.2010. <sup>1</sup>H-NMR (Acetone-d<sub>6</sub>, δ/ppm relative to TMS): 0.94 (t, 3H, *J* = 7.3 Hz), 1.32–1.42 (m, 2H),

1.87–1.97 (m, 2H), 4.05 (s, 3H), 4.36 (t, 2H,  $J = 7.2$  Hz), 7.72–7.79 (m, 2H), 9.12 (s, 1H).  $^{13}\text{C}$  (Acetone- $d_6$ ,  $\delta$ /ppm relative to TMS): 12.87, 19.05, 31.80, 35.65, 49.19, 121.13 (q,  $J_{\text{C-F}} = 318.7$ ), 122.48, 123.73, 136.74.  $^{19}\text{F}$ -NMR (Acetone- $d_6$ ,  $\delta$ /ppm relative to  $\text{CFCl}_3$ ): –79.53.

**Methyltrioctylammonium trifluoromethanesulfonate: [Oct<sub>3</sub>NMe][TfO].** A solution of Aliquat 336 (4.04 g, 10 mmol) in H<sub>2</sub>O (50 mL) and a solution of Ba(TfO)<sub>2</sub> (5.22 g, 12 mmol) in H<sub>2</sub>O (50 mL) were mixed with stirring at RT. After 2 h, CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was added and the aqueous solution was washed with CH<sub>2</sub>Cl<sub>2</sub> (2 × 30 mL). The organic layers were combined and evaporated. The liquid salt was dried for 4 h at 100 °C at a pressure of 0.05 mmHg to afford [Oct<sub>3</sub>NMe][TfO] (4.76 g, 92%) as a pale yellow liquid. Chloride was not detected either by the silver nitrate test or HRMS. HRMS (FAB) calcd. for C<sub>51</sub>H<sub>102</sub>NO<sub>3</sub>F<sub>3</sub>S, [2C<sup>+</sup>, TfO<sup>-</sup>]<sup>+</sup>: 922.7484, Found: 922.7469.  $^1\text{H}$ -NMR (Acetone- $d_6$ ,  $\delta$ /ppm relative to TMS): 0.88 (t, 9H,  $J = 6.7$  Hz), 1.25–1.55 (m, 36H), 1.89 (br s, 6H), 3.25 (s, 3H), 3.44–3.55 (m, 6H).  $^{13}\text{C}$  (Acetone- $d_6$ ,  $\delta$ /ppm relative to TMS): 14.08, 22.32, 22.89, 26.50, 32.06, 32.18, 54.18, 61.71, 121.46 (q,  $J_{\text{C-F}} = 319.5$  Hz), 122.48.  $^{19}\text{F}$ -NMR (Acetone- $d_6$ ,  $\delta$ /ppm relative to  $\text{CFCl}_3$ ): –79.37.

### Preparation of heterogeneous catalysts

Nafion SAC-13 and Laponite were obtained from DuPont Research & Development and Rockwood Additives Limited respectively.

**Preparation of laponite-exchanged catalysts.** To a solution of the bis(oxazoline) (1 mmol) in methanol (20 mL), was added 1 mmol of Cu(OTf)<sub>2</sub>. Laponite (1 g) was slowly added to the above blue solution and the suspension was stirred at room temperature for 24 h. The solid was filtered off, thoroughly washed with methanol and then with dichloromethane, and dried under air before use.

**Preparation of Nafion SAC-13 exchanged catalysts.** Before exchange with the chiral catalyst Nafion SAC-13 was transformed into its sodium form by passing a solution of NaCl 2 M through a column of the solid until neutral pH was obtained. The solid was then washed with deionised water and dried under vacuum at 150 °C for 4 h. To a solution of the bis(oxazoline) (2 mmol) in methanol (20 mL) was added 2 mmol of Cu(OTf)<sub>2</sub>. To this blue solution was added the sodium form of the support (3 g) and the suspension was stirred at room temperature for 24 h. The solid was filtered off, thoroughly washed with methanol and then with dichloromethane. Before use the catalyst was dried under vacuum and ground in a mortar.

### Cyclopropanation reactions

**Reactions in ionic liquids.** The complexes were prepared *in situ* by dissolving the appropriate copper salt (0.038 mmol) and the ligand (0.038 mmol) in the ionic liquid (0.5 mL). The mixture was stirred at room temperature until a clear pale green solution was obtained. To this solution, under an Ar atmosphere, was added styrene (395 mg, 3.8 mmol). In some cases a clear solution was obtained only after the addition of styrene. Ethyl diazoacetate (433 mg, 3.8 mmol) was slowly added (2 h) using a syringe pump. The reaction mixture was stirred at room temperature for 20 h. After this time the products were extracted with hexane (3 × 4 mL) and *n*-decane (100 mg) was added to the hexane solution as an internal standard for the GC analysis. The remaining solution of the catalyst in the ionic liquid was reused following the same method.

In the last three entries of Table 3 the amounts were: 0.019 mmol copper salt and ligand, 0.75 mL ionic liquid, 1.9 mmol styrene and ethyl diazoacetate.

**Reactions with solid catalysts.** To a suspension of the corresponding supported catalyst (150 mg of laponite catalyst or

300 mg of SAC-13 catalyst) in a solution of styrene (5 mmol) and *n*-decane (100 mg) in dichloromethane (5 mL), was added ethyl diazoacetate (2.5 mmol) in the same solvent (0.5 mL), under an argon atmosphere, during 2 h using a syringe pump. The reaction was monitored by gas chromatography, and after consumption of the diazoacetate, a second portion of this reagent was added in the same way. After the reaction the catalyst was filtered off, washed with dichloromethane and dried. The recovered catalysts were reused following the same method.

**Determination of the reaction results.** Yield and *trans/cis* selectivity: methyl silicone column, oven temperature program: 70 °C (3 min), 15 °C min<sup>-1</sup> to 200 °C (5 min); retention times: ethyl diazoacetate 4.28 min, styrene 5.03 min, *n*-decane 6.93 min, *cis*-cyclopropanes (**2**) 11.84 min, *trans*-cyclopropanes (**1**) 12.35 min. Asymmetric inductions: Cyclodex B column, oven temperature program: 125 °C isotherm; retention times: (1*S*,2*R*)-cyclopropane (2*S*) 28.9 min, (1*R*,2*S*)-cyclopropane (2*R*) 29.8 min, (1*R*,2*R*)-cyclopropane (1*R*) 34.3 min, (1*S*,2*S*)-cyclopropane (1*S*) 34.9 min.

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# Emulsifier-free ultrasonic emulsion copolymerization of styrene with acrylic acid in water

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A copolymer of styrene with acrylic acid (Poly(St-co-AA)) was directly synthesized by random emulsion copolymerization under ultrasonic irradiation without any volatile organic solvent (VOC) and emulsifier being used. Only water was used as solvent. The copolymer has been characterized by FT-IR spectra and H-NMR; its characteristic viscosity has been used to measure its average molecular weight. Our results show that high monomer conversion and short induction period were achieved. The effects of ultrasonic power and time on the average molecular weight and monomer conversion are discussed. The self-assembly behavior of the copolymer into regular pattern structures was imaged by atomic force microscopy (AFM).

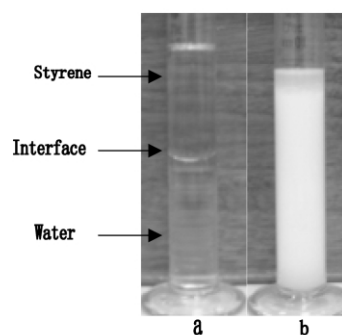
## Introduction

Finding alternative solvents is one of the important area in green chemistry. Water is a typical green solvent that has been used recently in organic synthesis.<sup>1</sup> It is also widely used as the hydrophilic phase in emulsion reactions with an organic phase. To stabilize the emulsion, emulsifier is usually required. For example, in emulsion copolymerization of styrene with methyl acrylate (MA), an aqueous solution of the surfactant SDS aqueous is used as emulsifier. Under strong stirring conditions an emulsion is formed, then the reaction is initiated and the copolymer formed.<sup>2</sup> Since surfactants are usually low molar mass molecules, they present some drawbacks, such as their high mobility. This makes them migrate to the interface with solid substrates, which can lead to a poor adhesion of the water-bone coating on artificial bone implants. Moreover, when used in large concentration during the emulsion polymerization, they result in a broad particle size distribution.<sup>3</sup> To overcome these drawbacks, a reactive surfactant or polymer surfactants have been proposed.<sup>4,5</sup> Is it possible to carry out emulsion polymerization free of surfactants?

Ultrasound assisted chemical reaction is a potential method for this purpose, which may also provide a potential green chemistry method.<sup>6</sup> Due to the extreme environment created by ultrasonic cavitation, *i.e.* extremely high local temperature and pressure, as well as heating and cooling rates for chemical reaction, radicals can easily be generated from decomposition of initiator, monomer, or rupture of polymer chains; these radicals can further initiate chemical reaction, *e.g.*, polymerization of monomer. Additionally the motion caused by ultrasonic irradiation of fluid around the bubbles results in a very efficient mixing of water and oil phases. It is the so-called ultrasonic emulsification effect that makes the organic phase easily form an emulsion with water free of surfactant.<sup>7</sup> It is reported that such emulsions are stable for a long period of time and do not separate for days or even months.<sup>8</sup> Fig. 1 shows a mixture of benzene with water before and after ultrasonic irradiation after 10 s at 300 W. It clearly shows that an efficient emulsion is formed.

A copolymer of styrene with acrylic acid (poly(St-co-AA)) has been attracting much attention for its potential application as a macromolecular surfactant, dispersant in ink, and support for polymer complex catalysts *etc.*<sup>9</sup> However, there are no reports on the direct copolymerization of styrene with acrylic acid. Usually, a copolymer of styrene with acrylate is prepared, and then hydrolysis of the acrylate into acrylic acid is performed.<sup>3,10</sup>

In this paper, the aqueous copolymerization of styrene with acrylic acid was directly carried out free of emulsifier with ultrasonic assisted emulsification.



**Fig. 1** Photograph of mixture of benzene with water in a 1:1 ratio. (a) Typical phase separation is observed. (b) Emulsion formed after ultrasonic irradiation 10 s at a power of  $0.166 \text{ W cm}^{-3}$ .

FT-IR and proton nuclear magnetic resonance ( $^1\text{H NMR}$ ) spectroscopy were used to determine its composition and structure. Moreover, the change of molecular weight with experimental factors such as time and ultrasonic power is described by characteristic viscosity curve. Atomic force microscopy (AFM) is used to study the phase separation occurring in copolymers on the surface of a solid substrate.

## Experimental

### General

Styrene and acrylic acid used in the experiment (Shanghai Chemical Reagents Company, CP) were purified by reduced pressure distillation. AIBN (Shanghai Chemical Reagents Company, CP) as initiator was purified by recrystallization from alcohol. Dimethyl sulfoxide- $d_6$  was used as solvent for NMR (Beijing Chemical Industry Factory),  $\text{NH}_3\text{-H}_2\text{O}$  (ammonia, 30%), and tetrahydrofuran (THF, purified) were used.

A 20 KHz ultrasonic generator with power output range from 1 W to 650 W dial reading (JY92-2D, Xinzhi) with a titanium horn (tapered,  $\phi$  6 mm) was used. The actual acoustic energy entering the reaction was measured with a calorimeter. The temperature of the reactor was controlled by a water bath surrounding the reaction vessel.

### Ultrasonic emulsion copolymerization

A mixture of purified styrene, acrylic acid and distilled water in proportions of 1 : 1 : 2 was added into a vessel. Then the initiator AIBN was added at a concentration of  $0.016 \text{ g ml}^{-1}$ . The water-bath temperature was kept at  $50^\circ\text{C}$  and the ultrasonic output power



was adjusted from  $0.082 \text{ W cm}^{-3}$  to  $0.263 \text{ W cm}^{-3}$ . After copolymerization a white viscous liquid was obtained. Then it was washed with toluene in order to remove styrene homopolymer and monomer, and dried. Residual acrylic acid monomer was removed with distilled water, and the product was then dried under vacuum again. Finally the products were obtained.

### Copolymer characterization

FT-IR spectra were recorded by using a Bruker spectrometer (KBr). A  $^1\text{H}$  NMR spectrometer (Bruker company, 300 MHz) was used to study the polymer structure with  $\text{DMSO-d}_6$  as solvent. The characteristic viscosity was obtained using an Ubbelohde viscometer.

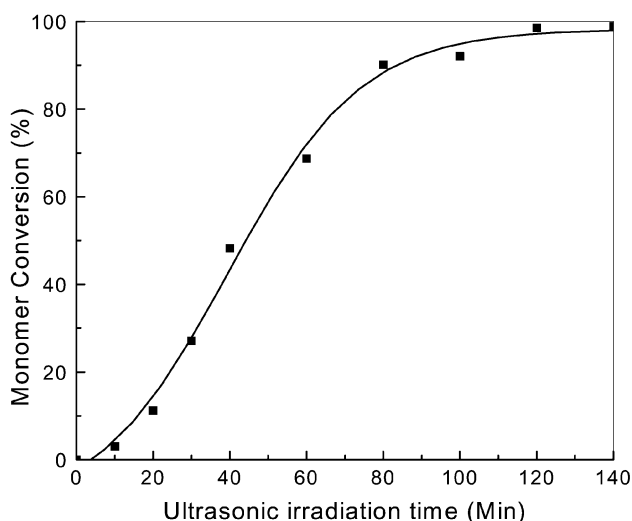
### Sample prepared for AFM measurement

Thin copolymer films were solvated in THF or ammonia respectively, and then a droplet (20  $\mu\text{l}$ ) of them was deposited onto newly cleaved mica. After spin coating at a speed of 1300 rpm for 8 s and then 4000 rpm for 30 s, dried films were formed. Topographic images of the copolymer film on mica were measured by atomic force microscopy (AFM, Nanoscope IIIa, D.I.) in tapping mode with silicon TESP cantilevers.

## Results and discussion

FT-IR spectroscopy and  $^1\text{H}$  NMR were used to characterize the structure of the copolymer. The characteristic absorption bands for  $-\text{OH}$  and  $\text{C}=\text{O}$  bonds of acrylic acid units appear at 3432, 1702  $\text{cm}^{-1}$ , respectively, and those for the aromatic ring of the styrene units appear at 1601, 1493, and 1453  $\text{cm}^{-1}$  respectively.  $^1\text{H}$  NMR shows that the signal at about 12 ppm corresponding to the acrylic acid group, and the peaks at 7.2 ppm and 6.7 ppm can be assigned to the aromatic protons in the styrene. According to the integral area of the characteristic chemical shift, the mole ratio of styrene to acrylic acid is 2.141 : 1.<sup>11</sup>

Fig. 2 shows the effect of ultrasonic time on copolymer yield when the power is fixed at  $0.121 \text{ W cm}^{-3}$ , reaction temperature is  $50^\circ\text{C}$ , and at an initiator AIBN concentration of  $0.016 \text{ g ml}^{-1}$ . Obviously there is a sharp increase of the reaction rate at around 30 min, and the induction time is about 10 min, which is shorter than that of conventional experimental methods. In the early stages, the reaction rate was slow because of an induction period.<sup>12</sup> With better distribution of initiator and monomers in efficient microscopic mixing facilitated by ultrasound<sup>13</sup> and self-emulsification effect of the amphiphilic copolymer the reaction rate increases, and when the reaction time is 100 min, over 90% of monomer is converted. After



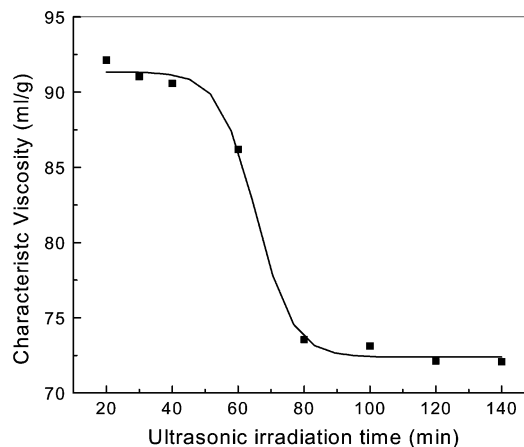
**Fig. 2** Relationship of ultrasonic irradiation time and monomer conversion rate at fixed the reaction condition as St : AA : Water = 1 : 1 : 2, ultrasonic output power of  $0.121 \text{ W cm}^{-3}$ , reaction temperature  $50^\circ\text{C}$ , and initiator AIBN concentration of  $0.016 \text{ g ml}^{-1}$ .

80 min, the reaction rate gradually decreases according to the emulsion polymerization rate equation<sup>14,15</sup> due to the decrease in concentration of monomers and initiator [eqn. (1)].

$$R_p = K_p N C_m n / N_A \quad (1)$$

where  $K_p$  is the propagation rate coefficient,  $N$  is the number of particles,  $C_m$  is the monomer concentration in the particles,  $n$  is the average number of radicals per particle, and  $N_A$  is Avogadro's constant.

