Impact Factors and Awards

It is especially pleasing to be able to start this editorial with the news that that the impact factor for this journal has reached the dizzy heights of 2.477 for the year 2001. This is our first "official" score, although we did receive an unofficial rating of 2.2 for the year 2000. This is a tremendous achievement especially for a new journal and can be attributed to the very high quality of articles that we are attracting. I would like to take the opportunity to thank my colleagues at Cambridge and York for all of their hard work and my colleagues on the editorial board for their excellent support in making this the premier journal for green chemistry research and information. We have come a long way since those long planning meetings some four years ago when we were able to turn a dream into a reality.

Green chemistry can indeed turn dreams into reality as was further witnessed this July when the world's first supercritical fluids reaction plant was opened in Durham, England. The plant which belongs to the Thomas Swan company is the latest in a long line of environmentally responsible technologies introduced by the company. The new facility will exploit proven new technology to replace conventional solvents by inert supercritical fluids for several key chemical technologies. Behind this excellent example of green chemical technology at work is a very successful academic–industrial collaboration with the University of Nottingham's Chemistry Department (UK). Congratulations to the company and to the academic scientists involved in the associated pioneering research.

Congratulations are also due to this years winners of the US Presidential Green Chemistry Awards. These nicely illustrate the range of applications for green chemistry. Supercritical solvents are also featured here with a new cleaning application and a new family of CO_2-soluble materials. The vital importance of green chemistry in the synthesis of pharmaceuticals is demonstrated in the new cleaner and simpler manufacture of Sertraline. Improvements include a reduction in the number of steps and in the number of solvents used – nicely illustrating the concept of green chemistry as being a series of reductions. I have written before about the (literally) growing importance of renewable feedstocks for sustainable chemicals manufacturing and the associated reduction in the use of fossil feedstocks. This will require continuous innovation in the way that we exploit biomass. The award for NatureWorks™ a new family of plastics manufactured entirely from renewable resources is a splendid example of this especially as production in the first world-scale 140,000 t/y plant began just a few months ago – another proven commercial-scale application of green chemistry. The US awards also honour another green chemistry reduction, that of reduced toxicity, for a new arsenic-free and chromium-free wood preservative. You can read more about these awards in this issue of *Green Chemistry*.

James Clark
York, UK
July 2002

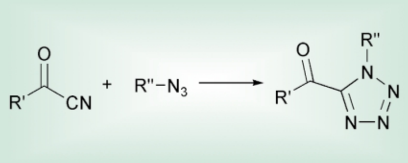
DOI: 10.1039/b206504p

Highlights

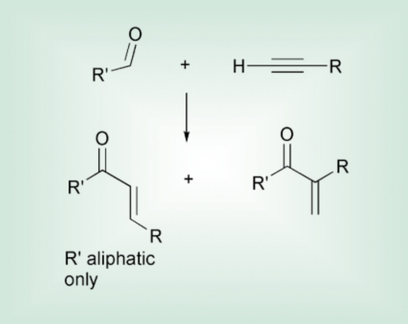
Duncan Macquarrie reviews the recent literature on green chemistry

Additions

Cycloadditions can provide an excellent clean route to functional heterocycles. Zachary Demko and Barry Sharpless of the Scripps Institute, La Jolla, USA, have recently reported examples of such chemistry which run without solvent and in almost quantitative yields (*Angew. Chem., Int. Ed.*, 2002, **41**, 2113). They have found that heating acyl cyanides with azides at 120 °C yields the tetrazole in yields of over 90%. No solvent is required for the reaction, and the isolation step is relatively straightforward, but could often be omitted in a multi-step synthesis. The products are versatile synthons for a range of further elaborations.



Additions of aldehydes to alkyne derivatives is another potentially very clean route to highly versatile enone derivatives. Chul-Ho Jun and co-workers from Yonsei University in Seoul, South Korea, have now published details of the relatively unexplored addition of aldehydes to terminal alkynes (*Angew. Chem., Int. Ed.*, 2002, **41**, 2146). They found that the Rh catalysed addition of the two components proceeded smoothly under mild conditions in toluene, to produce the branched enone as the major component (for aromatic aldehydes, this product was formed exclusively). Yields varied from 63% to 98%, with most examples being above 80%.



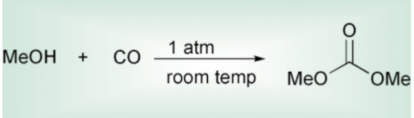
CFCs

The problem of what to do with CFCs is still a pressing one. Some work has been done which has provided routes whereby the CFCs can be converted to useful, non-ozone-depleting raw materials such as tetrafluoroethene, but this approach cannot be used for *e.g.* $ClCF_3$. Now Noriyoki Sonoyama and Tadayoshi Sakata of the Tokyo Institute of Technology have described an electrochemical route which allows the production of trifluoroacetic acid from $ClCF_3$ (*Chem. Lett.*, 2002, 444) They mixed the two gases under pressure in an autoclave and then electrolysed them in the absence of oxygen. The CF_3^- anion formed is rapidly quenched by CO_2 to give the carboxylic acid in yields of up to 85%, with current efficiencies of around 70%.

$$ClCF_3 \xrightarrow{\text{electrolysis}} CF_3CO_2H$$

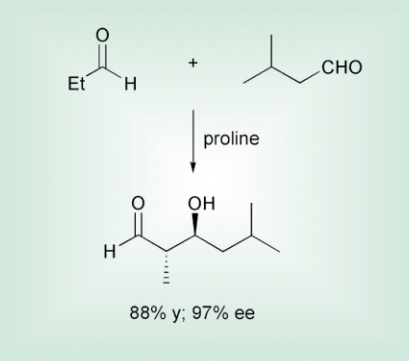
Carbonylations

Dimethyl carbonate as seen as a safe alternative to phosgene for carbonylation reactions. Current synthetic routes to this material have room for improvement, and mild and efficient conditions are still sought. The group led by Ichiro Yamanaka of the Tokyo Institute of Technology, Japan, have now published details of an electrolytic one-step route to dimethyl carbonate from methanol and CO under mild conditions (*Chem. Lett.*, 2002, 448). Since existing electrochemical routes are relatively inefficient, the group redesigned both the cell and the electrode (Pd on a vapour grown carbon fibre) in order to enhance the concentration of the two reaction components at the electrode surface. They achieved 67% current efficiency and 82% selectivity based on CO under 1 atmosphere of CO and at room temperature.



Aldol reactions

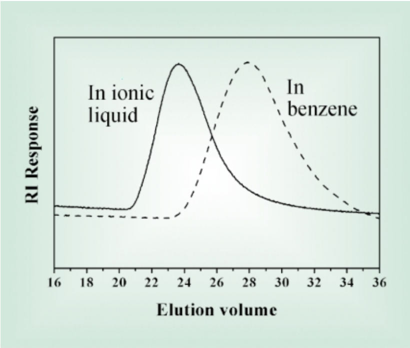
The aldol addition is one of the most effective methods for building up complex organic molecules. In particular, those which do not require pre-activation / protection sequences are particularly attractive from a green chemicals perspective, and several groups have made advances in this area. One of the most challenging situation is that where two aldehydes must be coupled, and so far little has been achieved in this area. Now, Alan Northrup and David MacMillan of the California Institute of Technology, USA, have shown that not only is this possible, but that it can be done with excellent selectivity, using proline as catalyst (*J. Am. Chem. Soc.*, 2002, **124**, 6798). Slow addition of an aldehyde donor (typically propionaldehyde) to the aldehyde acceptor in a range of solvents at 4 °C gave yields of around 80%, with *anti*:*syn* ratios of 3 : 1 to 24 : 1 and ee's of > 95%.



Ionic liquids

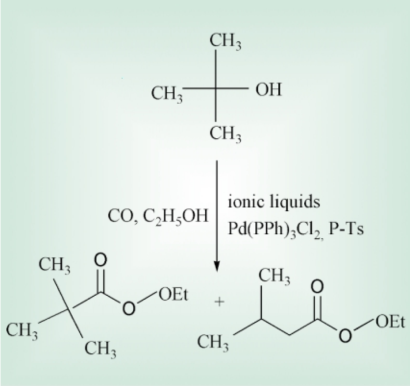
Ionic liquids have been shown to be very versatile solvents for a wide range of reactions. The US group led by Jimmy Mays, Christopher Brazel and Robin Rogers from the Universities of Alabama and Tennessee, and the Oak Ridge National Laboratory have now shown that these liquids are useful in the free-radical polymerisation of methyl methacrylate and styrene (*Chem. Commun.*, 2002, 1368). They found that polymerisation in these liquids proceeded smoothly to give polymers with higher molecular weights than those formed in organic solvents. The polymer separated from the ionic liquid as the reaction proceeded, and further purification with methanol or

DOI: 10.1039/b206505n



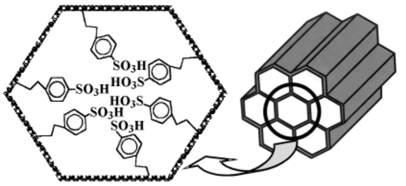
aqueous ethanol could be used to remove traces of the ionic liquid. In a second paper, they also show that the ionic liquids can behave as plasticisers in the polymers, potentially giving a direct route to plasticised materials (*Chem. Commun.*, 2002, 1370). Additionally (*Chem. Commun.,* 2002, 1394) they demonstrate the alternating copolymerisation of styrene and CO.