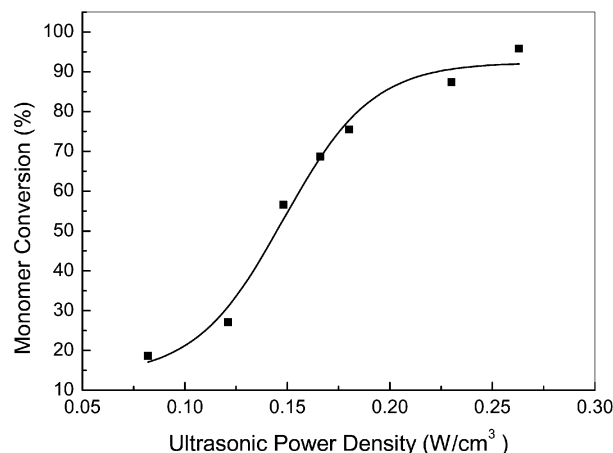
The characteristic viscosity was recorded with THF as solvent, and it gives information of the polymer's average molecular weight. Fig. 3 shows the plot of the characteristic viscosity *versus*



**Fig. 3** Relationship of ultrasonic irradiation time and the characteristic viscosity of copolymer at fixed reaction conditions: St : AA : Water = 1 : 1 : 2, ultrasonic output power of  $0.121 \text{ W cm}^{-3}$ , reaction temperature  $50^\circ\text{C}$ , and initiator AIBN concentration of  $0.016 \text{ g ml}^{-1}$ .

the sonication time with power of  $0.121 \text{ W cm}^{-3}$ , reaction temperature  $50^\circ\text{C}$ , and with the initiator AIBN concentration  $0.016 \text{ g ml}^{-1}$ . With the reaction time increasing, the characteristic viscosity (or average molecular weight) of the copolymer decreases<sup>16</sup> and the curve is nearly steady after 80 min. The possible reason may be the growth and explosive collapse of microscopic bubbles as the sound wave propagates through the mixing liquid; the motion of the fluid around the bubbles rapidly results in effective shear degradation of polymer chains in the vicinity of the cavitation bubbles<sup>17</sup> as long as the molecular weight of polymer exceeds a certain value. So at the last stage of the reaction, the degradation of polymer chains is not obvious and the polymer has a certain average molecular weight.

Fig. 4 shows the plot of monomer conversion rate *versus* ultrasonic power with reaction temperature  $50^\circ\text{C}$ , the initiator

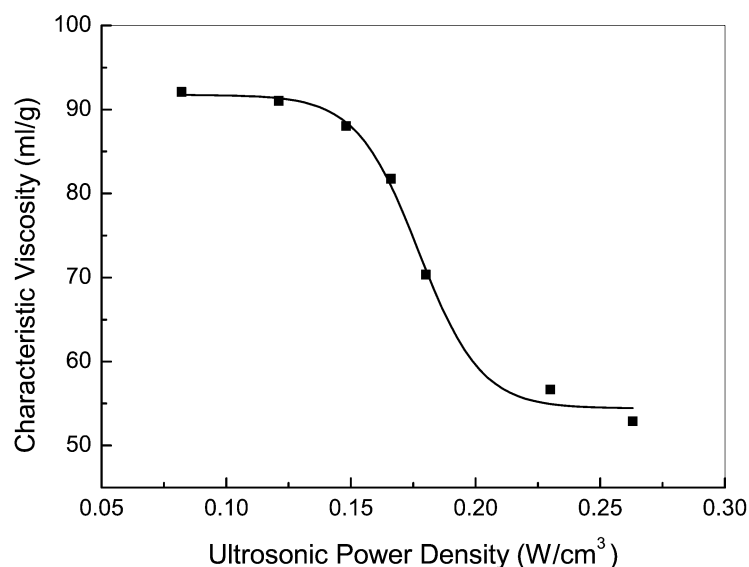


**Fig. 4** Effect of ultrasonic power on the monomer conversion rate at fixed reaction conditions: St : AA : Water = 1 : 1 : 2, reaction time of 30 min, reaction temperature  $50^\circ\text{C}$ , and initiator AIBN concentration of  $0.016 \text{ g ml}^{-1}$ .

concentration  $0.016 \text{ g ml}^{-1}$  and reaction time 30 min. The curve can also indicate the change in reaction rate. It is found that the monomer conversion rate grows with the increase of ultrasonic power under the same reaction conditions. In other words, the ultrasonic power can enhance the reaction rate of the copolymerization. The possible main reason might be that the larger the ultrasonic output power is, the larger the number of microbubbles forming, growing and collapsing in a very short time.<sup>17</sup> Then many radicals start the polymerization reaction, which can be generated due to decomposition of the chemical initiator or the solvent or rupture of polymer chains.<sup>18</sup> So an increase in output power can accelerate the copolymerization reaction. Comparing Fig. 4 to Fig. 2 it can be seen that 90% conversion rate is achieved at 30 min for  $0.23 \text{ W cm}^{-3}$  and 100 min for  $0.121 \text{ W cm}^{-3}$ , indicating that higher power results in quicker reaction rate.

Fig. 5 shows the effect of ultrasonic power on characteristic viscosity. It also shows a decrease of characteristic viscosity with increasing ultrasonic power, which is similar to Fig. 3. The degradation of polymer chains under high ultrasonic power is greater than that under lower ultrasonic power. When the ultrasonic output power increases, the more rapid motion can result in effective shear degradation of polymer chains in the vicinity of cavitation bubbles, and so the decomposition of the polymer chains is more vigorous. As expected, with the increase of power output, the molecular weight of copolymer decreases.

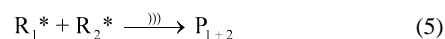
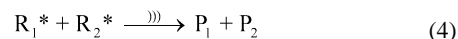
In order to understand the polymerization mechanism, a series of experiments were carried out with three different systems (styrene and acrylic acid without solvent, styrene and acrylic acid with water as solvent, styrene and acrylic acid plus water and AIBN) as shown in Table 1. For pure styrene and acrylic acid the conversion rate is about 9%, suggesting that radicals can come from the ultrasonic irradiation of monomers. For the monomers plus water system (the ratio of volume of styrene, acrylic acid and water is 3 : 3 : 6), the conversion rate is only 3%, indicating that the radicals do not efficiently initiate chain propagation, and radical termination happens easily in aqueous solution. However, after adding the initiator AIBN (concentration:  $0.016 \text{ g ml}^{-1}$ ) into the emulsion, the initiation rate increases significantly, and the conversion rate can reach up 27%. Based on all the results, the initiation mechanism of ultrasonically initiated emulsion polymerization copolymerization could be proposed as follows:



**Fig. 5** Effect of ultrasonic power on the characteristic viscosity of copolymer at fixed reaction conditions: St : AA : Water = 1 : 1 : 2, reaction time of 30 min, reaction temperature at  $50 \text{ }^\circ\text{C}$ , and initiator AIBN concentration of  $0.016 \text{ g ml}^{-1}$ .

**Table 1** Ultrasonic assistant copolymerization of styrene with acrylic acid in different system

Polymerization system	Reaction conditions	Conversion (%)
St + AA (1 : 1)	$50 \text{ }^\circ\text{C}$ , 30 min	> 9%
St + AA + water (1 : 1 : 2)	$50 \text{ }^\circ\text{C}$ , 30 min	< 3
St + AA + water (1 : 1 : 2)	$50 \text{ }^\circ\text{C}$ , 30 min, AIBN	> 27%

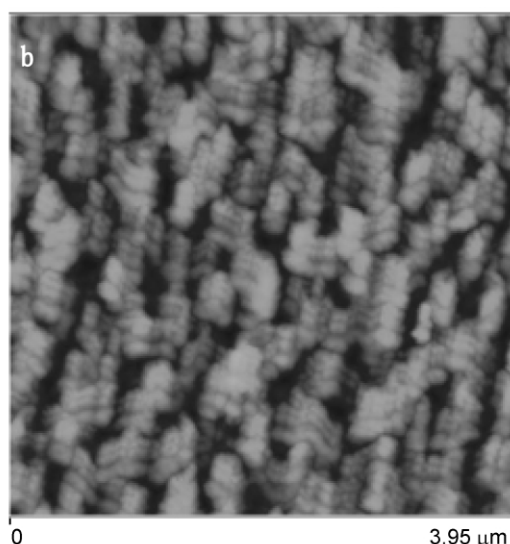
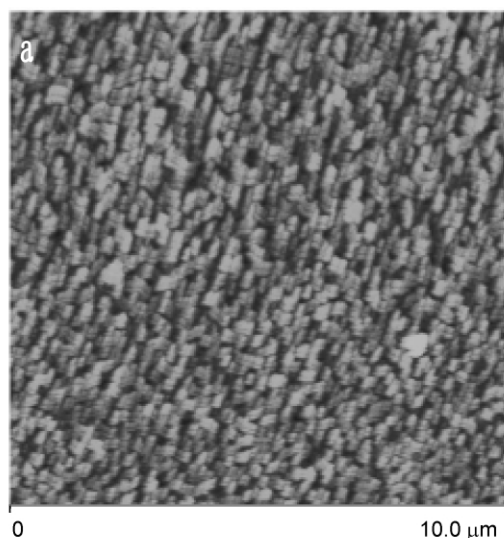


where AA and St are monomers,  $\text{R}_i^*$  is the radical species, and  $\text{P}_i$  is the polymer chain.

Although radicals can be generated from the excitation of monomers because of the ultrasonic extreme conditions with high temperature and pressure, obviously it is not the decisive factor that initiates polymerization. The thermolysis of the initiator AIBN is the main reason for copolymerization.

In addition, because AIBN is easily dissolved in the styrene, styrene was first initiated and polymerized, and then acrylic acid was initiated at the interface of the emulsion. This causes the styrene content to be higher than acrylic acid, which is consistent with the NMR result.

Both Fig. 6 and 7 show AFM topographic images of the product copolymer film on the surface of mica. The copolymer ( $0.263 \text{ W cm}^{-3}$ , 30 min,  $50 \text{ }^\circ\text{C}$ , AIBN) was solvated in ammonia ( $9.14 \text{ mg ml}^{-1}$ ) and THF ( $8.58 \text{ mg ml}^{-1}$ ), respectively. Then  $20 \text{ } \mu\text{l}$  of the solution was deposited onto the surface of newly cleaved mica, and after being spin-coated the samples were dried before AFM measurements. The solvent used to prepare the copolymer films has a strong influence on the morphology of the film. For the film prepared from ammonia solution it shows obvious hydrophilic behavior, while the film prepared from THF solution displays some hydrophobic properties. The solubility of the constituent units is different in ammonia and THF, which leads to different microstructure formation in the solutions and subsequently affects the self-assembly in the film. For ammonia, the weak alkalinity damages the stronger H-bond interaction among the carboxylic acid groups that connect different copolymer chains to form large aggregates, so the particles of copolymer in solution should be small. Furthermore the hydrophilic environment led to the copolymer forming a core-shell structure with polystyrene as the core and poly(acrylic acid) as the shell. However, for THF, the environment is more hydrophobic than ammonia, which can extend

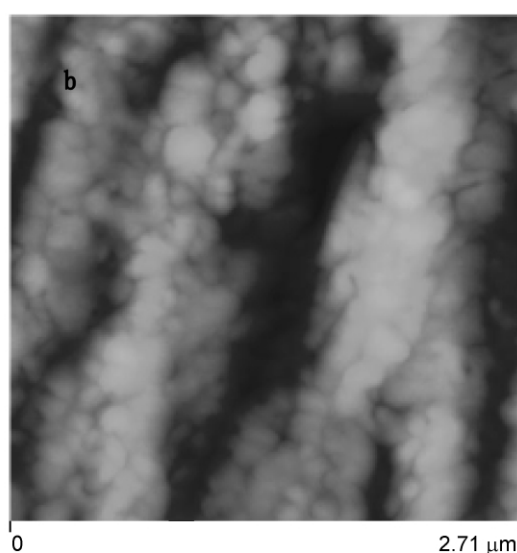
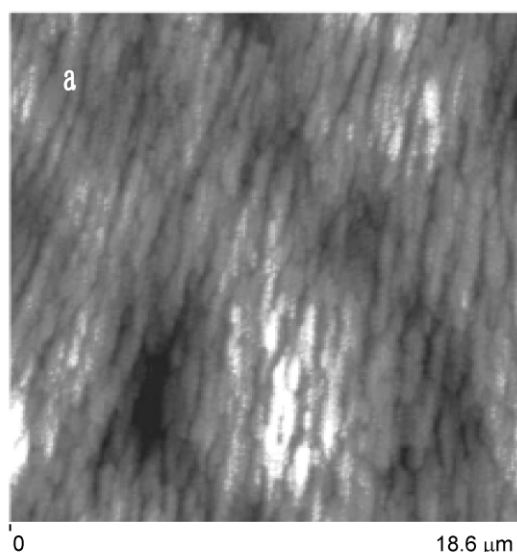


**Fig. 6** (a) AFM image of copolymer film on newly cleaved mica prepared by spin coating (1300 rpm for 8 s and 4000 rpm for 30 s) 20  $\mu\text{l}$  of its ammonia solution with concentration of  $9.14 \text{ mg ml}^{-1}$ . (b) Zoom in AFM image of (a).

both polystyrene and poly(acrylic acid) chains. Since there exist stronger interchain H-bond interactions among carboxylic acid groups, many copolymer chains aggregate together, and this results in the formation of larger particles than those in ammonia. By comparing Fig. 6 and Fig. 7 it can be found that the basic particles in Fig. 7 are bigger than in Fig. 6, which is consistent with this suggestion. After deposition on the substrate, the interaction among hydrophilic or hydrophobic surfaces of the particles could lead to self-assembly into the observed pattern structures. The mechanism of the self-assembly of the particles will be studied with dynamic laser scattering in future work.

## Conclusion

In this paper, a novel, ultrasonically assisted aqueous emulsion polymerization free of emulsifier was reported. Styrene can copolymerize with acrylic acid in water without emulsifier by making use of the emulsification effect of ultrasonic irradiation. At higher ultrasonic power, a short induction period and high monomer conversion rate were achieved. The effect of ultrasonic conditions on polymerization rate and the average molecular weight were also studied, and it was found that increasing output power and reaction time result in a decrease in the average molecular weight. Based on the experimental results, a free radical



**Fig. 7** (a) AFM image of copolymer film on newly cleaved mica prepared by spin coating (1300 rpm for 8 s and 4000 rpm for 30 s) 20  $\mu\text{l}$  of its THF solution with concentration of  $8.58 \text{ mg ml}^{-1}$ . (b) Zoom in AFM image of (a).

mechanism for ultrasonically initiated emulsion copolymerization of styrene with acrylic acid was proposed.

In addition, copolymer films were prepared by spin coating and the morphologies were measured by AFM. The copolymers form a patterned structure resulting from the self-assembly of the nanoparticles.

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# Studies on selective adsorbents for oxo-anions. Nitrate ion-exchange properties of layered double hydroxides with different metal atoms

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Layered double hydroxides (LDHs) with different kinds of metal ions (Mg–Al, Co–Fe, Ni–Fe, and Mg–Fe) in the brucite layers were prepared and their anion exchange properties were studied by measurements of distribution coefficient ( $K_d$ ) and ion exchange capacity. The basal spacing of LDHs varied depending on the kind of metal ions in the brucite layer. A relatively high  $K_d$  value for  $\text{NO}_3^-$  ions was observed on Ni–Fe type LDHs, and a markedly high  $K_d$  value for the hydrothermally-treated Ni–Fe type LDHs (Ni–Fe (HT)), prepared at 120 °C. These high  $K_d$  values correlated with the basal spacing of 0.81 nm observed for this sample, where the interlayer distance (0.33 nm) is suitable for the stable fixing of  $\text{NO}_3^-$  ions (ionic size = 0.33 nm). A chemical analysis study showed a  $\text{Cl}^-/\text{NO}_3^-$  ion-exchange mechanism for  $\text{NO}_3^-$  adsorption on Ni–Fe (HT). The  $\text{NO}_3^-$  uptake by Ni–Fe (HT) was nearly constant ( $\text{NO}_3^-/\text{Fe} = 0.7$ ) over a pH range between 5 and 10, which also supports the adsorption mechanism of  $\text{Cl}^-/\text{NO}_3^-$  ion exchange. The Ni–Fe (HT) could remove  $\text{NO}_3^-$  ions from seawater effectively ( $\text{NO}_3^-$  uptake = 168  $\mu\text{mol g}^{-1}$ ) even though seawater contains an extremely large amount of coexisting anions. This novel adsorbent thus has a  $\text{NO}_3^-$  ion-sieve property and will prove beneficial for the selective removal of  $\text{NO}_3^-$  ions from industrial effluents and seawater to clean the environment.

## Introduction

Nitrate is a source of nitrogen that is essential for plant life, but toxic to human, animal and marine life health. Nitrate contamination in the environment comes mainly from poorly or untreated human and animal waste, agricultural fertilizers and industrial effluents. Nitrate ions are highly soluble in water, which causes them to be washed from the land into rivers, lakes or the sea. Nitrate pollution of ground and surface water has become a common concern in both industrial and developing countries. An increased nitrate uptake affects human health, causing methaemoglobinemia.<sup>1</sup> Enriched nitrate ions in the hydrosphere fertilize plant life, causing it to grow markedly, but the subsequent decay process of plants consumes available oxygen in environmental water. A lack of oxygen causes life in the affected aqueous medium to migrate to other places or to die.

We are interested in adsorption technology for the removal of nitrate ions, since the adsorption method is advantageous for the selective recovery of elements with markedly low concentrations. However, there have been few adsorbents to date suitable for the removal of nitrate ions from solutions which also contain high concentrations of chloride, sulfate, or carbonate ions, since most of the adsorbents show low selectivity toward nitrate ion compared to the other anions.

Layered double hydroxide (LDHs) consists of positively charged metal hydroxide layers separated by counter anions and water molecules. The chemical composition can be expressed in general as  $[\text{M}(\text{II})_{1-x}\text{M}(\text{III})_x(\text{OH})_2]^{x+}[\text{A}^{n-}]_{x/2} \cdot z\text{H}_2\text{O}$ , where  $\text{M}(\text{II})$  and  $\text{M}(\text{III})$  are divalent and trivalent cations in the octahedral interstices of the hydroxide layer and  $\text{A}^{n-}$  is the charge-balancing interlayer gallery anion. Due to the presence of a large interlayer space and exchangeable counter anions, LDHs can act as good anion adsorbents.<sup>2–12</sup> They are attractive in the field of green sustainable chemistry, since they are useful for the removal of harmful oxo-anions (phosphate, nitrate ions, etc.) from aqueous solutions. LDHs of Mg and Al, Mg and Fe have been studied in detail with regard to preparation and anion exchange properties.<sup>2,3,13–18</sup> Those of Ni and Fe with chloride anions as the counter anions in the interlayer space have not been prepared so far, although the material in carbonate

form, which exists naturally as the mineral reevesite,<sup>19</sup> has been synthesized.<sup>20–22</sup> LDHs of Co and Fe are less studied materials.<sup>23,24</sup> Although there have been many studies on the adsorptive properties of LDHs for various anions, there have been relatively few studies on their anion selectivity mechanism.<sup>2,14,16,25</sup> So far, there has been no report on the adsorption behavior of nitrate ions with LDHs in competitive conditions.

In the present paper, we studied the nitrate ion-exchange properties of LDHs consisting of different skeletal metal atoms. From studies of distribution coefficients, we found that the layered double hydroxide has a nitrate ion-sieve property depending on the basal spacing of the brucite layer. The LDHs with Ni or Fe as skeletal metal atoms had a high selectivity for nitrate ions. A  $\text{Cl}^-/\text{NO}_3^-$  ion exchange mechanism could be proposed from the chemical analysis and pH dependence studies. From an application standpoint, they were found to be a good adsorbent for  $\text{NO}_3^-$  removal from seawater. They could remove nitrate ions effectively, even in seawater where an enormous amount of  $\text{Cl}^-$ ,  $\text{SO}_4^{2-}$ , and  $\text{CO}_3^{2-}$  ions coexists with  $\text{NO}_3^-$  ions. To the best of our knowledge, this is the first report that shows the effective removal of  $\text{NO}_3^-$  ions from seawater by an adsorption method.

## Results and discussion

### Characterization of the starting LDHs

The chemical compositions of different LDHs were calculated by analyzing their metal ion, carbonate, and water contents. The carbonate contents were determined from the total carbon contents and the water contents were derived from TG analysis. All the samples contain small amounts of carbonate ions. In spite of precautions taken during the synthesis of LDHs samples,  $\text{CO}_2$  from the atmosphere entered slightly into the product LDHs. The chloride and hydroxide contents were calculated on the basis of electroneutrality assuming a typical LDHs composition (Table 1). The Cl content could be determined by ion chromatography. The experimentally determined  $\text{Cl}/\text{M}(\text{II})$  mole ratios are given in Table 1. The mole ratios agree comparatively well with the calculated ones for samples Mg–Al, Ni–Fe, Ni–Fe(HT), and Mg–Fe. It is

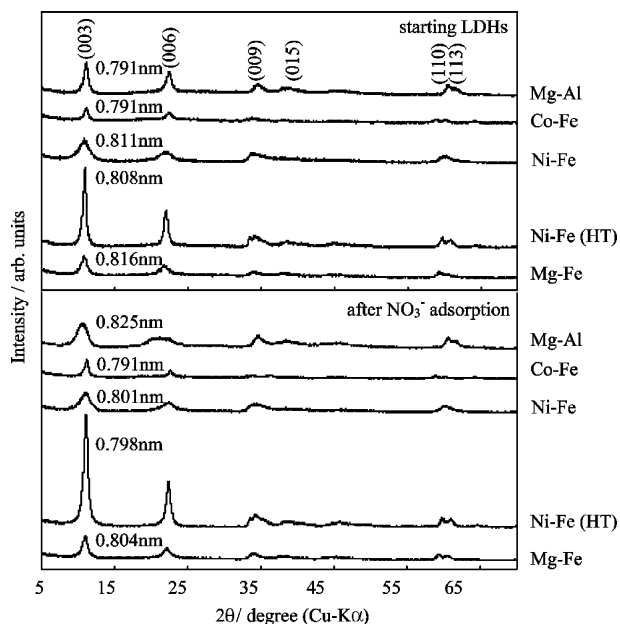
**Table 1** Chemical composition, Cl and NO<sub>3</sub> contents, and lattice parameters of LDHs

LDHs	Chemical composition	Cl/M(m) <sup>a</sup>				Lattice parameter/nm	
		Calculated	Determined	Cl/M(m) after NO <sub>3</sub> <sup>-</sup> exchange	NO <sub>3</sub> <sup>-</sup> /M(m) after NO <sub>3</sub> <sup>-</sup> exchange	<i>a</i>	<i>c</i>
Mg–Al	Mg <sub>0.706</sub> Al <sub>0.294</sub> (OH) <sub>2</sub> Cl <sub>0.271</sub> (CO <sub>3</sub> ) <sub>0.012</sub> ·0.586H <sub>2</sub> O	0.92	0.95	0.10	0.66	0.306	2.373
Co–Fe	Co <sub>0.737</sub> Fe <sub>0.263</sub> (OH) <sub>2</sub> Cl <sub>0.227</sub> (CO <sub>3</sub> ) <sub>0.018</sub> ·0.801H <sub>2</sub> O	0.86	0.70	0.06	0.51	0.312	2.373
Ni–Fe	Ni <sub>0.787</sub> Fe <sub>0.213</sub> (OH) <sub>2</sub> Cl <sub>0.154</sub> (CO <sub>3</sub> ) <sub>0.029</sub> ·0.705H <sub>2</sub> O	0.72	0.65	0.03	0.63	0.308	2.433
Ni–Fe(HT)	Ni <sub>0.790</sub> Fe <sub>0.210</sub> (OH) <sub>2</sub> Cl <sub>0.174</sub> (CO <sub>3</sub> ) <sub>0.018</sub> ·0.631H <sub>2</sub> O	0.83	0.85	0.08	0.72	0.310	2.424
Mg–Fe	Mg <sub>0.844</sub> Fe <sub>0.156</sub> (OH) <sub>2</sub> Cl <sub>0.131</sub> (CO <sub>3</sub> ) <sub>0.013</sub> ·0.680H <sub>2</sub> O	0.84	0.84	0.04	0.67	0.312	2.448

<sup>a</sup> M(m): trivalent metal.

slightly smaller than the calculated one for Co–Fe; this suggests that a small portion of amorphous iron hydroxide phase coexists in the solid. The theoretical AEC (anion exchange capacity) for each sample was calculated from the chemical compositions, as is described in the literature.<sup>3</sup> It decreases in the order Mg–Al (3.65 mmol g<sup>-1</sup>) > Co–Fe (2.26 mmol g<sup>-1</sup>) > Mg–Fe (1.92 mmol g<sup>-1</sup>) > Ni–Fe (HT) (1.88 mmol g<sup>-1</sup>) > Ni–Fe (1.87 mmol g<sup>-1</sup>).

The XRD pattern of synthesized Ni–Fe (HT) consists of sharp, symmetrical peaks and some asymmetrical peaks at high angles, which are characteristics of a typical LDHs compound with well ordered layered structure (Fig. 1). Although the intensities of the



**Fig. 1** XRD pattern of LDHs before and after nitrate ion exchange.

peaks are weak in the Mg–Al, Co–Fe, Ni–Fe, and Mg–Fe patterns, these samples also show the patterns for typical layered compounds of LDHs. The difference in the crystallinity can be related to the conditions of synthesis, because hydrothermal treatment (for Ni–Fe (HT) only) usually gives higher crystalline phases. The *d*-spacings (*d*<sub>003</sub>) of these LDHs samples are also shown in Fig. 1. The lattice parameters *a* of the LDHs samples corresponding to the average cation–cation distance within the layers can be calculated from the *d*<sub>110</sub> diffraction. The lattice parameters *a* are nearly equal. The lattice parameter *c*, which corresponds to the sum of the thickness of one brucite-like layer and the interlayer distance, is commonly calculated from the *d*<sub>003</sub> diffraction peaks.<sup>3</sup> The lattice parameters *c* depend on the kind of metal of the brucite layer.

TG-DTA curves of different LDHs are shown in Fig. 2. Samples Mg–Al, Ni–Fe, Ni–Fe (HT) and Mg–Fe show decomposition profiles typical of LDHs material. The first endothermic peaks below 200 °C are associated with the dissipation of interlayer water. The endothermic peaks between 200–500 °C are due to dissipation of hydroxyl groups in the brucite layer and of interlayer chloride anions. The DTA curve of Co–Fe showed only one endothermic

peak around 170 °C. A similar behavior has also been observed for Co–Fe layered double hydroxides in the literature.<sup>24</sup> It is not clear why Co–Fe type LDHs does not have two endothermic peaks. A possible explanation is that the exothermic oxidation of Co<sup>2+</sup> takes place simultaneously during the endothermic reaction by the release of hydroxyl group and chloride. The weight loss by the release of hydroxyl group and chloride may be compensated for by the weight gain by the absorption of oxygen gas.

The IR spectra of different LDHs show the patterns typical of LDHs samples, as shown in Fig. 3. The broad bands in the region between 3400 to 3700 cm<sup>-1</sup> can be assigned to OH stretching vibrations of hydroxyl groups in the brucite layers and interlayer water molecules. The broad band around 3400 cm<sup>-1</sup> can be assigned to the vibrations of interlayer water molecules and the shoulder around 3650 cm<sup>-1</sup> that of hydroxyl group of brucite layer. The bending mode of interlayer water molecules is responsible for a small intense band recorded at 1628 cm<sup>-1</sup>. The absorption peak in the region 1355–1395 is assigned to the vibrations of carbonate ions. This carbonate absorption band has also been reported for the nitrate forms of other LDHs samples in the literature.<sup>26,27</sup> Bands recorded below 800 cm<sup>-1</sup> are due to lattice vibration of the brucite structure.

The SEM images of starting LDHs showed stacking of particles in a layer-like morphology (Fig. 4, left). All the samples consist of layered double hydroxides. The stacking of the layers in Mg–Al, Ni–Fe, Ni–Fe (HT) and Mg–Fe was more pronounced than in Co–Fe.

#### Distribution coefficient (*K<sub>d</sub>*)

The *K<sub>d</sub>* and the separation factor (*α*) values of different anions on LDHs samples are shown in Table 2. The selectivity sequence is NO<sub>3</sub><sup>-</sup> ≪ HPO<sub>4</sub><sup>2-</sup>, SO<sub>4</sub><sup>2-</sup>, CO<sub>3</sub><sup>2-</sup> on Mg–Al, SO<sub>4</sub><sup>2-</sup> < NO<sub>3</sub><sup>-</sup> ≪ HPO<sub>4</sub><sup>2-</sup> < CO<sub>3</sub><sup>2-</sup> on Co–Fe, SO<sub>4</sub><sup>2-</sup> < HPO<sub>4</sub><sup>2-</sup> < NO<sub>3</sub><sup>-</sup> ≪ CO<sub>3</sub><sup>2-</sup> on Ni–Fe, SO<sub>4</sub><sup>2-</sup> < HPO<sub>4</sub><sup>2-</sup> ≪ NO<sub>3</sub><sup>-</sup>, CO<sub>3</sub><sup>2-</sup> on Ni–Fe (HT), and SO<sub>4</sub><sup>2-</sup> < NO<sub>3</sub><sup>-</sup> < HPO<sub>4</sub><sup>2-</sup>, CO<sub>3</sub><sup>2-</sup> on Mg–Fe. High *K<sub>d</sub>* values of CO<sub>3</sub><sup>2-</sup> ions are observed for all the samples, while the *K<sub>d</sub>* values of other anions vary depending on the metal species in the brucite layer. The Mg–Al and Mg–Fe with Mg atoms show a high selectivity for HPO<sub>4</sub><sup>2-</sup> ions. This suggests a strong interaction between the skeletal Mg atoms and HPO<sub>4</sub><sup>2-</sup> ions. Since Mg<sup>2+</sup> and phosphate ions form a stable and slightly soluble magnesium phosphate, we can expect a strong chemical interaction between skeletal Mg and HPO<sub>4</sub><sup>2-</sup>. Mg–Al shows a high selectivity while the other samples show low selectivity for SO<sub>4</sub><sup>2-</sup>.

The *K<sub>d</sub>* value of NO<sub>3</sub><sup>-</sup> ions varies strongly with the kinds of double hydroxide. Sample Ni–Fe (HT) shows markedly high selectivity, Ni–Fe relatively high selectivity, Mg–Fe moderate selectivity, and Mg–Al and Co–Al low selectivity for NO<sub>3</sub><sup>-</sup> ions. Unlike HPO<sub>4</sub><sup>2-</sup>, NO<sub>3</sub><sup>-</sup> ions cannot form slightly soluble compounds with the skeletal metal atoms. Therefore, it is reasonable to think that the selectivity of NO<sub>3</sub><sup>-</sup> is controlled mainly by physical, but not chemical, interaction. The *K<sub>d</sub>* of NO<sub>3</sub><sup>-</sup> ions is found to be a function of the basal spacing of the LDHs samples. It is maximal for Ni–Fe (HT) with a basal spacing of 0.808 nm, which corresponds to an interlayer distance of 0.33 nm, assuming the



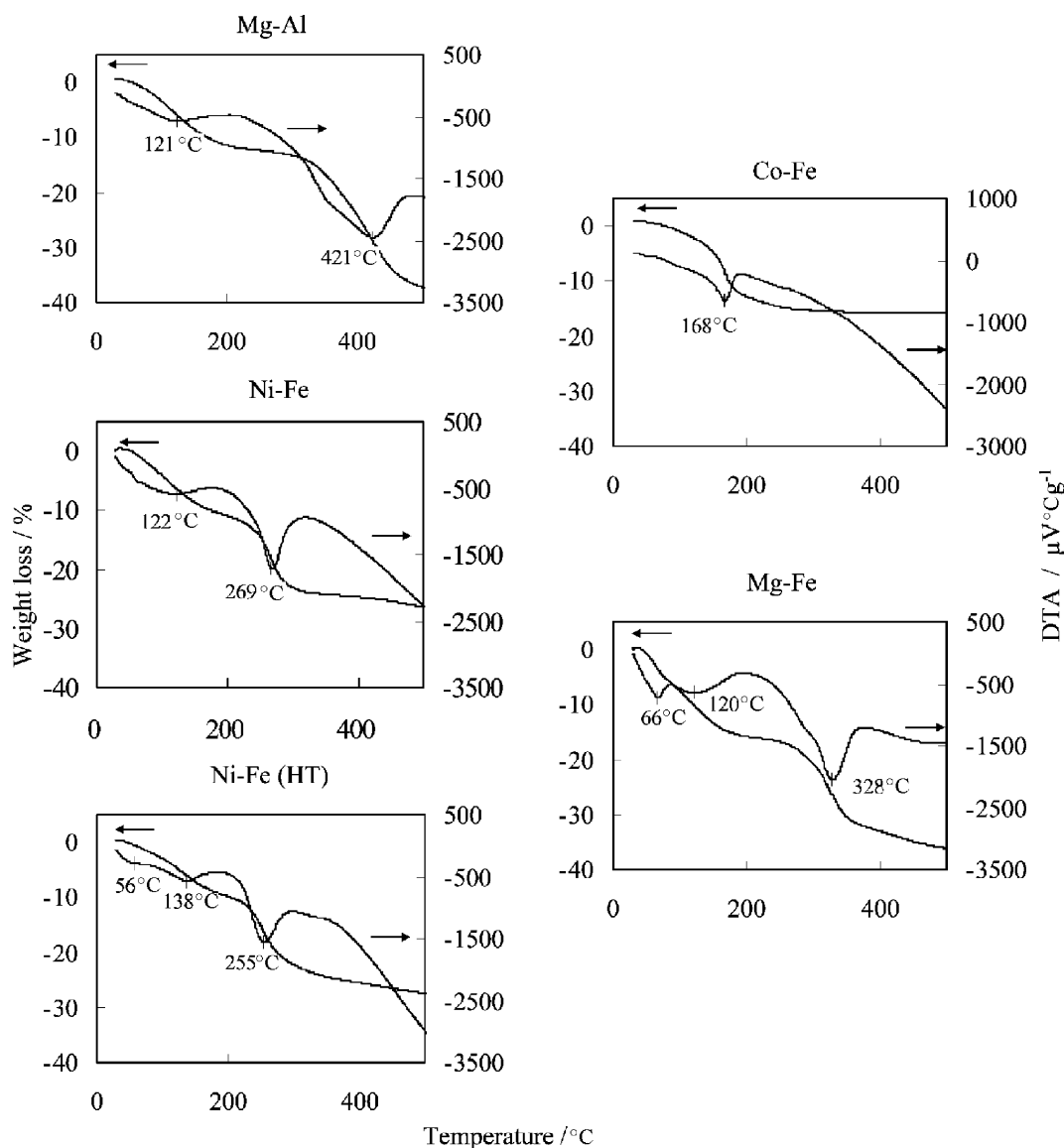


Fig. 2 TG-DTA curves of LDHs.