A further application of ionic liquids has been published. Kun Qiao and Youquan Deng of the Chinese Academy of Sciences in Lanzhou, China, have shown that carbonylation / esterification reactions can be eficiently carried out (*New J. Chem.,* 2002, **26**, 667). By using a transition metal / phosphine system in the presence of *p*-toluene sulfonic acid in ionic liquids they could react *t*-butanol with CO and ethanol to produce ethyl *iso*-valerate and ethyl *t*-valerate in total yields of up to *ca.*80%. Conventional solvents gave yields of <38%, with the main products in ethanol and toluene being isobutene and ethyl isobutyl ether. In general a 4:1 selectivity towards the *iso*-ester was found.



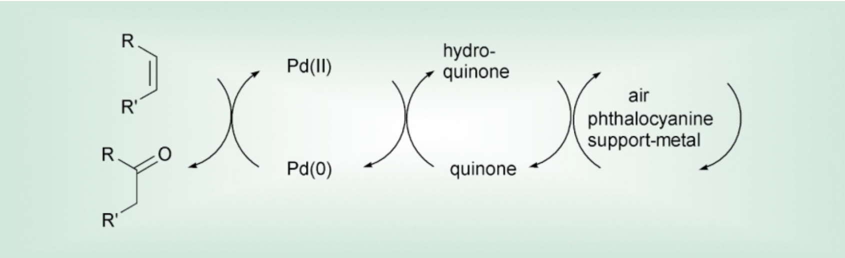
Mesoporous materials

The development of strongly Bronsted acidic solids has been a lively theme in catalysis for some time. One potentially clean method for the preparation of such materials is the formation of suitably substituted mesoporous silicas using neutral templates, which can be washed out and recovered. Juan Melero and colleagues from Rey Juan Carlos University in Madrid, Spain, have now published details of a new silica-arene sulfonic acid material, which has a higher acidity that the propane sulfonic acid-functionalised materials previously available (*J. Mater. Chem.*, 2002, **12**, 1664). They condensed 2(4-chlorosulfonylphenyl)-ethyltrimethoxysilane with tetraethoxysilane under aqueous conditions in the presence of a poly(alkylene oxide) surfactant to give the material, which was capable of catalysing the Fries rearrangement of phenyl acetate with an activity similar to that of an amberlyst resin and about twice that of an alkane sulfonic acid-functionalised silica.



Oxidations

An interesting extension of a known class of oxidation catalysts has been published by Didier Villemin and colleagues at the University of Caen (*Synth. Commun.*, 2002, **32**, 1501). They have coupled the known ability of supported metal phthalocyanines to catalyse the aerobic oxidation of *e.g.* hydroquinone to quinone to the ability of quinone to re-oxidise transition metals such as Pd and Ru (see below). In this way they have developed methods for the aerobic oxidation of alcohols to aldehydes, alkenes to ketones and 1,3-hexadiene to 1,4-diacetoxycyclohexene. Yields in the first two reaction types were very high, with excellent selectivity, while the third reaction type gave a yield of 50%.



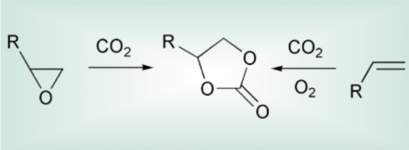
Catalysis

J. Mol. Catal., A volumes 182-183 contain papers from the 10th International Symposium on Relations between Homogeneous and Heterogeneous Catalysis, many of which are of interest in a green context.

In particular, the following two papers are of interest:

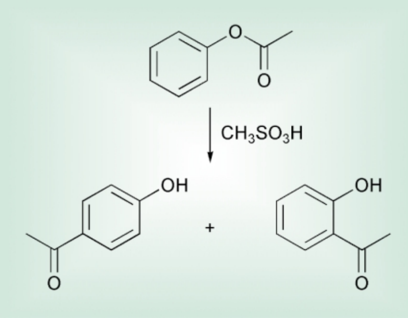
CO_2 as a raw material

Michele Aresta and Angela Dibenedetto of the University of Bari, Italy, have published details on work relating to the use of CO_2 as a raw material (*J. Mol. Catal., A*, 2002, **182-3**, 399). They have investigated both the reaction of CO_2 with styrene oxide to give the carbonate, and the direct reaction of styrene with oxygen and CO_2 to give the carbonate via an intermediate epoxidations. Yields are good with the epoxide, but considerably lower in the direct reaction. Nonetheless, mechanistic work on the latter hints at possible improvements which might make the latter a very useful route to generating functional molecules in a clean and efficient fashion.



Fries rearrangement

Annie Commarieu and colleagues from Atofina in Lacq, France have described the use of methanesulfonic acid as a biodegradable strong acid catalyst for the Fries rearrangement, which is normally carried out industrially using HF or $AlCl_3$ (*J. Mol. Catal., A*, 2002, **182-3**, 399). Looking at the first step of the paracetamol process, they have optimised



reaction conditions such that the desired *para* isomer can be produced selectively (*p*/*o* up to 88.5 has been achieved at high conversions). Anhydrous conditions are necessary to avoid hydrolysis. Reaction conditions are relatively mild—temperatures around 100 ºC and short reaction times (typically about 1 hour is sufficient).

Reviews

Asymmetric Michael additions

A useful microreview on asymmetric Michael additions has been published by Dieter Enders and colleagues from the RWTH Aachen (*Eur. J. Org. Chem.*, 2002, 1877).

Lanthanide chemistry

The latest issue of *Chemical Reviews* (2002, **102**, Part 6) is dedicated to lanthanide chemistry. Amongst several reviews covering many aspects of the chemistry of lanthanides are several on the catalytic and synthetic applications of lanthanide complexes (Gary Molander and Jan Antoinette Romero, (page 2161); Masakatu Shibasaki and Naoki Yoshikawa (page 2187); Junji Inanaga and colleagues (page 2211); and lanthanide triflates (Shu Kobayashi and co-workers (page 2227).

Presidential Green Chemistry Challenge Awards 2002

The following are the recipients of these prestigious US awards which recognize outstanding chemical technologies that incorporate the principles of green chemistry into chemical design, manufacture, and use, and that have been or can be utilized by industry in achieving their pollution prevention goals

Professor Eric J. Beckman, University of Pittsburgh–*for design of non-fluorous, highly CO_2-soluble materials*

Carbon dioxide, an environmentally benign and nonflammable solvent, has been investigated extensively in both academic and industrial settings. Solubility studies performed during the 1980s had suggested that CO_2's solvent power was similar to that of *n*-alkanes, leading to hopes that the chemical industry could use CO_2 as a ‘drop-in’ replacement for a wide variety of organic solvents. It was learned that these solubility studies inflated the solvent power value by as much as 20% due to the strong quadrupole moment of CO_2, and that carbon dioxide is actually a rather feeble solvent compared to alkanes. As the 1980s drew to a close, a number of research groups began to explore the design of CO_2-philic materials, that is, compounds that dissolve in CO_2 at significantly lower pressures than do their alkyl analogs. These new CO_2-philes, primarily fluoropolymers, opened up a host of new applications for CO_2, including heterogeneous polymerization, protein extraction, and homogeneous catalysis.

Although fluorinated amphiphiles allow new applications for CO_2, their cost (approximately $1 per gram) reduces the economic viability of CO_2 processes, particularly given that the use of CO_2 requires high-pressure equipment. Furthermore, data have recently shown that fluoroalkyl materials persist in the environment leading to the withdrawal of certain consumer products from the market. The drawbacks inherent to the use of fluorinated precursors, therefore, have inhibited the commercialization of many new applications for CO_2, and the full promise of CO_2-based technologies has yet to be realized. To address this need, Professor Eric Beckman and his group at the University of Pittsburgh have developed materials that work well, exhibiting miscibility pressures in carbon dioxide that are comparable or lower than fluorinated analogs and yet contain no fluorine.

Drawing from recent studies of the thermodynamics of CO_2 mixtures, Professor Beckman hypothesized that CO_2-philic materials should contain three primary features:

- relatively low glass transition temperature
- relatively low cohesive energy density
- number of Lewis base groups

Low glass transition temperature correlates to high free volume and high molecular flexibility, which imparts a high entropy of mixing with CO_2 (or any solvent). A low cohesive energy density is primarily a result of weak solute–solute interactions, a necessary feature given that CO_2 is a rather feeble solvent. Finally, because CO_2 is a Lewis acid, the presence of Lewis base groups should create sites for specific favorable interactions with CO_2.

Professor Beckman’s simple heuristic model was demonstrated on three sets of materials: functional silicones; poly(ether-carbonates); and acetate-functional polyethers. Poly(ether-carbonates) were found to exhibit lower miscibility pressures in CO_2 than perfluoropolyethers, yet are biodegradable and 100 times less expensive to prepare. Other families of non-fluorous CO_2-philes will inevitably be discovered using this model, further broadening the applicability of CO_2 as a greener process solvent.

SC Fluids, Inc.—*for SCORR (Supercritical CO_2 Resist Remover)*

The semiconductor industry is the most successful growth industry in history, with sales totaling over $170 billion in the year 2000. The fabrication of integrated circuits (ICs) relies heavily on photolithography to define the shape and pattern of individual components. Current manufacturing practices use hazardous chemicals and enormous amounts of purified water during this intermediate step, which may be repeated up to 30 times for a single wafer. It is estimated that a typical chip-fabrication plant generates 4 million gallons of waste water and consumes thousands of gallons of corrosive chemicals and hazardous solvents each day.

SC Fluids, in partnership with Los Alamos National Laboratory, developed a new process, SCORR, that removes photoresist and post-ash, -etch, and -CMP (particulate) residue from semiconductor wafers. The SCORR technology outperforms conventional photoresist removal techniques in the areas of waste minimization, water use, energy consumption, worker safety, feature size compatibility, material compatibility, and cost. The key to the effectiveness of SCORR is the use of supercritical CO_2 in place of hazardous solvents and corrosive chemicals. Neat CO_2 is also utilized for the rinse step, thereby eliminating the need for a deionized water rinse and an isopropyl alcohol drying step. In the closed loop SCORR process, CO_2 returns to a gaseous phase upon depressurization, leaving the silicon wafer dry and free of residue.

SCORR is cost-effective for five principal reasons. It minimizes the use of hazardous solvents, thereby minimizing costs required for disposal and discharge permits. It thoroughly strips photoresists from the wafer surface in less than half the time required for wet-stripping and far outperforms plasma, resulting in increased throughput. It eliminates rinsing and drying steps during the fabrication process, thereby simplifying and streamlining the manufacturing process. It eliminates the need for ultra-pure deionized water, thus reducing time, energy, and cost. Supercritical CO_2 costs less than traditional solvents and is recyclable.

SCORR will meet future, as well as current technology demands. To continue its astounding growth, the semiconductor industry must develop ICs that are smaller, faster, and cheaper. Due to their high viscosity, traditional wet chemistries cannot clean small feature sizes. Vapor cleaning technologies are available, but viable methods for particle removal in the gas phase have not yet been developed. Using SCORR, the smallest features present no barriers because supercritical fluids have zero surface tension and a 'gaslike' viscosity and, therefore, can clean features less than 100 nm. The low viscosity of supercritical fluids also allows particles less than 100 nm to be removed. The end result is a technically enabling 'green' process that has been accepted by leading semiconductor manufacturers and equipment and material suppliers.

SCORR technology is being driven by industry in pursuit of its own accelerated technical and manufacturing goals. SCORR was initially developed through a technical request from Hewlett Packard (now Agilent). A joint Cooperative Research and Development Agreement between Los Alamos National Laboratory and SC Fluids has led to the development of commercial units (SC Fluids' Arroyo™ System). Other industry leaders, such as IBM, ATMI, and Shipley, are participating in the development of this innovative technology.

Pfizer, Inc.—*for green chemistry in the redesign of the Sertraline process*

Sertraline is the active ingredient in the important pharmaceutical, Zoloft®. Zoloft® is the most prescribed agent of its kind and is used to treat an illness (depression) that each year strikes 20 million adults in the U.S. and that costs society $43.7 billion (1990 dollars). As of February 2000, more than 115 million Zoloft® prescriptions had been written in the US.

Applying the principles of green chemistry, Pfizer has dramatically improved the commercial manufacturing process of sertraline. After meticulously investigating of each of the chemical steps, Pfizer implemented a substantive green chemistry technology for a complex commercial process requiring extremely pure product. As a result, Pfizer significantly improved both worker and environmental safety. The new commercial process (referred to as the 'combined' process) offers substantial pollution prevention benefits including improved safety and material handling, reduced energy and water use, and doubled the overall product yield.

Specifically, a three-step sequence in the original manufacturing process was streamlined to a single step in the new sertraline process. The new process consists of imine formation of monomethylamine with a tetralone, followed by reduction of the imine function and *in-situ* resolution of the diastereomeric salts of mandelic acid to provide chirally pure sertraline in much higher yield and with greater selectivity. A more selective palladium catalyst was implemented in the reduction step, which reduced the formation of impurities and the need for reprocessing. Raw material use was cut by 60%, 45%, and 20% for monomethylamine, tetralone, and mandelic acid, respectively.

Pfizer also optimized its process using the more benign solvent ethanol for the combined process. This change eliminated the need to use, distill, and recover four solvents (methylene chloride, THF, toluene, hexane) from the original synthesis. Pfizer's innovative use of solubility differences to drive the equilibrium toward imine formation in the first reaction of the combined steps eliminated approximately 140 metric tons/year of the problematic reagent titanium tetrachloride. This process change eliminates 100 metric tons of 50% NaOH use, 150 metric tons of 35% HCl waste, and 440 metric tons of solid titanium dioxide wastes per year.

By eliminating waste, reducing solvents, and maximizing the yield of key intermediates, Pfizer have demonstrated significant green chemistry innovation in the manufacture of an important pharmaceutical agent.

Cargill Dow LLC—*for the NatureWorks™ PLA Process*

Nature Works™ polylactic acid (PLA) is the first family of polymers derived entirely from annually renewable resources that can compete head-to-head with traditional fibers and plastic packaging materials on a cost and performance basis. For fiber consumers, this will mean a new option for apparel and carpeting applications: a material that bridges the gap in performance between conventional synthetic fibers and natural fibers such as silk, wool and cotton. Clothing made with Nature Works™ fibers features a unique combination of desirable attributes such as superior hand, touch and drape, wrinkle resistance, excellent moisture management and resilience. In packaging applications consumers will have the opportunity to use a material that is natural, compostable, and recyclable without experiencing any tradeoffs in product performance.

The Nature Works™ PLA process offers significant environmental benefit in addition to the outstanding performance attributes of the polymer. Nature Works™ PLA products are made in a revolutionary new process developed by Cargill Dow LLC that incorporates all 12 green chemistry principles. The process consists of three separate and distinct steps that lead to the production of lactic acid, lactide, and PLA high polymer. Each of the process steps is free of organic solvent – water is used in the fermentation while molten lactide and polymer serve as the reaction media in monomer and polymer production. Each step not only has exceptionally high yields ($>95\%$), but also utilizes internal recycle streams to eliminate waste. Small (ppm) amounts of catalyst are used in both the lactide synthesis and polymerization to further enhance efficiency and reduce energy consumption. Additionally, the lactic acid is derived from annually renewable resources, PLA requires 20 to 50% less fossil resources than comparable petroleum-based plastics, and PLA is fully biodegradable or readily hydrolyzed into lactic acid for recycling back into the process.

While the technology to create PLA in the laboratory has been known for many years, previous attempts at large scale production were targeted solely at niche biodegradable applications and were not commercially viable. Only now has Cargill Dow been able to perfect the Nature Works™ process and enhance the physical properties of PLA resins to successfully compete with commodity petroleum-based plastics. Cargill Dow is currently producing approximately 4,000 metric tons of PLA per year to meet immediate market development needs. Production in the first world-scale 140,000 metric ton/yr plant began 1st November 2001.

The Nature Works™ process embodies the well-known principles of green chemistry by preventing pollution at the source through the use of a natural fermentation process to produce lactic acid, substituting annually renewable materials for petroleum-based feedstock, eliminating the use of solvents and other hazardous materials, completely recycling product and by-product streams, and efficiently using catalysts to reduce energy consumption and improve yield. In addition, Nature Works™ PLA products can be either recycled or composted after use.

CSI–*for ACQ Preserve®, the environmentally advanced wood preservative*

The pressure-treated wood industry is a \$4 billion industry, producing approximately 7 billion board feet of preserved wood per annum. More than 95 percent of the pressure-treated wood used in the United States is currently preserved with chromated copper arsenate (CCA). Approximately 150 million pounds of CCA wood preservatives were used in the production of pressure-treated wood in 2001, enough wood to build 435,000 homes. About 40 million pounds of arsenic and 64 million pounds of hexavalent chromium were used to manufacture these CCA wood preservatives.

Over the past few years, scientists, environmentalists, and regulators have raised concerns regarding the risks posed by the arsenic that is either dislodged or leached from CCA-treated wood. A principal concern is the risk to children from contact with CCA-treated wood in playground equipment, picnic tables, and decks. This concern has led to the increased demand for and use of alternatives to CCA.

Chemical Specialties, Inc. (CSI) developed its alkaline copper quaternary (ACQ) wood preservative as an environmentally advanced formula designed to replace the CCA industry standard. ACQ formulations combine a bivalent copper complex and a quaternary ammonium compound in a 2:1 ratio. The copper complex may be dissolved in either ethanolamine or ammonia. Carbon dioxide (CO_2) is added to the formulation to improve stability and to aid in solubilization of the copper.