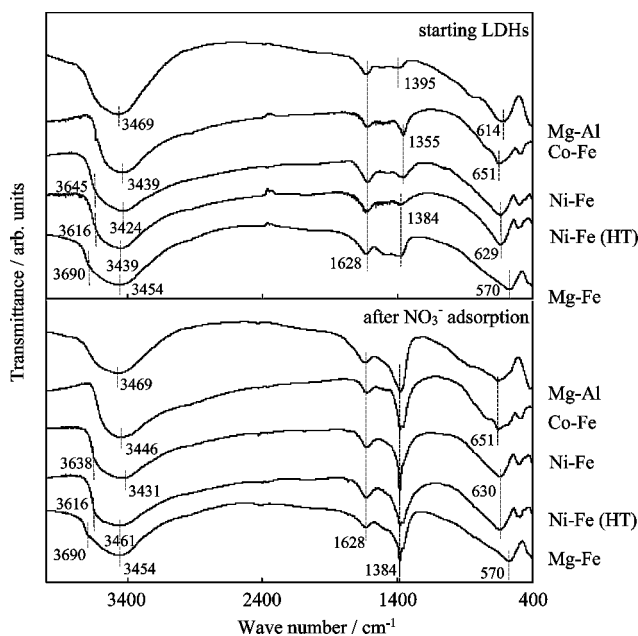


Fig. 3 IR spectra of LDHs before and after nitrate ion exchange.

thickness of the brucite layer to be 0.48 nm, as in the literature.<sup>28</sup> The interlayer distance is thus close to the ionic size (0.33 nm) of  $\text{NO}_3^-$  ions, suggesting that the basal spacing (0.81 nm) of the Ni-Fe type is advantageous for fixing  $\text{NO}_3^-$  ions in the interlayer from a steric standpoint. This suggests that the selectivity of  $\text{NO}_3^-$  on LDHs is largely influenced by the ion-sieve produced by the spatial limits between the brucite layers.

Ion-sieve properties have been extensively studied for inorganic cation exchange materials, like zeolite,<sup>29</sup> acidic salt of multivalent metal,<sup>30</sup> crystalline porous metal oxides,<sup>31,32</sup> etc. Alberti *et al.* have summarized the alkali metal ion-exchange property of layered acid salts of multivalent metal.<sup>33</sup> Alkali metal ion-sieve properties ( $\text{Li}^+$ ,  $\text{Na}^+$ , and  $\text{K}^+$ -sieve properties) have been observed on these samples which have different basal spacing values ( $d = 0.71\text{--}0.78$  nm) depending on the kind of central metal atom. We have observed that spinel-type manganese oxide with a  $[1 \times 3]$  network, hollandite-type manganese oxide with  $[2 \times 2]$ , and  $[2 \times 4]$  tunnel-type manganese oxide show lithium, potassium, and rubidium ion-sieve properties, respectively depending on their tunnel size.<sup>34,35</sup> The present data suggest that the concept of the ion-sieve is also effective for understanding the origin of anion selectivity on inorganic ion-exchange materials.

#### $\text{NO}_3^-$ ion-exchange properties

The  $\text{NO}_3^-$  exchange capacity was measured by a batch method using a 0.1 M  $\text{NaNO}_3$  solution. The  $\text{Cl}/\text{M}(\text{III})$  and  $\text{NO}_3/\text{M}(\text{III})$  mole

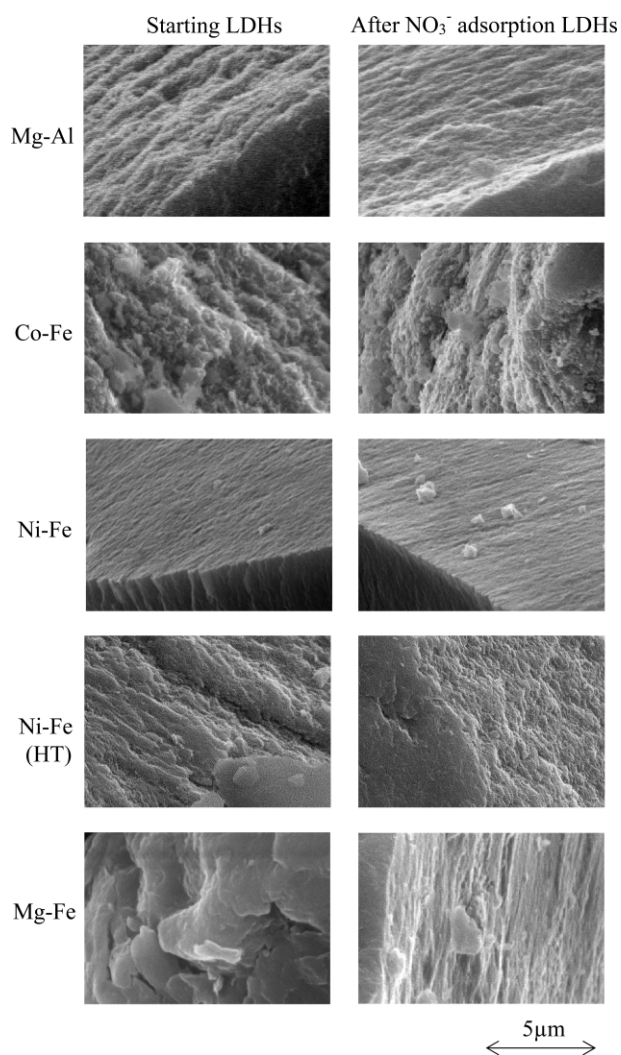


Fig. 4 SEM image of LDHs.

ratios after the  $\text{NO}_3^-$  exchange are given in Table 1. The  $\text{Cl}/\text{M}(\text{III})$  mole ratios decrease significantly by the  $\text{NO}_3^-$  exchange for all the samples. The differences in  $\text{Cl}/\text{M}(\text{III})$  ratio before and after the exchange agree well with the  $\text{NO}_3^-/\text{M}(\text{III})$  ratios for Ni-Fe and Ni-

Fe (HT). The chemical analysis of  $\text{CO}_3$  content showed that the  $\text{CO}_3/\text{M}(\text{III})$  mole ratio did not change by the  $\text{NO}_3^-$  adsorption. The  $\text{CO}_3/\text{Fe}(\text{III})$  mole ratio of Ni-Fe(HT) was 0.17 after the  $\text{NO}_3^-$  exchange; this shows that the adsorption of  $\text{CO}_3^-$  is negligible during the  $\text{NO}_3^-$  exchange. These results clearly show that the  $\text{NO}_3^-$  adsorption progresses mainly by the  $\text{Cl}^-/\text{NO}_3^-$  ion exchange mechanism and  $\text{CO}_3^{2-}/\text{NO}_3^-$  exchange does not proceed due to the high selectivity of  $\text{CO}_3^{2-}$  for LDHs. The  $\text{NO}_3^-$  contents of the other three samples are slightly smaller than those expected from the difference in  $\text{Cl}/\text{M}(\text{III})$  ratio. Since these samples have low selectivity for  $\text{NO}_3^-$  ions, the competitive adsorption of  $\text{CO}_3^{2-}$  ions may take place more easily.

XRD patterns of  $\text{NO}_3^-$ -exchanged LDHs were measured in order to study the  $\text{NO}_3^-$  exchange properties in more detail. The exchange reaction progresses topotactically, maintaining the layered structure (Fig. 1, bottom). The basal spacing of Mg-Al increases from 0.791 to 0.825 nm with  $\text{NO}_3^-$  loading. However, the basal spacings of Mg-Fe, Ni-Fe and Ni-Fe (HT) decrease slightly to 0.804, 0.801 and 0.798 nm with the  $\text{NO}_3^-$  exchange while that of Co-Fe remains constant after  $\text{NO}_3^-$  loading. These results suggest that the interlayer of Mg-Al can expand more easily than those of the other LDHs, and therefore it can exchange a large amount of guest anions, although less selectively. On the other hand, the other LDHs have a less expansive character and, therefore, they may have a strong ion-sieve effect for guest anions. The  $K_d$  measurement and the capacity study suggest that the Ni-Fe (HT) sample has a  $\text{NO}_3^-$  ion-sieve property from a microamount to a macroamount of adsorption.

The IR spectra do not change with the  $\text{NO}_3^-$  exchange except for the appearance of a sharp band around  $1384\text{ cm}^{-1}$ , which could be assigned to the vibration of  $\text{NO}_3^-$  anions intercalated in the interlayer space<sup>36,37</sup> (Fig. 3, bottom). The band exists at the same position independent of the metal species of the brucite layer, suggesting that the interlayer  $\text{NO}_3^-$  ions exist in the same state as those in the bulk solution because of their weak interaction with ion exchange sites on the brucite layer. SEM observation shows that the stacked layer structure is maintained after the  $\text{NO}_3^-$  exchange, as is shown in Fig. 4.

### The pH dependence

It is well known that in an aqueous solution hydroxyl groups form on the surface of metal oxide; they show cation or anion exchange behavior depending on the nature of the central metal atom of

Table 2 Distribution coefficients ( $K_d$ 's) and separation factors ( $\alpha$ 's)<sup>a</sup> on LDHs

Sample	pH	Ions	$\text{NO}_3^-$	$\text{HPO}_4^{2-}$	$\text{SO}_4^{2-}$	$\text{CO}_3^{2-}$
Mg-Al	6.4	$K_d$ $\alpha$	16 > 600	> $10^4$ —	> $10^4$ —	> $10^4$
Sample	pH	Ions	$\text{SO}_4^{2-}$	$\text{NO}_3^-$	$\text{HPO}_4^{2-}$	$\text{CO}_3^{2-}$
Co-Fe	7.6	$K_d$ $\alpha$	5 2	10 29	290 > 35	> $10^4$
Sample	pH	Ions	$\text{SO}_4^{2-}$	$\text{HPO}_4^{2-}$	$\text{NO}_3^-$	$\text{CO}_3^{2-}$
Ni-Fe	7.5	$K_d$ $\alpha$	120 1.1	130 1.7	220 45	> $10^4$
Sample	pH	Ions	$\text{SO}_4^{2-}$	$\text{HPO}_4^{2-}$	$\text{NO}_3^-$	$\text{CO}_3^{2-}$
Ni-Fe (HT)	7.3	$K_d$ $\alpha$	150 2	320 > 31	> $10^4$ —	> $10^4$
Sample	pH	Ions	$\text{SO}_4^{2-}$	$\text{NO}_3^-$	$\text{HPO}_4^{2-}$	$\text{CO}_3^{2-}$
Mg-Fe	6.4	$K_d$ $\alpha$	160 2.4	380 > 26	> $10^4$ —	> $10^4$

<sup>a</sup>  $\alpha_m^n = K_d(n)/K_d(m)$ .

oxide. When these surface hydroxyl groups or hydroxide ions are concerned with the  $\text{NO}_3^-$  adsorption, the  $\text{NO}_3^-$  uptake depends on the pH of solution. Since the exchange reaction can be written as  $\overline{\text{OH}^-} + \text{NO}_3^- \rightleftharpoons \overline{\text{NO}_3^-} + \text{OH}^-$ , where the bar describes the species in solid phase, the  $\text{NO}_3^-$  uptake should decrease with pH. In the present case, however, the  $\text{NO}_3^-$  uptake by Ni-Fe(HT) is pH independent; the  $\text{NO}_3^-/\text{M(III)}$  ratios are almost constant in the pH range between 5 and 10 (Fig. 5). This shows that the surface

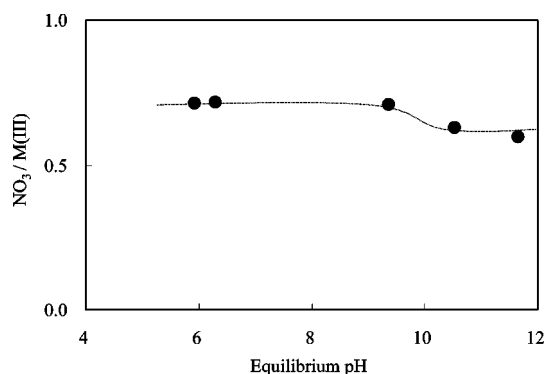


Fig. 5  $\text{NO}_3^-/\text{M(III)}$  on Ni-Fe (HT).

hydroxyl group or hydroxide ions plays little part in the adsorption of  $\text{NO}_3^-$  on Ni-Fe(HT). This also supports the  $\text{NO}_3^-/\text{Cl}^-$  ion exchange mechanism for the present  $\text{NO}_3^-$  adsorption.

### $\text{NO}_3^-$ uptake from seawater

Nitrate ion adsorption from seawater was studied by adding LDHs (0.10 g) to  $\text{NO}_3^-$ -enriched seawater ( $[\text{NO}_3^-] = 0.03 \text{ mM}$ , 1 L). The  $\text{NO}_3^-$  removals from solution were < 1, < 1, 40, 56, and 27% for samples Mg-Al, Co-Fe, Ni-Fe, Ni-Fe (HT) and Mg-Fe, respectively. The corresponding  $\text{NO}_3^-$  uptakes by LDHs were 0.4, < 1, 120, 168, and 81  $\mu\text{mol g}^{-1}$ , respectively. Ni-Fe and Mg-Fe samples could remove  $\text{NO}_3^-$  ions effectively, even in seawater containing large amounts of coexisting anions (2.3 mM of carbonate ions, 14 mM of sulfate ions, 550 mM of chloride ions, etc.). To the best of our knowledge, this is the first report that shows the effective removal of  $\text{NO}_3^-$  ions from seawater by an adsorption method. The Mg-Al sample has a relatively small  $\text{NO}_3^-$  uptake from seawater although it has the largest theoretical exchange capacity. Since Mg-Al has high selectivity for carbonate and sulfate ions, the competitive adsorption of these ions probably decreases the  $\text{NO}_3^-$  uptake markedly.

Dissolution of Ni and Fe from Ni-Fe(HT) was studied by analysis of Ni and Fe concentrations in seawater after the adsorption. The degrees of dissolution were less than 0.6% for Ni and less than 0.1% for Fe, indicating that this adsorbent is stable enough in seawater.

### Conclusion

Ni-Fe type LDH shows a high selectivity for  $\text{NO}_3^-$  ions as compared to other LDHs. Especially, high crystalline sample Ni-Fe(HT) shows a strong nitrate ion-sieve property, probably owing to its suitable interlayer spacing for fixing  $\text{NO}_3^-$  ions. These properties are beneficial for the selective removal of  $\text{NO}_3^-$  ions from multi-component solutions containing large coexisting ions. From the standpoint of adsorbent design, the concept of an "ion-sieve effect" is beneficial for the development of a novel adsorbent for selective removal of harmful oxo-anions including nitrate ions.

### Experiment

#### Preparation of different LDHs

Samples (10 mL) of 1 M (1 M = 1 mol L<sup>-1</sup>) mixed metal chlorides (Mg, Al, Fe, Co, Ni) with different M(II)/M(III) ratios and a 1 M

NaOH solution were added simultaneously to 200 mL of deionized water, while maintaining the pH around 10 and stirring vigorously at room temperature. For the Ni<sup>2+</sup>-Fe<sup>3+</sup>, Mg<sup>2+</sup>-Fe<sup>3+</sup> and Co<sup>2+</sup>-Fe<sup>3+</sup> systems, the precipitates were aged for 1 d at room temperature, however for the Mg<sup>2+</sup>-Al<sup>3+</sup> system, the precipitate was aged at 60 °C for 3 h followed by aging for 1 d at room temperature. The precipitate of the Ni<sup>2+</sup>-Fe<sup>3+</sup> was autoclaved at 120 °C for 1 d. The precipitates were centrifuged, washed with deionized water and dried at 50 °C for 1 d. The samples were designated as Ni-Fe, Ng-Fe, Co-Fe, Mg-Al and Ni-Fe (HT), respectively.

### Physical analysis

X-Ray diffraction analysis was carried out using a Rigaku type RINT 1200 X-ray diffractometer with a graphite monochromator. DTA-TG curves of adsorbents were measured on a Rigaku Thermoplus TG 8110 at a heating rate of 10 °C min<sup>-1</sup> in air. SEM observations were carried out on a Hitachi type S-2460 N scanning electron microscope.