Replacing CCA with ACQ is one of the most dramatic pollution prevention advancements in recent history. Because more than 90 percent of the 44 million pounds of arsenic used in the U.S. each year is used to make CCA, replacing CCA with ACQ will virtually eliminate the use of arsenic in the United States. In addition, ACQ Preserve® will eliminate the use of 64 million pounds of hexavalent chromium. Further, ACQ avoids the potential risks associated with the production, transportation, use, and disposal of the arsenic and hexavalent chromium contained in CCA wood preservatives and CCA-treated wood. In fact, ACQ does not generate any RCRA (Resource Conservation and Recovery Act) hazardous waste from production and treating facilities. The disposal issues associated with CCA-treated wood and ash residues associated with the burning of treated wood will also be avoided.

In 1996, CSI commercialized ACQ Preserve® in the United States. More than 1 million active pounds of ACQ wood preservatives were sold in the U.S. in 2001 for use by thirteen wood treaters to produce over 100 million board feet of ACQ-preserved wood. In 2002, CSI plans to spend approximately \$20 million to increase its production capacity for ACQ to 30 million active pounds. This will convert 60% of CSI's production from CCA to ACQ, with a plan to continue to increase ACQ sales while phasing out CCA production. Through investment in ACQ, CSI has helped to trigger a significant market shift away from arsenic-based wood preservatives that will continue over the next several years. This shift will result in major benefits to public health and the environment.

Green chemistry educational initiatives

The following are two recent initiatives in green chemistry education in US universities

Green chemistry earns a PhD

A new green chemistry PhD programme is underway at the University of Massachusetts, Boston. It is offered by the department of environmental sciences and administered by the department of chemistry.

This programme, which started last autumn, is believed to be the first of its kind in the world. It is the brainchild of Professor John Warner. Student training will be essentially similar to other chemistry PhD students but will emphasise skills to design materials and processes that have minimal impact on human health and the environment. Major research areas include: biodegradation, bioremediation, clean synthesis and environmental monitoring. The course requires students to take courses in environmental law and policy, toxicology, industrial chemistry, environmental fate and transport. The course has been praised by a number of leaders in the world of green chemistry including Professor Terry Collins of Carnegie Mellon University, Professor Janet Scott from the Centre for Green Chemistry at Monash University in Australia and Dr Mary Kirchoff of the US Green Chemistry Institute. The Vice President of pharmaceutical sciences at Pfizer Global R & D, Berkeley Cue, has noted that a green chemistry PhD would be a big plus for chemists interested in process development.

The first student enrolled in UMB's green chemistry PhD programme is Amy Cannon. She is working on constructing solar energy devices in a more environmentally benign manner.

The University of Oregon opens $1 million green chemistry laboratory

The University of Oregon celebrated the official opening of its new $1 million Green Chemistry Laboratory and the adjacent Alice C Tyler Instrumentation Center in a noon time ribbon-cutting ceremony on 16th May 2002.

UO President Dave Frohnmayer has said that the Green Chemistry Laboratory will make a significant contribution to sustainable and environmentally friendly advances in chemistry.

The concept of green chemistry involves substituting more benign solvents and reagents for the hazardous chemicals traditionally used in organic chemistry laboratories. In the Green Chemistry Laboratory, students learn the fundamentals of organic chemistry using less hazardous chemicals - an approach that is both more environmentally friendly and safer for students and teachers. Students also gain valuable experience identifying more environmentally benign (greener) chemical practices.

All organic chemistry students at the UO—about 200 each term—are now using the new lab and practicing green chemistry. Adjacent to the Green Chemistry Laboratory is the new Alice C Tyler Instrumentation Center that will serve all undergraduates taking chemistry—about 1000 students a year. The new lab is spacious enough to have 48 students working comfortably and safely at one time.

The instrumentation center, funded with a grant of $300,000 from the Alice C Tyler Perpetual Trust, gives students access to the full range of instruments essential in green chemistry. The Green Chemistry Institute of the American Chemical Society also supported the project with a $100,000 grant. Approximately $500,000 came from private donors and supplementary university funds. Together the lab and instrumentation center comprise approximately 4000 square feet on the first floor of Klamath Hall, 1370 Franklin Blvd. Unlike many university laboratories known for their cramped feeling, the new lab has high ceilings and many windows.

Chemistry professors Jim Hutchison and Ken Doxsee are among the staff closely involved in the new initiative. Also participating in the ribbon-cutting ceremony were Allyn Brown, representing the Alice C Tyler Perpetual Trust and Dennis Hjeresen, director of the Green Chemistry Institute for the American Chemical Society.

For further information contact Ross West (rwest@oregon.uoregon.edu) or Professor Jim Hutchison. (hutch@oregon.uoregon.edu) or see website http://www.uoregon.edu/~hutchlab/greenchem/

LEFT TO RIGHT – Allyn Brown, Dave Frohnmayer, Dennis Hjeresen, Ken Doxsee and Jim Hutchison

DOI: 10.1039/b206505n

Green lubricants. Environmental benefits and impacts of lubrication

Review

Steve Boyde

Uniqema Lubricants, Wilton, UK. E-mail: stephen.boyde@uniqema.com

Received 4th March 2002
First published as an Advance Article on the web 22nd July 2002

This paper is a review of the environmental impact of lubricants and lubrication, from a chemical perspective. It is intended to give an overview of our current understanding and to provide some specific examples of how optimising lubricant chemistry can contribute to reducing the environmental impact of human activities. Lubricants affect this impact in many ways, but they have a particularly important contribution to make in relation to energy conservation, minimisation of waste and development of durable products. Truly green lubricants are those that optimise energy efficiency and minimise wear in the machinery which they lubricate and which have maximised service lifetimes in order to reduce the amount of lubricant required. Increasing importance of these criteria in lubricant selection and design is expected to lead to more widespread use of high performance synthetic basefluids and effect additives.

1 Introduction. What is a lubricant?

This section outlines the functions and performance requirements of a lubricant and describes the chemical components of a modern lubricating oil formulation, in order to provide a brief introduction for those unfamiliar with this area of technology.

1.1 The role, functions and requirements of a lubricant

A lubricant is a material used to facilitate relative motion of solid bodies by minimising friction and wear between interacting surfaces. Most, although not all, lubricants are non-aqueous liquids. This paper concentrates on such lubricating oils, which are used in a very wide range of equipment, on scales ranging from industrial metal rolling mills, through car engines and gear boxes to computer disk drives. The paper also considers related functional fluids used in applications where their primary purpose is not friction and wear reduction, although some degree of lubricity may be required. Examples of such applications include hydraulic fluids, electrical transformer fluids, heat transfer fluids and metal working coolants.[1,2]

In addition to the primary purposes of reducing friction and wear, lubricating oils are also required to carry out a range of other functions, including removal of heat, corrosion prevention, transfer of power, providing a liquid seal at moving contacts and suspension and removal of wear particles.[3,4] In order to perform these roles, lubricating oils must have specific physical and chemical characteristics.

Perhaps the fundamental requirement is that a lubricating oil should be liquid over a broad temperature range. In practice the usable liquid range will be limited by the pour point at low temperatures and the flash point at high temperatures. The pour point should be low to ensure that the lubricant is pumpable when equipment is started from extremely low temperatures. The flash point should be high to allow safe operation, with minimum volatilisation, at the maximum operating temperature. For the most demanding applications, such as aviation jet engine lubricants, an effective liquid range of over 300 °C may be required.

The efficiency of a lubricating oil in reducing friction and wear is is greatly influenced by its viscosity. The relationship of the coefficient of friction in a lubricated system to the lubricant viscosity is shown schematically in Fig. 1.[3,4] At high speed, high viscosity or low load, sufficient hydrodynamic pressure is generated that the solid surfaces are fully separated by a thin film of lubricant. This condition is known as hydrodynamic lubrication. At lower speeds and viscosities, or higher loads, the hydrodynamic pressure generated is insufficient to fully separate the surfaces and asperities on the opposing surfaces come into contact. This condition is known as boundary lubrication. To minimise friction and wear, equipment is designed for hydrodynamic lubrication where possible. For any given lubricated system, the optimum lubricant viscosity depends on the relative velocities of the surfaces, and on the

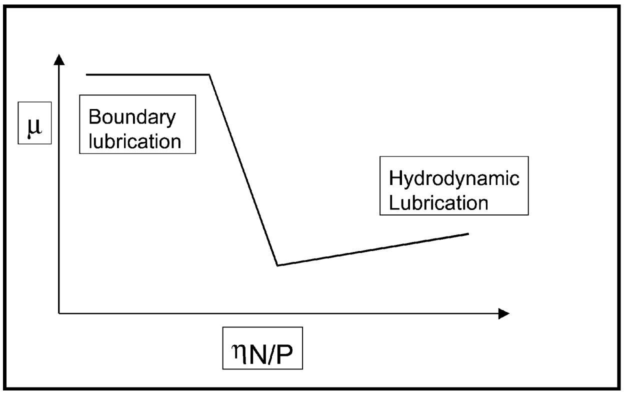


Fig. 1 The Stribeck curve. Schematic dependence of coefficient of friction, μ, on lubricant viscosity, η, relative velocity N, and load, P. (ref. 4, p. 227).

Green Context

Lubricants are ubiquitous, but are often overlooked in terms of environmental impact compared to *e.g.* fuels, which are continually under the spotlight. This overview places lubrication in context, in terms of its function currently, environmental impact and future trends, in particular from a green perspective. ***DJM***

DOI: 10.1039/b202272a

load to be supported. Since velocities and loads vary enormously between different types of machine, and even between different locations in the same machine, a correspondingly wide range of lubricant viscosities are required. Industrial lubricants are normally classified according to their ISO grade, the approximate viscosity in cSt at 40 °C.[5] Lubricants in current commercial use span a range of ISO grades from <10 to >1000. (Car engine oils are usually classified according to the SAE grade system, which gives greater discrimination over the viscosity range of interest in the application[6]).

For a given load and velocity, too high a viscosity means that the hydrodynamic lubricant film is thicker than necessary and energy is wasted in shearing the thick lubricant film. The excess energy is converted to heat, which increases both the local temperature and the bulk lubricant temperature. This accelerates lubricant decomposition reactions and mechanical failure of the surfaces, leading to reduced lifetime for the lubricant and for the equipment.[3,4]

Too low a viscosity means that the the system will operate in the boundary lubrication regime. Friction coefficients are much higher in boundary than in hydrodynamic lubrication, because energy is required for surface deformation and to overcome adhesion.[7] Energy is wasted in overcoming the higher frictional forces. Wear of the metal components also occurs, again leading to reduced equipment lifetime.

Viscosity of a fluid is a function of temperature, pressure, and in some cases, shear rate. It is generally desirable that the viscosity of a lubricating oil should change as little as possible over the temperature range of operation. The temperature dependence of viscosity of lubricants varies significantly, and is normally expressed in terms of an empirical parameter known as Viscosity Index (VI), where a higher VI implies a lower rate of change of viscosity with temperature.[8]

The pressure-dependence of viscosity is also a critical parameter in lubricant selection. The true hydrodynamic pressure in some lubricated contacts can exceed 1 GPa. Under these pressures, fluid viscosities may be orders of magnitude higher than their ambient pressure values.[9,10] Some fluids effectively solidify under these high pressures. For many applications, this increase in viscosity with pressure is essential to maintain a liquid film in the contact and prevent failure of components. In other applications a low viscosity increase is preferable to minimise friction and energy consumption.

The lubricant must maintain its physical properties throughout a long operating lifetime, during which time it is exposed to high temperatures in the presence of atmospheric oxygen. Thermal degradation and autoxidation affect fluid physical properties, so a lubricant must have extremely good thermal and oxidative stability in order to maintain performance.[11] It must also be inert to any other potential chemical reactants to which it may be exposed, *e.g.* water, fuels and process gases. A lubricant must also be stable under the extremely high shear rates characteristic of lubricated contacts, which are capable of mechanically fragmenting large molecules.

In addition to having the correct viscometrics and stability, a lubricant must deliver many other application effects. One of the most important of these is antiwear activity. This is a function of the lubricant chemistry under the extreme conditions occurring where asperities on the surfaces of opposing mechanical elements come into contact. Asperity contact gives rise to very high local flash temperatures and causes emission of electrons as the metal is deformed. The passivating metal oxide layer may be removed, exposing virgin metal surfaces. Any lubricant in proximity to an asperity collision is therefore subjected to extreme thermal and electrochemical excitation, while in contact with a potentially catalytic metal surface.[12,13] The lubricant must react under these conditions, for example by formation of an adherent, viscoplastic layer, which can be deformed sacrificially to relieve stress on the underlying metal surfaces and prevent wear.

The interfacial physical and chemical characteristics under milder conditions are equally important. The lubricant must contribute to minimising friction between contacting surfaces and prevent corrosion of metals. Wear and soot particles must be maintained in dispersed suspension to avoid formation of sludge and surface deposits. At the liquid air interface, low foaming and rapid air release are required.[1–4]

With such a range of physical and chemical parameters to consider, as well as economic, safety and environmental constraints, it is clear that lubricant design and formulation inevitably involves compromises between the different performance requirements of any given application. There is no single ideal lubricant, only more or less appropriate lubricants for any particular purpose.

Lubricants are best viewed as liquid materials. Their study and development requires a broad, interdisciplinary, materials science approach. However, lubricants are *molecular* materials, and their chemistry underlies the delivery of all of their physical and chemical properties, as well as being fundamental to their manufacturing processes and fate at end of life. Lubricant chemistry is therefore the key to understanding, quantifying and minimising the environmental impact of lubricants and lubricated systems.

1.2 The chemical composition of lubricants

Until the mid 19th century, essentially all lubricating oils were based on natural oils, *i.e.* animal fats, vegetable oils and marine oils, which are triglycerides of mixed C_8–C_{22} linear fatty acids.[14] Natural oils have some good lubricant properties, including high viscosity indices, high flash points and low boundary friction coefficients. However, natural oils have a limited viscosity range because of their limited range of structures. They also suffer from poor low temperature fluidity, and very poor thermal and oxidative stability, which leads to rapid degradation, thickening and deposit formation in use.[15]

Industrial development during the 19th century, mainly based on coal-fired, steam-powered equipment, increased the demand for lubricants, but the industry was completely transformed at the end of that century by the widespread adoption of the gasoline-powered internal combustion engine. This created a new demand for lubricants which rapidly exceeded the supply of natural oils. However, the increased exploitation of petroleum as a fuel source also provided a new raw material, mineral oil, which was co-produced when crude oil was refined for gasoline production.

Mineral oils are extremely complex mixtures of C_{20}–C_{50} hydrocarbons containing a range of linear alkanes (waxes), branched alkanes (paraffinics), alicyclic (naphthenic), olefinic and aromatic species. They also contain significant concentrations of heteroatoms, mainly sulfur.[1,4]

Mineral oils were found to be more stable than natural oils. However, although also cheaper and more readily available in a wider range of viscosities, early mineral oils did not immediately replace natural oils. One problem was that mineral oils from different oil fields had different characteristics. Another was that straight mineral oils gave inferior performance in several other key respects. For example, mineral oils have broader molecular weight distributions than natural oils. Volatilisation of low molecular weight components leads to a tendency to thicken in use. The low molecular weight components also reduce the flash point of mineral oils relative to natural oils of the same viscosity. Mineral oils also typically have low viscosity indices and high boundary friction coefficients compared to natural oils.

During the 20th century, the rapid growth in the number of vehicles led to a volume of demand for lubricants which could only be met by mineral oils and technical developments have overcome many of their performance deficiencies. Improvements in refinery technology have given refiners better control over the composition and characteristics of the mineral oil basefluid. At the same time, the developments of the science of chemistry and of the petrochemical industry have made available a diverse range of chemical products for use as performance additives.[1,16]

Hindered phenols and aromatic amines are used as antioxidants which retard the rate of autoxidation of lubricant basefluids and extend their useful lifetime. Long chain fatty acids and diacids are used as rust and corrosion inhibitors. They adsorb to ferrous metal surfaces, displacing water and preventing corrosion. Benzotriazole and other heterocyclics act as metal passivators which bond strongly to non-ferrous metals such as copper and its alloys, modifying the surface properties so as to prevent chemical attack and electrochemical processes at junctions between dissimilar metals.

Zinc dialkyldithiophosphates (ZDDPs) and other S- or P-containing compounds such as dithiocarbamates and trialkyl phosphates are used as antiwear agents which react under tribochemical conditions to form a protective film on the metal surfaces. ZDDPs are also powerful antioxidants.

High molecular weight polymers such as poly(acrylates) and styrene–butadiene copolymers are used as viscosity index improvers. The polymer molecules are more strongly solvated by the basefluid, and therefore thicken the fluid more effectively, at higher temperatures. This effect counteracts the decrease in viscosity with increasing temperature and increases the viscosity index.

Amphiphilic molecules with a polar ionic headgroup, *e.g.* a sulfonate, phenate or salicylate, attached to an oil-soluble hydrocarbon tail, act as detergents which adsorb to wear and soot particles to keep them in colloidal suspension in the basefluid. In over-based detergents, the amphiphilic molecules stabilise a colloidal suspension of a basic oxide or carbonate, *e.g.* $CaCO_3$, which neutralises acidic combustion gases to limit corrosivity. Non-ionic amphiphiles such as alkyl succinimides are used as dispersants which associate with the polar molecules formed by oxidative and tribochemical reactions in the lubricant to prevent formation of sludge and deposits.