### Chemical analysis

A solid sample (0.05 g) was dissolved in a 0.5 M HCl solution and the metal concentrations were determined with a Shimadzu AA-760 atomic absorption spectrometer or with a Seiko SPS 7800 atomic emission plasma spectrometer. Carbonate contents were calculated from the total carbon contents which were determined by carbon analyzer, Horiba EMIA-U511. Water contents were determined from the weight losses by the heating at 200 °C in the DTA-TG curves. Chloride contents were determined by ion chromatography after the solid was dissolved in a concentrated H<sub>2</sub>SO<sub>4</sub> solution.

### Distribution coefficient ( $K_d$ )

$K_d$  values of  $\text{NO}_3^-$ ,  $\text{CO}_3^{2-}$ ,  $\text{HPO}_4^{2-}$ , and  $\text{SO}_4^{2-}$  were determined by a batch method using a mixed solution of NaCl, Na<sub>2</sub>CO<sub>3</sub>, NaNO<sub>3</sub>, NaH<sub>2</sub>PO<sub>4</sub>, and Na<sub>2</sub>SO<sub>4</sub> (1 mM each). A solid sample (0.10 g) was added to the mixed solution (10 mL) and shaken for 3 days at room temperature. After equilibration, the concentration of each anion in the supernatant solution was determined by ion chromatography (Shimadzu, LC-10Ai). Anion uptakes were calculated by the decrease of anion concentrations relative to their initial concentrations. The  $K_d$  values were calculated using the following equation;  $K_d \text{ (mL g}^{-1}\text{)} = \text{anion uptake (mg g}^{-1}\text{)}/\text{equilibrium anion concentration (mg mL}^{-1}\text{)}$ .

### $\text{NO}_3^-$ exchange properties

The  $\text{NO}_3^-$  exchange capacity of each LDH was measured by mixing the LDHs (0.10 g) in a 0.1 M NaNO<sub>3</sub> solution (100 mL) for 3 days at room temperature. The solids were separated by filtration and the  $\text{NO}_3^-$  content was determined by ion chromatography after the solid was dissolved in a concentrated H<sub>2</sub>SO<sub>4</sub> solution.

The pH dependence of  $\text{NO}_3^-$  uptake was studied for Ni-Fe by a batch method. Samples of Ni-Fe (0.10 g) were immersed in  $6 \times 10^{-3} \text{ M}$  NaNO<sub>3</sub> solutions (100 mL) with different pH values. The pH of the solution was adjusted by using 0.1 M HNO<sub>3</sub> or 0.1 M NaOH. After equilibration, the solids were separated by filtration and the  $\text{NO}_3^-$  concentrations of the supernatant solutions were determined by ion chromatography. The  $\text{NO}_3^-$  uptakes were calculated from the differences between the initial and final concentrations. The pHs of the supernatant solutions were measured with a Horiba M8s pH meter.

The  $\text{NO}_3^-$  uptake from seawater was studied using  $\text{NO}_3^-$ -enriched seawater ( $\text{NO}_3^-$ -concentration = 0.030 mM) at room temperature. An LDHs sample (0.10 g) was immersed in the  $\text{NO}_3^-$ -enriched seawater (1 L) and stirred for 3 days. After stirring, the solid was separated by filtration. The  $\text{NO}_3^-$  concentration in the supernatant solution was determined with an automatic  $\text{NO}_3^-$

analyzer. The  $\text{NO}_3^-$  uptake was calculated from the difference between the initial and final  $\text{NO}_3^-$  concentrations.

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# Halogenation of carbazole and other aromatic compounds with hydrohalic acids and hydrogen peroxide under microwave irradiation

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Novel effective application of microwave irradiation to the chlorination, bromination, and iodination of carbazole and other aromatic compounds in the presence of a hydrogen peroxide–hydrohalic acids system is described as a new environmentally benign method for the synthesis of halogenoarenes.

## Introduction

Halogenated aromatic compounds belong to an important class of organic intermediates that are used as precursors of organometallic compounds applied for the manufacture of a number of natural and bio-active substances as well as pharmaceuticals.<sup>1</sup> Therefore, there are several known methods available in the literature that have been developed for the chlorination, bromination, and iodination of aromatic compounds.<sup>2</sup> However, the classical direct chlorination and bromination involves the use of potentially hazardous, difficult to store and handle elemental halogens or/and catalysts such as mineral acids or metal chlorides, which can decompose during the reaction and work-up to produce corrosive side products that create separation and disposal problems at the end. Iodine is the least reactive of the halogens in aromatic substitution; therefore synthetic methods have to involve a source of iodide cation (*i.e.* I<sup>-</sup>) which is most convenient for direct iodination, but requires molecular iodine to be used in combination with large amounts of mineral acids, high reaction temperatures, and metallic reagents, which in turn generate toxic waste. Moreover, the application of elemental halogens results in stoichiometric amounts of hydrohalic acids, which in general worsen atom economy for such processes. Thus, a range of new methods has been published lately, and the development of new halogenation protocols focused on environmentally acceptable techniques and materials with improved employment of all the atoms used in reactions has continued to receive wide attention.<sup>3,4</sup> Analyzing these literature data, one can see that the most promising examples of chlorination and bromination of arenes include a one-pot synthesis where elemental chlorine and bromine were generated *in situ* in the presence of hydrogen peroxide from hydrochloric and hydrobromic acids, respectively.<sup>3</sup> However, for iodination of aromatic compounds, such a protocol has not been broadly exemplified yet.

*In situ* liberation of elemental halogen by aqueous hydrogen



where: X = Cl, Br or I

**Scheme 1** Oxidation of hydrohalic acid using hydrogen peroxide.

peroxide–hydrohalic acid systems (Scheme 1) seems to have several advantages; however, the drawbacks are still the high cost of hydrogen peroxide and its undesirable decomposition during a

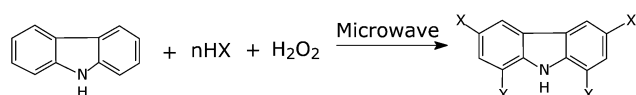
reaction at elevated temperatures and/or in the presence of metal catalysts.

The generation of halogens by hydrogen peroxide can be carried out either as a two-phase or one-phase reaction. When the reaction is carried out in a two-phase system *i.e.*, hydrogen peroxide solution–organic solvent, a substrate is dissolved in an organic phase, the reaction temperature is limited by the reflux temperature of the solvent, and, which is most important, halogen usage in such a process is much more efficient. When elemental halogen is used, half is lost as HX (HCl, HBr or HI) by-product. In the presence of H<sub>2</sub>O<sub>2</sub>, this by-product is reoxidised to elemental halogen and takes part in the halogenation reaction, which makes the net halogen consumption zero. As a result, the only effluent from the whole process is then water, the sole expected side product of the hydrogen peroxide reaction. An additional advantage is the fact that it is possible to maintain the halogen concentration in the reaction medium at the desired level by controlling the rate of addition of hydrogen peroxide. At last, the system is much easier to handle as halogen transfer and storage facilities are not required.

## Results and discussion

The accelerations of organic reactions by microwave irradiation have been largely exemplified<sup>5</sup> and, therefore, gained popularity in application to both homogeneous and heterogeneous processes. The reduced time of processing under microwave conditions found for a great number of chemical reactions was the main reason that microwave techniques became so attractive to chemists. Moreover, in many cases it was possible to provide pure products in a very high yield.<sup>6</sup> Since the application of microwave irradiation is one of the main interests of our laboratory, we decided to exploit the oxohalogenation of aromatic compounds under microwave conditions. Especially, we decided to focus on the oxohalogenation of carbazole as potential intermediates for use in the synthesis of photosensitive polymers based on 9-vinylcarbazole<sup>7</sup> as well as methacrylates/acrylates containing carbazole pendant groups.<sup>8</sup> Then, we examined the potential of elaborated oxohalogenation procedures for halogenation reactions of other aromatic compounds and tried to scale up some of them.

In the case of carbazole, the number of introduced halogen atoms can be easily controlled by the molar ratio of carbazol/hydrohalic acid (Scheme 2). During the reaction, substitution initially takes place at the 3-positions, then the reaction proceeds at the 6-, 1- and, finally, 8- positions. The bromination reactions to 3-bromocarbazole and 3,6-dibromocarbazole proceeded smoothly in the two-



**Scheme 2** Oxyhalogenation of carbazole.

phase system containing a water solution of hydrogen peroxide (30% wt.) and ethylene chloride as an organic phase. The hydrogen peroxide was added dropwise to the reaction systems over 5 min then the reaction was continued for another 5 min. The bromination reactions were carried out at a temperature of 50 °C in the microwave reactor Plazmatronika (Poland), which was equipped with a magnetic stirrer, continuous power regulation system, and fiber-optic thermometer to control reaction temperature. 1,3,6-Tribromocarbazole and 1,3,6,8-tetrabromocarbazole were obtained within 30 min because of the higher volume of hydrogen peroxide that was needed for the reactions (Table 1). The bromination reactions needed only stoichiometric amounts of both hydrobromic acid and hydrogen peroxide.

Since chlorination reactions are less selective than bromination, chlorine has a lower oxidation potential than bromine and HCl is much more volatile than HBr, in the case of chlorination reactions we needed a 3 fold molar excess of hydrochloric acid for each introduced chlorine atom. Moreover, to achieve a high conversion of carbazole, the reaction temperature was increased to 75 °C, and a small amount of catalyst ( $\text{Na}_2\text{WO}_4$ ) was necessary. When no catalyst was added the final reaction mixtures contained only the unchanged starting materials. Even though, under these catalysed conditions, a total conversion of carbazole was observed, the yield of chlorination reactions was lower, because of the lower selectivity of chlorine in comparison to bromine. The final desired chloroderivatives of carbazole were contaminated by more and/or less chlorinated derivatives, which is a common tendency when carbazole is chlorinated with elemental chlorine. In the case of 1,3,6,8-tetrachlorocarbazole, we managed to obtain this product in

only small yields, while the main product was 1,3,6-tribromocarbazole (Table 1).

Iodination of carbazole in the presence of hydrogen iodide and hydrogen peroxide, in the same reaction system as for chlorination and bromination reactions, did not give satisfactory results. Therefore, it was decided to change from a biphasic to a homogeneous reaction system and apply acetic acid as a solvent, in which all the reagents were soluble. Iodination had to be carried out at 100 °C in order to achieve total conversion of carbazole, but the use of catalyst,  $\text{Na}_2\text{WO}_4$ , as used in the chlorination reactions, was unnecessary. 3-Iodo- and 3,6-diiodocarbazole were prepared in good yields of 80 and 88%, respectively, within 30 min under microwave irradiation, whereas the attempts at synthesis of the tri- and tetra- substituted derivatives led to mixture of products.

Even though the amount of reagents was increased by a factor of 10, *i.e.* instead of 0.5 g of carbazole, 5.0 g was applied, the yield of the reactions remained at same level. However, in these cases it was more important to us that we still managed to maintain short reaction times for the preparation of 3-mono- and 3,6-di-substituted carbazole chloro- and bromo- derivatives (Table 2). These experiments clearly show another advantage of microwave synthesis besides the short reaction times that are usually mentioned.<sup>5</sup> It was shown that after the elaboration of microwave protocol on a small scale, it is relatively easy to scale up a procedure to preparative scale (Table 3).

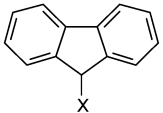
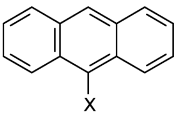
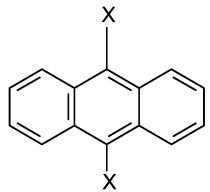
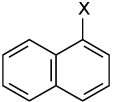
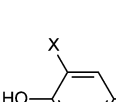
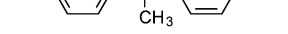
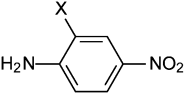
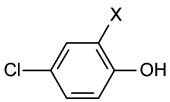
In the next stage of our investigation we decided to exploit the elaborated methods of chlorination, bromination, and iodination of carbazole in the halogenation reactions of other aromatic compounds (Table 2). In this case, different halogeno compounds (*i.e.* chloro-, bromo-, and iododerivatives) were obtained in high yield and short reaction time. Moreover, the example of anthracene shows that introduction of more than one halogen atom into the aromatic structure is also possible (see 9- and 9,10-dihalogenoanthracene). We have found that for aromatic compounds that are sensitive to oxidation no iodination was possible under such

**Table 1** Results of microwave-assisted oxohalogenation of carbazole<sup>ab</sup>

Product		Bromination <sup>c</sup>			Chlorination <sup>d</sup>			Iodination <sup>e</sup>		
		Yield [%]	Time/min	m.p./m.p. lit. <sup>10</sup> [°C]	Yield [%]	Time/min	m.p./m.p. lit. <sup>10</sup> [°C]	Yield [%]	Time/min	m.p./m.p. lit. <sup>10</sup> [°C]
	MW	76	10		73	15		80	30	
	Δ	59	10	197–198 °C/ 198–199 °C	56	15	200–202 °C/ 198 °C	59	30	195–197 °C/ 193–194 °C
	MW selectivity <sup>f</sup>	77	30		77	30		78	30	
	MW	92	10		62	30		88	30	
	Δ	74	10	209–210 °C/ 212–213 °C	53	30	204–205 °C/ 206–207 °C	68	30	211–212 °C/ 208–209 °C
	MW selectivity <sup>f</sup>	90	45		71	50		89	65	
	MW	96	30		64	30				
	Δ	71	30	180–182 °C/ 184 °C	49	30	146–147 °C/ 146–147 °C			
	MW selectivity <sup>f</sup>	92	55		62	60				
	MW	76	30		7	30				
	Δ	56	30	234 °C/ 234–235 °C	2	30	221–222 °C/ 224–224 °C			
	MW selectivity	74	75		7	65				
		0 : 0 : 23 : 76		0 : 5 : 86 : 7						

<sup>a</sup> Isolated yield. <sup>b</sup> Spectroscopic data consistent with those found in the literature. <sup>c</sup> Temperature of the process: 50 °C; HBr : substrate ratio was set to 1 : 1, 2 : 1, 3 : 1, 4 : 1 for mono-, di-, tri-, and tetrasubstituted derivatives, respectively. <sup>d</sup> Temperature of the process: 75 °C; HCl : substrate ratio was set to 3 : 1, 6 : 1, 9 : 1, 12 : 1 for mono-, di-, tri-, and tetrasubstituted derivatives, respectively. <sup>e</sup> Temperature of the process: 100 °C; HI : substrate ratio was set to 1 : 1, 2 : 1 for mono- and disubstituted derivatives, respectively. <sup>f</sup> Yields of mono- : di- : tri- : tetra- halogeno derivatives.

**Table 2** Results of microwave-assisted oxohalogenation of different aromatic compounds<sup>abc</sup>

Product		Bromination <sup>d</sup>			Chlorination <sup>e</sup>			Iodination <sup>f</sup>		
		Yield [%]	Time/min	m.p./m.p. lit. <sup>9</sup> [°C]	Yield [%]	Time/min	m.p./m.p. lit. <sup>9</sup> [°C]	Yield [%]	Time/min	m.p./m.p. lit. <sup>9</sup> [°C]
	MW	88	20		45	20		0 <sup>g</sup>	20	
	Δ	70	20	99–102 °C/ 102–104 °C	39	20	105–108 °C/ 109–111 °C	0	20	—
	MW	85	45		44	60		0	120	
	Δ	94	20	99–102 °C/ 98–101 °C	71	20	106–108 °C/ 108 °C	0 <sup>h</sup>	20	—
	Δ	70	20		39	20		0	20	
	MW	87 <sup>i</sup>	30		59 <sup>i</sup>	30		0 <sup>h</sup>	30	
	Δ	61	30	219–221 °C/ 218–220 °C	51	30	210–213 °C/ 213–215 °C	0	30	—
	MW	40	20		30	20		7	30	
	Δ	25	20	b.p.(10torr) 133–134 °C	30	30	b.p.(12torr) 117–120 °C	0	30	b.p.(5torr) 161–162 °C
	Δ	36	45		35	75		0	120	
	MW	62	30		55	30		—	—	—
	Δ	33	30	135–137 °C	29	30	109–111 °C/ 111–112 °C <sup>10</sup>	—	—	—
	MW	60	60		56	75		—	—	—
	MW	71	20		82	20		91	30	
	Δ	49	20	139–141 °C/ 138–141 °C	41	20	109–112 °C/ 107–110 °C	64	30	113–116 °C/ 111–113 °C <sup>11</sup>
	MW	69	45		79	60		79	75	
	Δ	75	20	37 °C/34–36 °C	61	20	41–44 °C/45 °C	69	30	75–77 °C/ 78 °C <sup>12</sup>
	Δ	52	20		49	20		39	30	
	Δ	74	45		59	50		69	80	

<sup>a</sup> Spectroscopic data consistent with those found in the literature. <sup>b</sup> Isolated yield. <sup>c</sup> Substrate : HX ratio 1 : 1 (for bromination and iodination) and 1 : 3 (for chlorination). <sup>d</sup> Temperature of the process: 50 °C. <sup>e</sup> Temperature of the process: 75 °C. <sup>f</sup> Temperature of the process: 100 °C. <sup>g</sup> 9-H-fluorenone as the only product (yield 29%). <sup>h</sup> 9,10-anthraquinone as the only product (yield 38%). <sup>i</sup> Substrate : HX ratio 1 : 2 for bromination and 1 : 6 for chlorination.