However, even with all of the additive chemistries now available, there are still some applications where performance requirements cannot be met by mineral oil formulations, and it is necessary to chemically synthesize a lubricant basefluid having the required properties. A variety of such synthetic lubricant basefluids have been developed.[17,18]

Poly(α-olefins) (PAOs) are synthetic hydrocarbons manufactured by cationic oligomerisation of C_8–C_{12} olefins, followed by hydrogenation and fractionation. They have characteristics similar to very highly refined paraffinic mineral oils, with the additional feature of a more narrowly defined molecular weight distribution. This gives particularly good low temperature fluidity and high temperature volatility characteristics. PAOs have been widely used as the main basefluid component of synthetic car engine oils.

Alkylbenzenes are synthetic hydrocarbons manufactured by Friedel–Crafts type alkylation of benzene. Monoalkylbenzenes are manufactured in large volumes for use in surfactant applications. Lubricant alkylbenzenes are typically derived from the dialkylbenzenes and diphenylalkanes which are formed as byproducts. Although the surfactant industry now uses almost exclusively linear alkylbenzenes, branched alkylbenzenes have better low temperature fluidity and are generally preferred in lubricant applications.

A very wide range of synthetic organic esters are used as lubricant basefluids. Examples include esters of C_8–C_{13} monoalcohols with diacids such as adipic acid (diesters) and esters of C_5–C_{18} monoacids with neopentyl polyols such as pentaerythritol (polyol esters). The presence of the ester group confers good low temperature fluidity and reduces volatility at high temperature, as well as providing some affinity for metal surfaces. Esters were originally developed for lubrication of aircraft jet engines, but have subsequently found more widespread use, particularly in applications where biodegradability is required.

Poly(alkylene glycols) (PAGs) are polymers of ethylene and/or propylene oxide. Control of molecular architecture gives access to a very wide range of viscosities. The polarity of PAGs can be varied to give materials which are soluble in water, mineral oils or neither. PAGs have exceptionally high viscosity indices and give very low friction when used as gear lubricants.

Phosphate esters are triesters of orthophosphoric acid with alkyl or aryl alcohols. They have particularly good fire retarding properties, and are used where this is an essential performance requirement, *e.g.* in aircraft hydraulic systems.

For applications where chemical stability is an overriding requirement, non-hydrocarbyl basefluids such as poly(dimethyl siloxanes) and perfluoroalkyl ethers may be used. However, the use of these non-hydrocarbyl lubricants is restricted both by their relatively high cost and by their incompatibility with other lubricants and standard additives.

All of the synthetic lubricant basefluids are normally used as formulations containing the same types of functional additives as are used in mineral oils. They are frequently blended with mineral oil or other synthetics in order to provide desired combinations of properties.

As a result of these technical developments, the chemical composition of lubricants has evolved over the last century from straight natural oils to today's complex formulations, containing one or more basefluids and a package of effect additives, tailored to meet the specific performance requirements of the intended application.

2 Environmental impact of lubricants and lubrication

This section considers various ways in which lubricants can impact the environment, in relation to the concepts of Green Chemistry and Life Cycle Analysis.

2.1 Assessing the scale

The annual global production of lubricants and related functional fluids (*e.g.* hydraulic fluids, transformer oils, heat transfer fluids and metal working coolants) is approximately 38 Mtes, of which lubricant additives account for 1.5–2 Mtes pa., while synthetic lubricant basefluids represent approximately 0.7 Mtes pa. [19] By comparison, annual global production of chemicals in total is estimated at 400 Mtes.[20] The latter figure includes additives and synthetic basefluids, but not mineral oils. If mineral oils are regarded as chemical products, the lubricants industry is responsible for approximately 8.5% of the total global chemical production by weight.

Manufacture and eventual disposal of this very large volume of material obviously represents an environmental burden. It is therefore not surprising that environmental aspects of lubricants and lubrication have been to the fore throughout the lifetime of the industry, and continue to be an active area of investigation.[21–23]

2.2 Life Cycle Assessment

A robust quantification of the overall environmental impact of lubricants would entail a detailed Life Cycle Assessment (LCA),[24] with a scope covering manufacturing, use and fate at end of life, and with system boundaries encompassing petroleum, petrochemical, oleochemical and engineering industry activities. This would be a dauntingly complex process, due to the very broad scope required, and also to some particular issues which are characteristic of the industry and the applications.

One complication is that lubricants are typically manufactured as coproducts in integrated product networks, based on petroleum refining, oleochemical refining or chemical processing. Consequently, allocation of resource requirements and environmental impacts to the lubricant elements of these networks is necessarily somewhat arbitrary.

Secondly, since different lubricant types differ greatly in their performance and in the amount required for a particular purpose, a detailed knowledge of application performance is required in order to define an appropriate functional unit for comparison. LCA comparisons are made on the basis of equivalent outputs so a simple comparison of different lubricant types, based only on their resource requirements per kg or per litre, would therefore give misleading results.

Thirdly, because lubricants are used so widely in many different products and applications, tracing fate at end of life is very difficult. End of life treatment of industrial lubricants used at a single manufacturing site can be controlled and monitored, but following the fate of used car engine oils is a more challenging problem. The eventual fate of a large proportion of overall lubricant production is not accurately known.

Finally, even where data are in principle available, they may be regarded as confidential to the product manufacturers or users, and not openly published. Publishable LCAs generally require coordination by an independent body to facilitate pooling of commercially sensitive information.

Practical illustrations of the magnitude of the task are provided by studies from related sectors of the chemicals industry. These include the 1995 European Life Cycle Inventory for detergent surfactants production[25] and the Eco Profiles of the European plastics industry.[26] This scope of the former study was an inventory of energy and resource requirements for production of seven major surfactant types, with no consideration of impact assessment. Even with these restrictions, the study required two years to prepare, involving 17 technical professionals from 13 companies. A key conclusion was that no technical basis existed to support a general environmental superiority claim either for an individual product type, or for the various options for sourcing raw materials from petrochemical, agricultural or oleochemical feedstocks.

For these reasons, no such comprehensive lubricant Life Cycle Assessment has yet been attempted, although lubricating oils and related fluids have been considered as elements of LCA studies focussing on particular application areas such as hydraulic equipment for forestry applications and municipal cleaning,[27] and domestic refrigerators.[28] Furthermore, most companies involved in the industry carry out more or less detailed analyses of environmental impact in order to guide their strategy and internal decision making. However, the results of these analyses are not generally made available externally, although some limited studies have been published,[29–31]]. Single company studies are limited by the access to data of the company involved, and may also raise concerns as to the independence of any conclusions from the commercial interests of that company.

2.3 Green Chemistry metrics

Although a full cradle to grave LCA study would be the ideal, its absence does not imply that no information is available. As Anastas has shown, the concepts of Green Chemistry[32] reinforce and complement those of Life Cycle Assessment.[33] This section will summarise some relevant available information and review its implications, in terms of the principles of Green Chemistry, in order to arrive at some general qualitative conclusions.

2.3.1 Lubricant manufacturing–mass efficiency and process energy requirements. The overall manufacturing process for a typical lubricant product involves a number of distinct steps, which can be broadly divided into basefluid manufacture, additive manufacture and formulation. The environmental impact of these processes can be assessed in terms of their reaction mass efficiencies[34] and process energy requirements.

By far the highest volume lubricant basefluid is mineral oil derived from petroleum processing. The typical energy requirement for mineral oil basefluid production has been estimated at 9 MJ kg^{-1}, or approximately 20% of the Energy of Material Resource (EMR) of the product (*ca.* 42 MJ kg^{-1}).[30] The required process energy in an integrated refinery is derived from combustion of a portion of the feedstock. Because a refinery produces a slate of different product types from LPG to asphalt, essentially all of the incoming raw material is either converted to products, or is used for energy production. Therefore, following the convention that raw materials used for energy production are not included in the overall mass balance, the mass efficiency of mineral oil basefluid production is essentially 100%.

A smaller proportion of lubricants are based on natural oils. Lubricants represent a minor application for natural oils as a whole and the range of sources of natural oils is very broad. Allocation of agricultural resource requirements to lubricant basefluids is therefore arbitrary and highly sensitive to assumptions about the raw material mix, geographical origin and the extent to which mechanised equipment and fertilisers are used. Data presented in the Surfactants LCI report[25] suggest a typical overall energy requirement of approximately 3 MJ kg^{-1} for vegetable oil production.

It is difficult to generalise about manufacturing metrics for lubricant additives and synthetic basefluids due to the wide variety of chemistries involved. Also, since both mass efficiencies and process energy requirements significantly affect variable costs of manufacture, this information is normally maintained as confidential by manufacturers.

From published information, lubricant additives are frequently manufactured in single vessel reactions with little subsequent processing of the reaction mixture, using as solvent a mineral oil which is included in the product as sold.[1,3,16] For products of this type, reaction mass efficiencies are generally in the range 95–98%, with losses due only to process inefficiencies such as reactor washouts and filtration losses. Although there is little published information on process energy specifically relating to lubricant additives, by reference to data for closely related materials in surfactant and polymer applications, it is estimated that overall process energy requirements for the entire manufacturing chain typically approximate the EMR of the products, *i.e.* 35–40 MJ kg^{-1}, to within a factor of 2.[25,26]

Similar arguments can be applied to the manufacture of synthetic basefluids. From process details disclosed in ref. 17, mass efficiency values for production of most synthetic basefluids may be estimated to be $>85\%$. Higher values will apply to products such as PAOs and PAGs which are produced by addition polymerisation, and lower values to products such as phosphate esters or silicones where the manufacturing route involves substitution reactions of a chlorinated raw material ($POCl_3$ or $SiCl_4$), with coproduction of HCl. Process energy requirements for the entire manufacturing chain for synthetic fluids are similar to those for lubricant additives, although the energy requirement for the final processing step involved in basefluid manufacture may be significantly lower than for mineral oil, particularly where distillation is not required.[29]

Lubricant formulation is typically a liquid blending operation, with a nominal 100% mass efficiency. Energy required for heating and agitation during the blending process is estimated at 3.6 MJ kg^{-1}.[29]

Overall then, the manufacturing of lubricants is characterised by high mass efficiencies, and relatively low process energy requirements, as would be expected for such high production volume materials.

2.3.2 Renewable raw materials. The natural fats and oils which were the first lubricants still provide a source of renewable raw materials. They are used in modern lubricants either directly, in formulations containing vegetable oils such as rapeseed and soybean oils, or after chemical processing as raw materials for the manufacture of synthetic basefluids and effect additives. The former approach has lower process energy requirements but gives a very restricted range of products, whose usefulness is restricted by their relatively poor stability and low temperature properties.[35,36] Also, the range of natural materials which can be used directly as fluids is obviously limited to those which are liquid over an appropriate temperature range.

Greater flexibility of utilisation is achieved through hydrolysis of natural fats and oils to produce the constituent fatty acids as raw materials for further chemical synthesis. A wide variety of natural sources, including solid fats and low grade or waste materials such as tallow from rendering of animal carcasses or tall oil from wood pulp processing, can be converted through controlled chemical processing into pure fatty acids of consistent quality.[37] Fatty acids of appropriate chain lengths and degree of unsaturation can then be used in the manufacture of synthetic basefluids or effect additives having precisely controlled structures which can be tailored for optimum application performance.

The major fatty acids derived from natural oils are linear, with an even number of carbon atoms, in the range C_8–C_{22}. For carbon numbers up to C_{16}, the natural fatty acids are typically fully saturated, with unsaturation or polyunsaturation becoming more common for higher carbon numbers.[14,37] Commercially, these C-even fatty acids and their derivatives are always derived from renewable resources. Because of their ready availability from natural oils, petrochemical routes to these materials have never been developed to a significant extent.

The saturated short chain acids, octanoic and decanoic, can be reacted with neopentyl polyols, such as trimethylolpropane, to give thermally stable esters that are used as components of high performance synthetic car engine oils and as textile lubricants. Saturated acids with higher carbon numbers and their ester derivatives are solids at room temperature and not generally suitable in synthesis of lubricant basefluids. However, esters of longer chain *cis*-unsaturated acids such as oleic (*cis* 9-octadecenoic) acid have lower melting points and can be used. In particular, the trioleate ester of trimethyolpropane is widely used as a basefluid in applications such as biodegradable hydraulic fluids and cutting fluids, where oxidative stability is less critical.[38]

Both saturated and unsaturated longer chain fatty acids, and their derivatives such as amides and glycerol monoesters, are used as surface active lubricant additives. Sulfurised unsaturated fatty acids and derivatives are used as antiwear agents under extreme pressure conditions.

An important atypical natural fatty acid is the hydroxy acid ricinoleic (12-hydroxyhexadecenoic) acid, which is obtained from castor oil. Castor oil consists mainly of glycerol triricinoleate. It is more viscous than typical vegetable oils, due to hydrogen bonding, and has relatively good oxidative stability and low temperature fluidity. It has been widely used as a lubricating oil in its own right. Ricinoleate esters and amides are used as lubricant additives, and ricinoleic acid can be hydrogenated to give 12-hydroxystearic acid, which is extensively used as a gellant in lubricating greases in the form of its alkali metal salts.[1]

Although they have good low temperature fluidity, polyunsaturated acids are not preferred for use in lubricant applications because of their poor oxidative stability. However, with oleic acid, they can be converted by acid catalysed oligomerisation and isomerisation, followed by hydrogenation, to give branched C_{18} monoacid (isostearic), C_{36} diacid (dimer acid) and C_{54} triacid (trimer acid), which are useful raw materials for the synthesis of high viscosity ester fluids.[37–39]

The double bond in the unsaturated acids offers many obvious possibilities for chemical derivatisation, some of which are already commercially exploited. For example, the linear diacids azelaic acid (C_9) and sebacic acid (C_{10}) are manufactured industrially by oxidation of oleic acid and alkali fusion of ricinoleic acid, respectively.[40] These diacids are raw materials for synthetic ester basefluids such as the respective diesters of 2-ethylhexanol.[38] The production of azelaic acid gives the C-odd monoacid nonanoic acid as coproduct. Another C-odd monoacid, heptanoic acid, is derived from ricinoleic acid by pyrolysis, as a coproduct in the manufacture of undecenoic acid. Nonanoic and heptanoic acids are used in the same way as their C-even homologues in manufacture of neopentyl polyol esters, where the C-odd chain lengths confers some low temperature fluidity benefits.[41] Manufacture of these C-odd monoacids from renewable resources is economically competitive with petrochemical routes, although the supply from the renewable route is limited by the demand for the more valuable co-product, in each case.

C_{19} diacid based on carbonylation of oleic acid, and C_{21} diacid from Diels–Alder addition of acrylic acid to conjugated dienic acids have also been developed and proposed for use as lubricant raw materials, although they have not found significant commercial application.[40] Many other fatty acid derivatives have been proposed for lubricant applications, including products of olefinic aralkylation, sulfonation, phosphation or halogenation,[42] epoxidation/addition products[43] and oligomeric estolides produced from oleic acid by 1,2 addition of the acid head group to the double bond.[44]

Currently, the vast majority of lubricant components are derived from fossil carbon sources, but because of the size of the overall market, even the relatively small proportion currently derived from renewable resources represents a large volume of material. It is estimated that lubricants derived from renewable raw materials account for approximately 2% of the European market, or 100 ktes pa.[45]

2.3.3 Fate at end of life. Reuse and recycling. Obtaining meaningful data on fate at end of life is challenging because of the enormous range of end use applications for lubricant products. The most comprehensive data are available for Europe, where studies have been carried out both by industry[46,47] and government,[48,49] typically focussing on automotive lubricants, hydraulic fluids and metal working fluids. All studies have reported a high degree of uncertainty, with a large proportion of material unaccounted for. According to the most recent survey,[42] annual lubricant demand in the EU is approx. 5.1 Mtes of which 2.65 Mtes (52%) is consumed in use. This leaves 2.45 Mtes (48%) generated as waste oils, of which 0.6 Mtes (25%) is unaccounted for and presumed to be burned illegally or dumped into the environment. The remaining 75% is collected, of which 36% is rerefined into lubricating oils and 64% burned as fuel. These data are summarised in Fig. 2.

Waste oil disposal in the EU is regulated according to Directive 75/439/EEC. This directive specifies a hierarchy of waste oils management which gives preference to regeneration or refining, but accepts burning under environmentally acceptable conditions. It was originally anticipated that the proportion of lubricant being refined would progressively increase from levels then estimated at around 30% in Germany and 5% in the UK. However, in practice, levels have not increased as expected[50] and are believed to be currently declining in favour of use as fuels. There has been much debate over whether it is environmentally preferable for used oils to be regenerated for reuse as lubricants or used as fuel. Inevitably, because of the

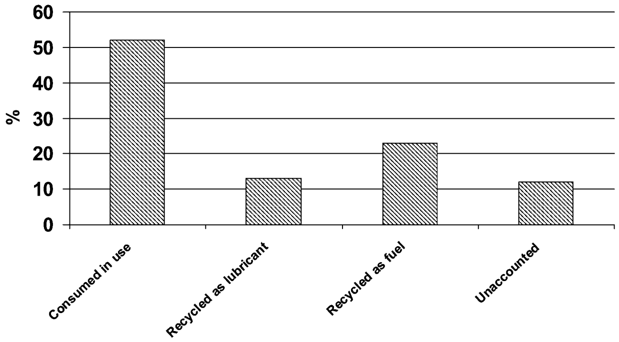


Fig. 2 Fate of waste oil in the EU (ref. 48).

wide range of product types and applications, there is no universally correct answer, and it is necessary to consider the details of each specific case.

The difficulty of re-refining used lubricating oils depends on the severity of the application, and the degree of control which can be applied to the recovery and collection process. For some industrial oils such as hydraulic fluids and transformer fluids, which are subject to regular condition monitoring, it has long been common practice to periodically 'launder' the oils by filtration, ion exchange and additive replenishment as required in order to restore them to a standard specification.[51] Material processed in this way is not recorded as used oil, so this type of re-use is not captured in the EU figures cited above.