**Table 3** Scale-up of carbazole halogenation

Carbazole <sup>a</sup> : HX ratio	Yields [%]				Time/min
	Mono-	Di-	Tri-	Tetra-	
<b>HX=HBr<sup>b</sup></b>					
1 : 1	74	16	—	—	25
1 : 2	—	91	9	—	25
<b>HX=HCl<sup>c</sup></b>					
1 : 3	67	23	1	—	35
1 : 6	27	61	2	—	60

<sup>a</sup> Typical amount of carbazole: 0.03mol (5 g). <sup>b</sup> Temperature of the process: 50 °C. <sup>c</sup> Temperature of the process: 75 °C.

conditions. The only products were the oxidized substrates *i.e.*, 9,10-anthraquinone and 9-fluorenone for the oxidation of anthracene and 9-fluorene, respectively. However, for arenes that were not conjugated, the desired halogenation products were obtained in high yields, and the position of the halogen atom in the aromatic ring conformed with the general orientation rules for substitution reactions in arenes.

## Summary

In conclusion, the influence of microwave irradiation on the oxohalogenation of carbazole and other arenes was observed, which resulted in shorter reaction times and the increase of product yield in comparison with conventional protocols. The investigations show that the described system of hydrohalic acid–hydrogen peroxide for halogenation of aromatic compounds under microwave conditions is a green alternative for other known halogenation systems, in which generation of stoichiometric amounts of side products (waste) is usually observed. Additionally, the simple set up of the process seems to be valuable for the synthesis of important halogeno compounds like, for example, chlorinated and brominated bisphenol A derivatives, which are known flame retardants for polymeric materials.

## Experimental

All the reactions were carried out in a multimode microwave reactor with a continuous power regulation (PLAZMATRONIKA,



Poland), which was equipped with magnetic stirrer and two inlets on the top and one side of the reactor. The inlets allowed application of an upright condenser and introduction of a fibre-optical sensor (ReFlex, Nortech) which was used to control temperature during microwave experiments. The reactions were carried in commercially available round-bottom Pyrex flasks, 100 mL and 250 mL in capacity for small and large scale experiments, respectively. IR spectra were recorded on a FT-IR BIORAD FTS-165 spectrophotometer as liquids on NaCl disks. <sup>1</sup>H-NMR spectra were collected on a Tesla 487C (80MHz) spectrometer using TMS as an internal standard. The progress of the reactions was monitored by a GC/MS 5890 SERIES II HEWLETT-PACKARD gas chromatograph equipped with Ultra 2 (25 m × 0.25 mm × 0.25 μm) column with HEWLETT-PACKARD 5971 Series Mass Selective Detector. Melting points, measured on Boetius-PHMK 05 microscope plates, are uncorrected.

All the chemicals were purchased from Aldrich and used as received.

*The general procedure for chlorination:* an aromatic compound (3 mmol) was dissolved in ethylene chloride (25 mL) and put into an open vessel that was placed in the microwave oven. Then a 33% water solution of HCl (10 mmol or an appropriate excess for obtaining multisubstituted derivatives) together with Na<sub>2</sub>WO<sub>4</sub> (0.1 g; 0.3 mmol) were added to the solution. Next, the solution was irradiated at 75 °C for specific periods of time (see Table 1 and 2), and, simultaneously, a 30% water solution of H<sub>2</sub>O<sub>2</sub> (10 mmol or an appropriate amount stoichiometric to HCl) was added dropwise to the mixture. The irradiation was continued for an additional 5 min and the reaction mixture was allowed to cool to room temperature. Upon completion, the phases were separated and ethylene chloride evaporated giving the desired product.

*The general procedure for bromination:* an aromatic compound (3 mmol) was dissolved in ethylene chloride (25 mL) and put into an open vessel in the microwave oven. Then a 40% water solution of HBr (3.3 mmol or an appropriate excess for obtaining multisubstituted derivatives) was added to the solution. Next, the solution was irradiated at 50 °C for specific periods of time (see Table 1 and 2), and, simultaneously, a 30% water solution of H<sub>2</sub>O<sub>2</sub> (3.3 mmol or an appropriate amount stoichiometric for HBr) was added dropwise to the mixture. The irradiation was continued for an additional 5 min and the reaction mixture was allowed to cool to room temperature. Upon completion, the phases were separated and ethylene chloride evaporated giving the desired product.

*The general procedure for iodination:* an aromatic compound (3 mmol) was dissolved in acetic acid (80% water solution, 25 mL) and put into an open vessel that was placed in the microwave oven. Then a 58% water solution of HI (3.3 mmol or 6.6 mmol to obtain diiododerivative) was added to the solution. Next, the solution was irradiated at 100 °C for specific periods of time (see Table 1 and 2). Simultaneously a 30% water solution of H<sub>2</sub>O<sub>2</sub> (3.3 mmol or 6.6 mmol to obtain diiododerivatives) was added dropwise to the mixture. Upon completion of the reaction the mixture was put into water and the precipitated product was separated by filtration.

## Acknowledgement

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# Pd-catalyzed completely selective hydrogenation of conjugated and isolated C=C of citral (3,7-dimethyl-2, 6-octadienal) in supercritical carbon dioxide

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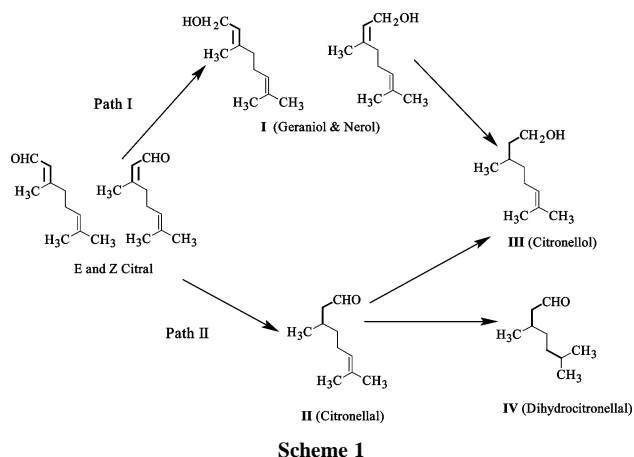
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Mesoporous Pd-MCM-48 as well as Pd/SiO<sub>2</sub>, Pd/Al<sub>2</sub>O<sub>3</sub> catalysts containing 1% of Pd were successfully used in the selective hydrogenation of citral in scCO<sub>2</sub>. The reported results show that it is possible to hydrogenate the conjugated and isolated C=C double bond forming a fully saturated aldehyde, dihydrocitronellal (3,7-dimethyloctanal) under mild conditions. The ascendancy of the scCO<sub>2</sub> medium is established in comparison with the conventional organic solvent and solventless conditions. Changes in different reaction parameters such as H<sub>2</sub> pressure, temperature and nature of the support do not affect the selectivity. Moreover, the catalyst can be recycled several times without any further treatment. Easy separation of the liquid product from the catalyst and the use of environmentally benign solvent make this procedure a viable and an attractive ideal green chemical process for large-scale application. Experimental findings are supported by the theoretical calculations to propose a plausible explanation for the reduction of the conjugated and isolated C=C double bonds in scCO<sub>2</sub>.

## Introduction

Selective hydrogenation of  $\alpha,\beta$ -unsaturated aldehydes is an important research area because of the relevance of these compounds to the pharmaceutical and fine chemical industries.<sup>1-4</sup> The liquid phase hydrogenation of  $\alpha,\beta$ -unsaturated aldehydes has been reviewed by Gallezot and Richard<sup>5</sup> Practically, the hydrogenation of either C=C or C=O is desirable for the manufacture of specialty and other fine chemicals. Among the  $\alpha,\beta$ -unsaturated aldehydes, citral (3,7-dimethyl-2,6-octadienal) is a substrate of special interest to the fragrance and flavors industry.<sup>6</sup> It is an attractive model molecule as it possesses an isolated C=C double bond besides the conjugated C=O and C=C double bonds. The potential products of citral hydrogenation are schematized in



Scheme 1

Scheme 1. The fully saturated aldehyde, dihydrocitronellal (IV), is obtained by the hydrogenation of citral through citronellal (II). Dihydrocitronellal is more stable than citral and could enhance the citrus effect of cologne; hence it can be used in fine fragrances. Several authors have reported the liquid phase hydrogenation of citral over noble metals on different supports,<sup>7-9</sup> bimetallic

catalysts<sup>10</sup> and basic catalysts<sup>11</sup> in various organic solvents to achieve the desired product. Conventionally, among the noble metals, Pd is one of the most active and selective catalysts for reducing the C=C double bond, forming a saturated aldehyde. However, the direct production of IV from citral is not possible in conventional organic solvents even using Pd catalyst. In a recent work, Aramendia *et al.*<sup>7</sup> observed that only the conjugated C=C double bond of citral is hydrogenated producing II using Pd catalyst in different solvents, either polar or non-polar. Traditionally, in organic solvent IV was obtained through the formation of acetals followed by hydrolysis in acidic medium.<sup>1</sup> Since the C=O double bond is replaced by an acetal group, the hydrogenation of the olefinic C=C double bond is favored. Additionally, liquid phase hydrogenations have suffered from serious drawbacks, such as tedious experimental procedure, harsh reaction conditions, long reaction time due to the low solubility of the H<sub>2</sub> which causes mass transfer limitations and the use of large quantities of environmentally damaging solvents. Therefore, the growing demand for a safer reaction poses the need for alternative solvents with low environmental impact.

Supercritical carbon dioxide (scCO<sub>2</sub>) is one of the frequently discussed environmentally benign alternative reaction media for organic synthesis.<sup>12</sup> It has the ability to dissolve many reactive gasses such as H<sub>2</sub> and O<sub>2</sub> to facilitate hydrogenation or oxidation reactions by eliminating the mass transfer limitations, leading to an increase in the reaction rate. Control of the density by altering operating conditions like the pressure and temperature make it easier to tune the solvent properties of the medium. The remarkable physicochemical properties, benign character and low cost of scCO<sub>2</sub> could have positive effects as an environmentally friendly option to achieve the goal of green chemistry. In fact, scCO<sub>2</sub> has also been proved to be a suitable "green medium", especially for hydrogenation in homogeneous<sup>13-16</sup> and heterogeneous catalysis.<sup>17-21</sup> Some recent literature also described scCO<sub>2</sub> as a suitable medium in the selective hydrogenation of  $\alpha,\beta$ -unsaturated aldehydes using a solid catalyst.<sup>22-25</sup> In the present work we report for the first time the exclusive formation of IV with 100% conversion

and selectivity by the hydrogenation of citral over 1% Pd catalysts on different supports in scCO<sub>2</sub> medium. The influence of different parameters such as CO<sub>2</sub> and H<sub>2</sub> pressure and temperature has also been investigated and the results are compared with organic solvent and solventless conditions to prove the efficiency of the scCO<sub>2</sub> medium. We also report theoretical calculations in support of our observations.

## Experimental

Palladium catalyst (1 wt%) was prepared by wetness impregnation with a 0.1 M aqueous solution of palladium chloride (Aldrich) on calcined mesoporous Si-MCM-48. The impregnated material was dried at 353 K for 4 h and calcined in air for 3 h at 573 K (heating rate 2 K min<sup>-1</sup>). The Pd mesoporous catalyst was named as Pd-MCM-48. Before impregnation, the wetting capacity of the support was measured by water titration. Pd/SiO<sub>2</sub> and Pd/Al<sub>2</sub>O<sub>3</sub> were also prepared in the same way as described above. The hydrogenation of citral was carried out in a 50 ml stainless steel batch reactor in the presence of 0.1 g of the Pd-MCM-48 catalyst and 6.5 mmol of the reactant. The reactor was sealed, flushed with CO<sub>2</sub> at 2 MPa pressure for 2–3 times, and then heated at 323 K. A known amount of hydrogen (4 MPa) was first loaded into the reactor. After that, liquid CO<sub>2</sub> was charged into the reactor by a high-pressure liquid pump to the desired pressure. Total pressure control was achieved by a back-pressure regulator. The reaction mixture was stirred continuously with a magnetic stirrer in scCO<sub>2</sub> during the reaction (2 h). At the end of the reaction, the reactor was cooled in ice-cold water and then depressurized carefully with the help of the back-pressure regulator. The liquid product was separated from the catalyst by filtration and identified by GC/MS followed by quantitative analysis using GC (HP 6890, DB-Wax column with

flame ionization detector). Quantification of the products was obtained by a multipoint calibration curve for each product. After the reaction, the catalyst was separated from the reactant and the product, then again mixed with fresh reactant and run for recycle studies of the catalyst. The percentage selectivity (*S*) for each product was calculated by the following expression:

$$\%S = \frac{C_i}{\sum C_p} \times 100$$

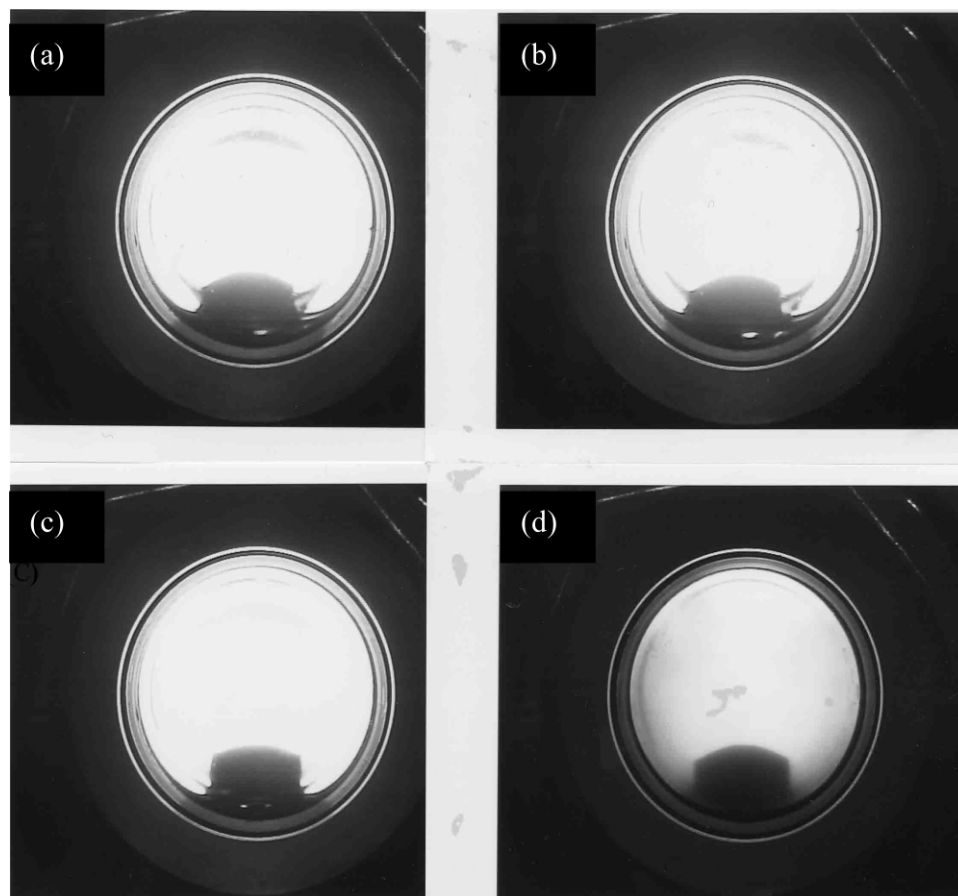
where *C<sub>i</sub>* is the concentration of the product 'i' and  $\sum C_p$  is the total concentration of the product.

Hydrogenations in organic solvents were also carried out in the same 50 ml high-pressure reactor. The reactor was charged with 6.5 mmol of citral, 0.1 g of the catalyst and 5 ml of the solvent and then heated at 323 K. After the introduction of H<sub>2</sub> (4 MPa) the reaction was conducted as described for the scCO<sub>2</sub> medium.

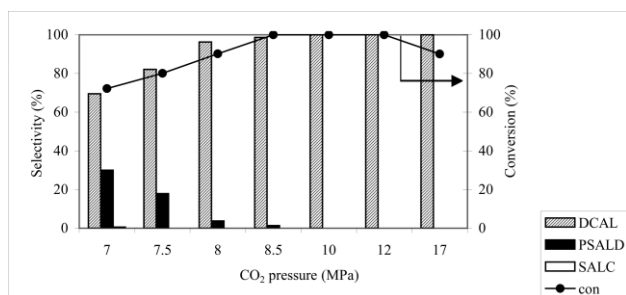
A phase behavior experiment of citral in scCO<sub>2</sub> was conducted at a temperature of 323 K in the presence of a hydrogen pressure of 4 MPa and varying the CO<sub>2</sub> pressure from 7.0 to 17.0 MPa using a 10 ml high-pressure view cell. From naked eye observation, it has been found that the system consisted of a liquid phase along with a CO<sub>2</sub> phase at lower pressure (7 MPa). However, the system revealed partial miscibility of liquid citral and CO<sub>2</sub> at 8–10 MPa pressure. With a further increase in pressure the amount of liquid phase decreased, and finally a homogeneous system was attained at around 11 MPa of CO<sub>2</sub> (Fig. 1).

## Results and discussion

The effect of CO<sub>2</sub> pressure variation on citral hydrogenation has been studied at a constant temperature of 323 K and a hydrogen



**Fig. 1** Visual observation of the reaction system at 323 K under the studied reaction conditions. The black oval shaped object at the bottom is a Teflon coated magnetic stirrer (a) At 7 MPa, liquid citral and gaseous CO<sub>2</sub>, (b) At 8.5 MPa (above the critical pressure of CO<sub>2</sub>), the amount of liquid at the bottom decreased, (c) At 10 MPa, corresponds to the decrease in liquid phase and change to the single phase, (d) At 12 MPa all the reactants were dissolved and a single phase appeared.



**Fig. 2** CO<sub>2</sub> pressure dependence on the conversion and selectivity of the citral hydrogenation. Reaction conditions: citral = 6.5 mmol, catalyst = 0.1 g (1 wt% Pd), P<sub>H<sub>2</sub></sub> = 4 MPa, reaction time = 2 h, Temperature = 323 K; **IV** = dihydrocitraonellal; **I** = geraniol + nerol; **II** = citronellal; **III** = citronellol.

pressure of 4 MPa. The results are summarized in Fig. 2. It is evident that only the conjugated and isolated C=C is hydrogenated following the formation of **IV** with 100% selectivity. As the pressure changes from 7.0 to 10 MPa the selectivity increases from 69.5 to 100%, then remains constant even for the highest CO<sub>2</sub> pressure of 17 MPa. In addition to that, a strong influence of pressure on the citral conversion is also observed (Fig. 2). Above a CO<sub>2</sub> pressure of 8 MPa, conversion strongly increased, reached its maximum at 10 MPa and remained constant when the pressure was further increased to 17 MPa. A slow decrease in conversion (90%) was observed at 17 MPa. Generally, in the dense phase, CO<sub>2</sub> pressure affects most of its properties. In particular, the density of the medium changes significantly with the change in pressure, for example with a change in CO<sub>2</sub> pressure from 8 to 14 MPa the density changes from 520.8 to 802.9 kg m<sup>-3</sup>. Accordingly, a sharp enhancement of the solubility of substrate in CO<sub>2</sub> is observed. From the phase behavior studies (experimental section) it can be stated that at the lower pressure (below 8 MPa) the system contains a liquid phase and a gas phase and that due to the gas-liquid mass transfer limitation the conversion is lower.<sup>26</sup> With increasing pressure as the density increases, the reactant concentration in scCO<sub>2</sub> increases, which results in higher conversion. Consequently, at around a pressure of 17 MPa, the additional amount of CO<sub>2</sub> dilutes the reactant concentration and reduces the conversion.

Table 1 compares the results obtained in scCO<sub>2</sub> with those in the conventional liquid solvent (Run 2–Run 4) as well as in a solventless medium (Run 5) under the studied reaction conditions. A remarkable change in the product distribution was observed when the reaction was conducted in organic solvent and in the solventless conditions. At the same conversion of 25%, the selectivity for **IV** is 100% in scCO<sub>2</sub>, whereas in the organic solvent and in the solventless medium ~73 to 90% **II** is obtained as the

major product. This distinguished behavior in scCO<sub>2</sub> is due to the difference in the adsorption geometry of the reactant to the metal surface. Presumably, α,β-unsaturated aldehyde can adsorb on the metal surface in different ways favoring C=C or C=O adsorption.<sup>27</sup> Under the scCO<sub>2</sub> medium there could be a variation of the adsorption geometry, favoring the hydrogenation of the conjugated and isolated C=C double bonds; generally solvent plays an important role in dictating the selectivity.

Compared to the scCO<sub>2</sub>, citral conversion is lower in hexane and under solventless conditions. Although the conversion is improved in methanol and benzene, the product distribution remains the same. So it is obvious from the results that the scCO<sub>2</sub> medium has a major role in the selective hydrogenation of the conjugated and isolated C=C of citral and significantly enhances the conversion.

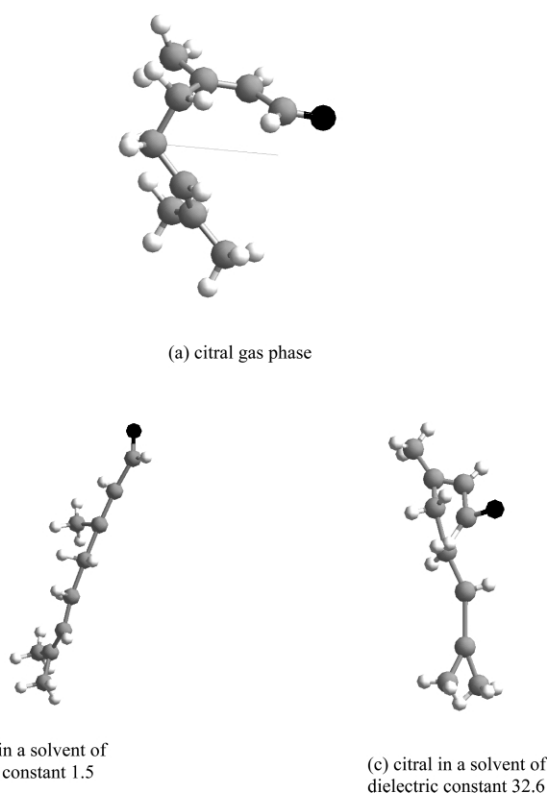
From the above experimental study it has been observed that the adsorption geometry of the reactant and the medium has a strong influence on dictating the selectivity of the reaction. We have performed a preliminary calculation to monitor the effect of solvent on the electronic structure and geometry of the isolated citral molecule considering a gas phase, a non-polar liquid phase with a dielectric constant of 1.6 and a polar solvent with a dielectric constant 32.6 using density functional calculations with B3LYP functional and 6-311G\*\* basis set. The geometries of the three conformers are shown in Fig. 3. The dielectric constant of scCO<sub>2</sub> at our studied pressure range corresponds well to the liquid phase with a dielectric constant of 1.5.<sup>28</sup> The results show that the dielectric constant influences the geometry. The structures of the liquid phases are different from the gas phase. The conformer obtained at very low dielectric constant close to scCO<sub>2</sub> is very linear and the charges derived from Mulliken population indicate that the charge on the terminal oxygen is very high which may result in the favorable C–C bond cleavage through an intermediate, which we are studying now. In contrast, for the conformer in high dielectric constant medium the geometry itself shows that the cleavage of the second C=C is improbable. Here the charge on the terminal oxygen is positive. Though these are preliminary results, at this point comparing the geometries of the conformer we can foresee the favorable nature of scCO<sub>2</sub> over organic solvent in terms of dielectric constant. The calculation indicates a drastic change in geometry and thus proposes a plausible interaction route.

The influence of hydrogen pressure has been considered to be an important factor in directing the conversion and selectivity of the hydrogenation reaction, as hydrogen is miscible in scCO<sub>2</sub>. The effect of H<sub>2</sub> pressure has been examined at a constant CO<sub>2</sub> pressure and temperature of 12 MPa and 323 K, respectively. The results are shown in Fig. 4. From Table 1 it has been observed that, compared to the organic solvents (Run 2 to Run 4) and solventless conditions (Run 5), conversion is higher in scCO<sub>2</sub>. This could be explained by

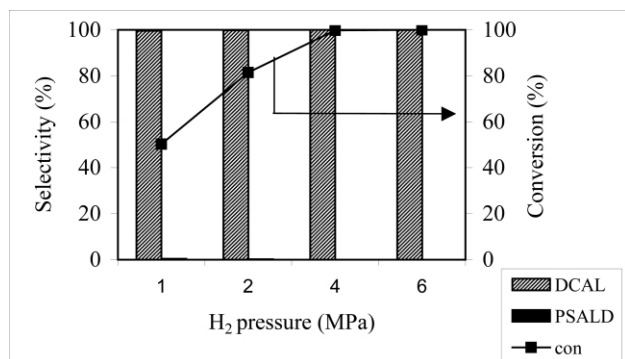
**Table 1** Hydrogenation of citral over Pd supported catalysts under conventional organic solvent medium and solventless conditions

Run	Catalyst	CO <sub>2</sub> pressure/MPa	Organic solvent	Conv. (%)	Selectivity (%)			
					<b>IV</b>	<b>I</b>	<b>II</b>	<b>III</b>
1	<sup>a</sup> Pd-MCM-48	12.0	—	99.8	100.0	0.0	0.0	0.0
2	<sup>a</sup> Pd-MCM-48	—	Benzene	89.5	(100.0)	(0.0)	(0.0)	(0.0)
3	<sup>a</sup> Pd-MCM-48	—	MeOH	90.3	16	1.3	73.0	9.7
4	<sup>a</sup> Pd-MCM-48	—	Hexane	40.5	(12.2)	(0.3)	(80.6)	(6.9)
5	<sup>a</sup> Pd-MCM-48	—	Solventless	14.2	0.2	2.2	88.1	9.5
6	<sup>b</sup> Pd/SiO <sub>2</sub>	12.0	—	96.0	(0.2)	(1.8)	(90.5)	(7.5)
7	<sup>b</sup> Pd/Al <sub>2</sub> O <sub>3</sub>	12.0	—	92.7	2.3	0.0	90.2	7.5
8	<sup>b</sup> Pd/C	12.0	—	97.8	(1.5)	(0.0)	(96.2)	(2.3)
					—	12.9	85.3	1.8

Reaction conditions: citral = 6.5 mmol, catalyst = 0.1 g (1 wt% Pd), P<sub>H<sub>2</sub></sub> = 4 MPa, reaction time = 2 h, Temperature = 323 K.<sup>a</sup> Without reduction. <sup>b</sup> After reduction. <sup>c</sup> Organic solvent = 5 ml. The data in the parentheses represent the selectivity at 25% conversion. **IV** = dihydrocitraonellal; **I** = geraniol + nerol; **II** = citronellal; **III** = citronellol.



**Fig. 3** The geometries of the three conformers of citral, using density functional calculation with B3LYP functional and 6-311G\*\* basis set (a) gas phase; (b) liquid phase with dielectric constant 1.6; (c) liquid phase with dielectric constant 32.6. Color code: black = oxygen; gray = carbon; white = hydrogen.



**Fig. 4** Influence of H<sub>2</sub> pressure on the conversion and selectivity of the citral hydrogenation. Reaction conditions: citral = 6.5 mmol, catalyst = 0.1 g (1 wt% Pd),  $P_{\text{CO}_2}$  = 12 MPa, reaction time = 2 h, Temperature = 323 K; **IV** = dihydrocitronellal; **I** = geraniol + nerol; **II** = citronellal; **III** = citronellol.

the complete miscibility of hydrogen in scCO<sub>2</sub>, increasing the hydrogen concentration in the vicinity of the solid catalyst. This is in close agreement with Fig. 4, which shows that an increase in hydrogen pressure from 1 to 4 MPa enhances the citral conversion from ~40 to 100% keeping the selectivity constant. It was reported that the liquid phase hydrogenation of citral over Ir/TiO<sub>2</sub> in n-heptane<sup>29</sup> and Pt/SiO<sub>2</sub> in hexane<sup>30</sup> was first order with respect to H<sub>2</sub> pressure, which is consistent with the present result until 4 MPa.

The catalyst support can also have a significant effect on the selectivity.<sup>30</sup> We have compared the conversion and selectivity over different Pd catalysts (Run 6–Run 8), other than a mesoporous support. Irrespective of the nature of the catalyst support (Table 1) high conversion to and selectivity for (100%) **IV** was obtained at a pressure of 12 MPa. This could be attributed to the Pd metal that promotes the highly selective hydrogenation of conjugated and isolated C=C in scCO<sub>2</sub> medium. The pronounced selectivity for **IV**

in scCO<sub>2</sub> being independent of the nature of the support may be a consequence of the interaction of the medium with the metal particle, as observed in the adsorption spectrum of small gold particles in scCO<sub>2</sub> medium<sup>28</sup> or a different energetic path of the reaction, which needs further detailed study.

The temperature does not have any strong influence on the selectivity of the described reaction in scCO<sub>2</sub> medium. As the temperature changes the conversion increases but the selectivity remain constant whereas, in the organic solvents the selectivity for **II** sharply decreases with increasing temperature.<sup>7</sup>

In this study recycling of the Pd catalyst is successfully carried out under the studied reaction conditions. After four successive cycles of operation the catalyst does not show any change in the conversion and selectivity. In liquid phase hydrogenation of citral deactivation of the catalyst was known to occur *via* concurrent side reactions, producing inhibited product<sup>31</sup> or by the leaching of the active metal site. To measure the probability of leaching of Pd, we analyzed the liquid product for the metal but no information about leaching was obtained. No significant deactivation of Pd mesoporous catalysts was observed during the reaction up to a long period of 16 h, though serious deactivation of the catalysts took place during hydrogenation of ethyl pyruvate in scCO<sub>2</sub> using conventional catalysts such as Pd/Al<sub>2</sub>O<sub>3</sub>.<sup>32</sup>

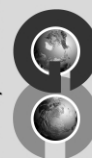
## Conclusions

In conclusion, this study demonstrated that scCO<sub>2</sub> medium is a unique reaction medium to achieve the selective hydrogenation of conjugated and also isolated C=C using different types of Pd catalysts. Experimental findings are also supported by the theoretical calculation. The change in different reaction parameters such as H<sub>2</sub> and CO<sub>2</sub> pressure does not change the selectivity. The highest conversion to and selectivity for **IV** is achieved only in scCO<sub>2</sub>. Furthermore, in the liquid phase reaction a separation procedure for the mixture of reactant and products is further required, but in scCO<sub>2</sub> medium the desired product can be separated easily by simple filtration and the catalyst can be reused several times without loss in the activity and selectivity. Clearly, the methodology presented here could be highly relevant for the further development of a clean chemical process to hydrogenate the different diene compounds with conjugated and isolated C=C based on Pd catalysts in a “green” and clean medium.

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# Indium metal mediated synthesis of homoallylic amines in poly(propylene)glycol (PPG)

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Reaction of aldimines and sulfonylimines with indium powder in poly(propylene) glycol (MW *ca.* 1000), a benign, recyclable reaction medium, results in the formation of corresponding homoallylic amines and sulfonamides in high yield.

## Introduction

The use of indium metal to mediate chemical reactions has gained prominence in recent years, specifically in those reactions which can be described as 'benign by design', such as modifications to standard Michael addition,<sup>1</sup> cross-aldol,<sup>2</sup> pinacol-coupling,<sup>3</sup> and *in situ* Barbier-type Grignard reactions.<sup>4</sup> This relates to the metal's unique characteristics which include a low first ionisation potential (5.70 eV), its ability to be recycled electrochemically, not being sensitive to boiling water or alkali, and not readily forming oxides in air.<sup>4</sup>

In the case of the Barbier addition to carbonyl containing compounds, it can be carried out in water, and has been shown to be functional group tolerant, for example with carbohydrates.<sup>3–5</sup> In contrast, extending such addition reactions to C=N containing compounds in aqueous media has been limited,<sup>6,7</sup> despite the importance of homoallylic secondary amines as fundamental building blocks for many biologically active compounds, such as antifungal agents,<sup>8,9</sup> and the synthesis of many nitrogen containing natural products such as amino acids,<sup>10</sup> amino sugars and  $\gamma$ -lactams.<sup>11</sup> This has been attributed to several inherent characteristics of imines which includes their sensitivity to water, their relatively low electrophilicity, and their tendency to deprotonate when they are derived from enolizable carbonyl compounds.<sup>12,13</sup> Therefore, in aqueous media aldimines can rapidly hydrolyse to the corresponding carbonyl compounds prior to allylation, thus affording secondary alcohols rather than the target secondary amines.<sup>6,7</sup>

One other non-aqueous 'benign' route to homoallylic amines which has been developed uses an electrochemical pathway.<sup>14</sup> However, although this method negated the hydrolysis of the starting aldimine, unidentified allylated products were also generated.

The difficulties associated with the use of aldimines in aqueous media has been largely overcome by their replacement by sulfonyl imines<sup>6,7</sup> which are both hydrolytically robust and more electrophilic. The sulfonyl group of the resultant secondary amine can, subsequently, be easily removed to give the corresponding primary amine.<sup>13</sup> However, despite this valuable synthetic property, in terms of the green chemistry metrics (benignness), the synthesis of homoallylic secondary amines *via* sulfonylimines is less than desirable given that their synthesis often incorporates indefinite reaction times and the use of highly reactive and toxic reagents such as TiCl<sub>4</sub>.<sup>15–17</sup> Aldimines, on the other hand, can be readily prepared with favourable green chemistry metrics involving a solvent free route.<sup>18</sup>

As a consequence current investigations have focused on developing more benign protocols for the allylation of aldimines.

Our previous studies looking at mediation by indium metal under solvent free conditions consistently produced a mixture of the homoallylic and the bis-allylated amine,<sup>18</sup> which we concluded derives from the formation of an iminium salt intermediate, which subsequently undergoes competitive nucleophilic attack from the persistent allylindium halide species.<sup>18</sup>

In turning from these solvent free and aqueous methodologies, several alternative reaction media have been considered including; ionic liquids, supercritical CO<sub>2</sub>, polyethylene glycol (PEG) and polypropylene glycol (PPG). PPG has several advantages over other potential reaction media, including; (i) it is commercially available, (ii) economic considerations (AUD\$86.60 for 500 g),<sup>†</sup> (iii) it is thermally robust, (iv) it can potentially be recycled,<sup>19</sup> (v) it has low toxicity, as highlighted by its frequent use in pharmaceuticals and cosmetics,<sup>20</sup> and (vi) significantly, unlike many volatile organic solvents, it can be obtained from non petroleum-based starting materials such as lactic acid derived from corn.<sup>21</sup>

Herein we now report a Barbier-type synthesis of homoallylic secondary amines from aldimines and sulfonylimines in PPG (MW *ca.* 1000). This MW PPG is liquid at room temperature with a viscosity of 150 centistokes at ambient temperatures. Its range of molecular weight components allows for isolation of volatile products to be performed by distillation under high vacuum from the higher boiling point (> 175 °C, 3 mmHg) components of the PPG. Conversely when less volatile products are formed, the lower molecular weight/lower boiling point components (< 125 °C, 3 mmHg) of PPG can be employed as the reaction media, with isolation of the organic components occurring by the removal of PPG by distillation. This minimizes the use of chromatographic techniques and associated use of relatively large volumes of organic solvents.

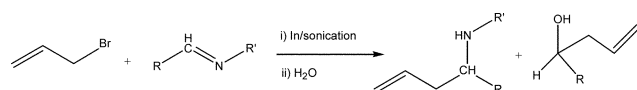
## Results and discussion

### Aldimines

The standard reaction procedure simply involved reacting the aldimine, indium powder and allyl bromide in PPG in a 1 : 1 : 1.5 ratio under sonication at room temperature (Scheme 1). Extraction of the homoallylic amine was by small amounts of diethyl ether. Overall these reactions went smoothly with no evidence of decomposition of the starting materials or of the production of bis-allylated species as we have described elsewhere for analogous solventless reactions.<sup>18</sup> <sup>1</sup>H NMR analysis of the crude ether extract

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R = Alkyl, Aryl groups  
R' = Alkyl, Aryl groups or SO<sub>2</sub>Ph

**Scheme 1** The synthesis of homoallylic secondary amines in PPG.

revealed the reaction products to be the target homoallylic amine and the homoallylic alcohol, which derives from hydrolysis of the aldimine. By pre-drying the PPG, thus preventing the hydrolysis process, yields were significantly improved by *ca.* 20%. When reactions were performed on aldimines derived from aromatic aldehydes (Entries 1–4, Table 1) relatively high yields (76–95%), were obtained comparable with analogous Barbier–Grignard reactions performed in VOC's using various metal mediators, namely; In,<sup>22,23</sup> Zn,<sup>24</sup> Mg,<sup>24</sup> Cd<sup>25</sup> and Sm.<sup>26</sup> Importantly, in comparison with the electrochemical route, improved yields were also observed.<sup>14</sup> When moving from the aldimines to the  $\alpha,\beta$ -unsaturated imine (Entry 12, Table 1) a reduction in yield was observed reflecting the decreased electrophilicity of these imines. However, in terms of chemoselectivity only the 1,2-adduct was observed (Entry 6, Table 1).

### Effects of sonication

The reactions were also conducted with only rapid stirring, however, there was an observable decrease in yields for all aldimines (by *ca.* 6–12%) from when the reactions were performed under sonication. This can be accounted for by the limited solubility

of the imines in PPG, which is improved by sonication, and the influence of sonic energy in creating a constantly clean metal surface.<sup>27</sup>

### Recycling

To investigate whether the PPG could possibly be recycled without compromising product yields, the reaction with benzylidene aniline was conducted three times in the same 10 ml of PPG. After each reaction and isolation of the homoallylic amine, phenyl(1-phenylbut-3-enyl)amine, by distillation, the PPG was washed with water (10 ml) and filtered to ensure complete removal of any inorganic salts, before being re-dried over anhydrous MgSO<sub>4</sub>. The use of the higher molecular weight fraction of the distilled PPG ensured the PPG and water would form two distinct layers with only a loss of < 3% of the PPG in each cycle through partitioning and re-collection. The very low solubility of this fraction of PPG in water meant that despite a slight increase in the amount of homoallylic alcohol, indicating that the PPG does not dry over the anhydrous MgSO<sub>4</sub> to previous levels, only a slight reduction in the yield of the amine, by a few percent in each cycle, was observed. This could be easily overcome by the development of a more efficient drying process which would maintain high product yields.

### Gallium

In contrast to indium we have previously established that gallium metal is efficient at producing homoallylic amines from imines under solvent free conditions.<sup>18</sup> Given the similar first ionisation

**Table 1** Indium mediated allylation reactions with aldimines and sulfonylimines under sonication

Entry	Imine	Allyl bromide	Product	Yield% <sup>a</sup>
1	PhC(H)=NPh			95
2	2-(MeO)PhC(H)=NPh			82
3	4-(MeO)PhC(H)=NPh			78
4	2-(OH)PhC(H)=NPh			76
5	PhC(H)=N-2,6-(Me)-Ph			34
6	PhC(H)=C(H)C(H)=NPh			62 <sup>b</sup>
7	PhCH=NSO <sub>2</sub> Ph			96
8	PhCH=NSO <sub>2</sub> Ph			93 <sup>b</sup> <i>anti</i> : <i>syn</i> 44 : 56
9	PhCH=NSO <sub>2</sub> Ph			91 <sup>b</sup> <i>anti</i> : <i>syn</i> 48 : 52
10	PhCH=NSO <sub>2</sub> Ph			32 <sup>b</sup> <i>anti</i> : <i>syn</i> 1 : 5
11	4-(MeO)PhC(H)=NSO <sub>2</sub> Ph			86
12	PhC(H)=C(H)C(H)=NSO <sub>2</sub> Ph			89

<sup>a</sup> Isolated yield. <sup>b</sup> Obtained as a mixture of diastereoisomers, with ratio of *syn* : *anti* being estimated by <sup>1</sup>H NMR.

potentials of indium, 5.70 eV, and gallium, 5.99 eV,<sup>28</sup> it was of interest to examine the comparative performance of gallium in PPG. However, we found no homoallylic amine was produced, even with extended reaction times (*ca.* 24 h) and sonication. More surprisingly, no homoallylic alcohol was produced either. This inertness most likely results from several factors; the reaction of the allylgallium species with the numerous hydroxyl groups present in PPG, the ease with which organogallium species are hydrolysed in the presence of H<sub>2</sub>O, and galloxane formation in the presence of KOH.<sup>29</sup> These factors are of no great concern when using indium.

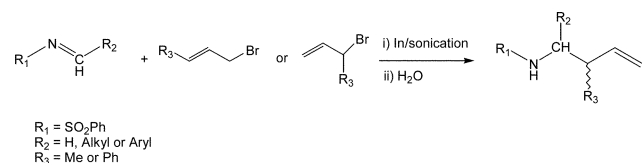
### Sulfonylimines

To extend the scope of the reaction protocols we also investigated the allylation of sulfonylimines with indium metal as a mediator. Initially reactions were performed using the higher boiling point components (> 175 °C, 3 mmHg) of the distilled PPG, accompanied by sonication. Although <sup>1</sup>H NMR spectra of the crude reaction mixtures indicated that the reactions had essentially gone to completion, when attempting to isolate the sulfonamides by vacuum distillation it was found that this was not a feasible extraction method due to their high boiling points. Furthermore, it has been established that sulfonamides can undergo thermal decomposition under reflux conditions at relatively low temperatures.<sup>30,31</sup> Therefore, an alternative method was established: using lower boiling point fractions (< 125 °C, 3 mmHg) of the pre-distilled PPG allowed the sulfonamides to be successfully isolated by removing the PPG under high vacuum from the crude reaction mixture.

In comparison with the homoallylic amines, there was a slight improvement in the yields for the sulfonamides, which can be explained by the increased electrophilicity of the C=N bond.<sup>13</sup> However, the yields are slightly lower than those obtained in aqueous solution<sup>7</sup> which could be attributed to the favourable role played by water as a complexing ligand. As observed in the aldimine reaction, only the 1,2-addition product was obtained (in 89% yield) when the  $\alpha,\beta$ -unsaturated sulfonimine, *N*-(3-phenylallylidene)benzenesulfonamide (Entry 12, Table 1) was employed.

### Selectivity

Loh *et al.* have described the effect of moving from one solvent to another on the selectivity of the Barbier–Grignard reaction.<sup>32,33</sup> Thus, we were interested in the regio- and diastereo-selectivity exhibited by sulfonylimines in PPG. Consequently, reactions of *N*-benzylidenebenzenesulfonamide were conducted with crotyl bromide, 3-bromo-2-methylpropene and cinnamyl bromide (Entries 8–10, Table 1) and it was found that the  $\gamma$ -allylation products were exclusively obtained (Scheme 2), which is in accordance with the



**Scheme 2** Regioselectivity of allylation reactions performed in PPG, with the  $\gamma$ -adduct predominating.

regioselectivity previously observed for indium mediated allylation reactions performed on carbonyl compounds in aqueous media.<sup>34</sup> This implies that the substituent is found  $\alpha$  to the new C–C bond irrespective of the position of the substituent on the substituted allyl bromide

Diastereoselectivity also appears to be in accordance with the aqueous systems<sup>35</sup> though the degree of selectivity increased as the size of the substituent increased on the allyl bromide. Approximately a 1 : 1 ratio between the *syn* : *anti* adducts resulted from the addition of crotyl bromide and 3-bromo-2-methylpropene bromide,

whilst additions performed using cinnamyl bromide resulted predominantly in the *syn* adduct (*ca.* 5 : 1, *syn* : *anti*).

### Conclusion

We have established that PPG is a versatile benign solvent for the indium metal mediated allylation of imines and sulfonylimines. In contrast, gallium metal is totally ineffective in this medium due to the susceptibility of the allylgallium intermediates to decomposition from entrained H<sub>2</sub>O, the hydroxyl groups and KOH. It clearly offers an alternative to organic solvents as a reaction media in synthesis and gives an alternative to other benign reaction media, such as water, which can only be used for hydrolytically robust processes. The possibility of recycling the PPG reaction medium was also established.

### Experimental

PPG is commercially available and was purchased from Aldrich, as was indium powder. The PPG we employed in reactions had an average MW of *ca.* 1000, with a viscosity of 150 centistokes at 25 °C and had a hydroxyl number of 111 mg KOH per g. Prior to use, the PPG was distilled, *in vacuo* (3 mmHg) up to 125 °C, and the distillate collected, dried over MgSO<sub>4</sub>, and used in the reactions with sulfonylimines. The higher boiling point (> 175 °C) components left behind were collected, filtered through a silica plug and dried over MgSO<sub>4</sub> before use in additions to aldimines.

Reactions employing sonication were performed in the Transtec Systems, Soniclean 80T model. This sonicator runs at 240 V with an operating frequency of 50/60 Hz. All aldimines were synthesised *via* the previously reported solvent free method.<sup>18</sup> The sulfonylimines were prepared following a previously reported synthesis for the synthesis of *N*-phosphinoyl imines, with alterations.<sup>15,16</sup> <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> on the Varian Mercury 300 at 300 MHz. Infra-red spectra were obtained on a Perkin-Elmer 1600 FTIR.

### Typical synthetic procedures for synthesis of homoallylic amine

**Synthesis of phenyl(1-phenylbut-3-enyl)amine.** To approximately 10 ml of previously dried PPG, 0.18 g of indium metal (1.6 mmol) and 0.28 g of benzylidene aniline (1.6 mmol) was added under an inert atmosphere of argon. To this suspension, 1.5 equivalents of allyl bromide (0.29 g, 2.4 mmol) were added. This was allowed to sonicate for 3 h, which resulted in the complete consumption of indium metal and the formation of an orange/brown precipitate, indicating the formation of the allylindium reactive species. The reaction mixture was then quenched with H<sub>2</sub>O (*ca.* 0.5 ml) and allowed to sonicate for a further 15 min. The reaction mixture was then purified by fractional distillation, under high vacuum, to afford the clear oil of phenyl(1-phenylbut-3-enyl)amine. The spectral properties of the homoallylic amine were in accordance with data previously reported.<sup>36</sup> Bp 138–140 °C (3 mmHg); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 30 °C, 300 MHz)  $\delta$  7.55 (4H, m, *o*-, *m*-H), 7.08 (1H, t, *p*-H), 6.78 (4H, m, *o*-, *m*-H), 6.51 (1H, d, *p*-H), 5.82 (1H, m, –CH=CH<sub>2</sub>), 5.11 (2H, d, –CH=CH<sub>2</sub>), 4.63 (1H, m, –CH–NH), 4.30 (1H, br m, –NH), 2.44 (2H, m, CH<sub>2</sub>–CH); MS ES (+) Calculated for C<sub>16</sub>H<sub>17</sub>N *m/z* 223.31 Found *m/z* 224.0.

**Synthesis of *N*-(4-methoxybenzylidene)benzenesulfonamide.** To a previously dried Schlenk flask, 0.63 g (4 mmol) of benzenesulfonamide was added. This was dissolved in approximately 20 ml of dry dichloromethane (molecular sieves). To this solution 0.54 g (4 mmol) of 4-methoxybenzaldehyde and 1.22 g (12 mmol) of anhydrous triethylamine was added and the mixture was then cooled to 0 °C in an ice bath whereupon 2.20 ml of TiCl<sub>4</sub> (1 M, CH<sub>2</sub>Cl<sub>2</sub>, 2.2 mol) was added over 5 min. The solution was then allowed to stir on ice for 2 h, followed by 12 h of stirring at room temperature. This resulted in a yellow solution with cream

precipitate of titanium dioxide. The solution was diluted with 75 ml of toluene with the titanium dioxide being removed by suction filtration over Celite. The residue was washed with a further 50 ml of dry toluene. The resulting solution was placed under high vacuum to remove any unreacted aldehyde and toluene. The resulting cream precipitate was recrystallised from toluene and hexane, affording the microcrystalline white precipitate of the desired imine. Spectral properties of the compound were consistent with spectra previously reported.<sup>15</sup> Mp 118–119 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 30 °C, 300 MHz) δ 9.03 (1H, s, –CH), 8.16 (2H, m, aromatic-H), 7.91 (2H, m, aromatic-H), 7.58 (3H, m, aromatic-H), 7.13 (2H, m, aromatic-H), 3.92 (3H, s, –OCH<sub>3</sub>); IR Nujol mull, 1590.3 cm<sup>-1</sup> (m, C=N), 1162.0 cm<sup>-1</sup> (m, sulfone), 722.6 cm<sup>-1</sup> (s, C–H aromatic), 688.3 cm<sup>-1</sup> (s, aromatic).

**Typical procedure for allylation of sulfonamides; synthesis of *N*-[1-(4-methoxyphenyl)-3-butenyl]benzenesulfonamide.** To a suspension of 0.73 mmol (0.2 g) of *N*-(4-methoxybenzylidene)benzenesulfonamide and 0.73 mmol (0.08 g) of indium metal in PPG, 1.5 equivalents (0.13 g, 1.09 mmol) of allyl bromide was added. This suspension was then allowed to sonicate for 3 h, which resulted in the complete consumption of indium metal and the formation of a white precipitate. The reaction mixture was then quenched with 0.5 ml of water. The PPG was removed from the reaction mixture under high vacuum at 125 °C. This resulted in the isolation of the white powder of the desired amine, which was further purified by crystallisation in a methanol–hexane solution. On analysis the spectral properties of the amine were in accordance with data previously reported.<sup>7</sup> Mp 70–72 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 30 °C, 300 MHz) δ 7.68 (2H, aromatic H, m), 7.48 (1H, aromatic-H, m), 7.35 (2H, m, aromatic-H), 6.89 (2H, aromatic-H, d, *J* = 9.4 Hz), 6.75 (2H, aromatic-H, d, *J* = 9.4 Hz), 5.58 (1H, m, –CH=CH<sub>2</sub>), 5.11 (2H, m, –CH=CH<sub>2</sub>), 4.80 (1H, br s, –NH), 4.36 (1H, dd, *J* = 7.1 Hz, –CH<), 3.78 (3H, s, –CH<sub>3</sub>), 2.42 (2H, m, –CH<sub>2</sub>–CH=); IR Nujol mull 3276.3 cm<sup>-1</sup> (m, amide), 1453.8 cm<sup>-1</sup> (s, sulfone), 1317.6 cm<sup>-1</sup> (m, alkene), 1161.2 cm<sup>-1</sup> (s, sulfone), 728.6 cm<sup>-1</sup> (s, C–H aromatic), 690.3 cm<sup>-1</sup> (s, aromatic).

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