Used car engine oils present much more of a challenge, both in terms of the degree of refining required and the difficulty of controlling the collection process in order to prevent contamination. However, collection and recycling processes are well established. Approximately 0.5 Mte pa of used engine oils are currently recycled in Europe,[46] and the capacity exists for a throughput of approximately 0.8 Mte pa.[52] A range of different refining processes have been commercialised, including acid/clay treatment, solvent extraction, distillation/clay treatment and distillation/hydrotreatment. All involve generation of process effluents such as acid sludge, solvent wastes, spent clays and catalysts. All also require significant process energy inputs, in some cases comparable to that required for original manufacture. Recovered base oil yields range from 60–95% depending on the technology and the quality of the input oil.[30,53]

In general, lubricant additives are not recyclable due to degradation in use.[46] They are therefore removed as sludge during lubricant re-refining and contribute to waste generation. However, most are combustible because they contain long chain hydrocarbon substituents in order to render them oil soluble. It is therefore not necessary to remove lubricant additives prior to combustion under suitable conditions. When used oils are used as fuel for cement and asphalt manufacture, any ash arising *e.g.* from presence of metal-containing additives may be sequestered in the product.

The case for recycling synthetic lubricant basefluids is stronger than that for mineral oils, due to the relatively higher process energy requirements in original manufacture of the synthetics. Additionally, oxygen-containing basefluids such as esters and polyalkylene glycols have significantly lower calorific value and therefore lower value as fuels than hydrocarbons. Where synthetic oils can readily be segregated and handled in large volume, reprocessing of specific high grade oils can be a realistic option, *e.g.* for the polyol esters used for aviation jet engine lubricants.[54]

Recycling technology continues to be an active area of research, with recent developments including separation of unoxidised baseoil components using supercritical fluid extraction,[55] separation of additives,[56] and separation of mineral oils from higher value synthetic basefluids.[57]

2.3.4 Fate in the environment. A very large proportion of overall lubricant production is dispersed into the environment on first use, either in the form of spills or leaks of virgin oils, spills and leaks of used oils, or emission of partially combusted oil derivatives in automotive exhausts. Lubricating oils are generally mobile liquids which are insoluble and less dense than water. They therefore tend to spread over surface waters in the form of highly visible oil slicks. These may have a damaging effect on aquatic life and are visually polluting. Consequently, considerable attention has been given to lubricant biodegradability and persistence in the environment.[58]

For complex substances, biodegradation is a multi-step process, and different measurements can be applied to the rate or extent of biodegradation, depending on the intended purpose of the measurement. The biodegradability of lubricants has generally been assessed according to two different types of test protocol, primary biodegradability and ultimate biodegradability.

As oils begin to biodegrade, they are first transformed into carboxylated or hydroxylated intermediates having higher water solubility, leading to disappearance of any visible oil slick. The rate of these first steps of the overall biodegradation pathway is described as primary biodegradability. It is normally determined by the CEC-L-33-A-93 test,[59] which measures the extent of disappearance of C–H stretching vibrations from the IR spectrum in a perhalogenated solvent extract of the test medium, over 21 days.

Disappearance of a visible slick does not imply that degradation is complete. In order to assess persistence in the environment, it is necessary to determine ultimate biodegradability. This is a measure of how readily the biodegradation process is completed and the test substance is fully mineralised, *i.e.* converted to carbon dioxide and water. Ultimate biodegradability of lubricating oils has generally been assessed according to the OECD 301 test protocols,[60] in particular OECD 301B which measures the amount of carbon dioxide evolved from a flask containing the test substance over 28 days and compares to the theoretical value based on the total organic carbon content of the sample. In general, biodegradability values of 100% are not obtained in the OECD 301B test because a portion of the substrate is converted into biomass rather than being fully oxidised to CO_2. A substance is considered readily biodegradable if the final test value after 28 days is $>60\%$, and if 50% biodegradation occurs within a 10 day period.

Typical values for biodegradability of a range of basefluids by OECD 301B and CEC-L-33-A-93 are listed in Table 1.[61] As expected, primary biodegradability values are generally significantly higher than ready biodegradability. From the viewpoint of assessing persistence in the environment, the OECD test protocols represent an extremely stringent test in relation to true environmental exposure, where microbes have the opportunity to acclimate to the substrate. A modified version has recently been proposed, involving preacclimation of the microbial innoculum and a longer test duration, in order to give a more practically useful indication of the likely extent of

Table 1 Primary and ready biodegradability of lubricant basefluids (ref. 54)

Lubricant type	Primary biodegradability CEC-L-33-A-94 21 days	Ready biodegradability OECD 301B 28 days
Mineral oil	10–45	10–40
PAO	20–80	5–60
Alkylbenzene	5–20	0–20
Diester (aliphatic)	75–100	50–95
Polyol ester	0–100	0–85
Vegetable oil	90–100	75–95

biodegradation in the environment. This measurement has been defined as inherent biodegradability and a draft protocol submitted for consideration by OECD.[62,63]

The results illustrate that biodegradability of mineral oils is generally much lower than that of vegetable oils, reflecting the adaptation of the microbial enzymic chemistry set to metabolism of naturally occurring substrates. In particular, microbes are equipped with enzymes for ester hydrolysis and oxidation of linear alkyl and alkenyl groups. Branched alkyl groups, particularly those containing quaternary branching, are more resistant to biodegradation.[64] These principles can be used to design and select synthetic basefluids having desired biodegradation characteristics.

Among synthetic basefluids, esters can have ready biodegradabilities essentially equivalent to those of natural oils. Poly(α-olefins) show higher biodegradability than mineral oils of equivalent viscosity because of their higher degree of linearity. Alkylbenzenes having a high degree of branching are generally of low biodegradability. The specialised non-hydrocarbon synthetic basefluid types such as silicones and perfluoroalkyl ethers are essentially non-biodegradable.

2.3.5 Hazards and toxicity. Lubricant basefluids and additives are generally low hazard materials. Because of the performance requirements, lubricating oils are viscous liquids with low vapour pressure, which are not highly flammable, have low VOC content and are not easily inhaled or ingested. Acute toxicity of lubricant basefluids and additives is also typically very low with $LD_{50} > 2g\ kg^{-1}$ for most major additive types.[65–68]

Some materials used historically as lubricant additives have been found to present potential hazards. Use of these materials, such as lead napthenates, chlorinated naphthalenes and tris(*o*-cresyl)phosphate, has generally been discontinued.[68] Some unrefined and lightly refined mineral oils have been shown to induce skin cancers, due to presence of polynuclear aromatic hydrocarbons (PAHs). Refined mineral oils with low PAH content are now specified for most applications.[68]

Current health issues with lubricants primarily relate to inhalation of mists and to skin contact. Prolonged skin contact with oils can lead to defatting of the skin, which can cause dermatitis, while some additives are classified as irritant or sensitising.[65] Avoidance of skin contact, through good working practices and appropriate protective clothing, is recommended for all lubricant products.

Used oils present a more complex toxicological picture. Their hazards are harder to quantify since used oils may have a wide range of compositions, reflecting the potential range of service conditions and possibilities of contamination. It is known that PAH concentration increases in used oils, particularly in petrol engine crankcase oils, but also for diesel engine oils and hydraulic fluids. It is believed that the greater part of the PAH content is derived from fuel combustion by-products, and a minor part from tribochemical or thermochemical decomposition of the lubricant. Because of PAH formation in service, used engine oil is recognised as a potential carcinogen.[65,69,70] One implication is that careful monitoring of re-refining processes is required in order to control the level of PAH in recycled oils, particularly as increasing lubricant drain intervals may offer more opportunity for accumulation of PAH during the service lifetime of a given lubricant charge.

2.3.6 Performance in use. The previous sections have illustrated that lubricants generally rate well against Green Chemistry metrics associated with manufacture and fate at end of life. Mass efficiencies in manufacture are high, the materials are generally low hazard, and routes for recycling or re-use are established.

However, the principles of Green Chemistry also include consideration of product use, and in particular the impact of the product on energy consumption and waste generation in the intended application.[32,33] It is in this area that there is the greatest scope for further optimisation.

The fundamental purpose of lubricants is to reduce friction in machinery. Reducing friction implies reduced energy consumption for equivalent output of useful work, so optimising friction performance offers the possibility of reducing overall consumption of energy and associated emissions to the environment. The potential for improvement is enormous.

As noted above, global annual lubricant production is approximately 38 Mtes. However, this is only approximately 1% of total refinery throughput of crude oil. The major petrochemical raw materials collectively represent approximately 3%, and other nonfuel uses (solvents, asphalt, waxes) another 1%.[71] The remaining 95% or approximately 3.6 Gtes pa are burned as fuel.

Crude oil in turn accounts for only approximately 40% of global annual energy consumption, with large contributions also arising from combustion of other fossil fuels including coal and natural gas. In total, this energy production is responsible for emission of approximately 6 Gtes of CO_2 expressed as elemental carbon (GtC)[72] and is the greatest source of atmospheric pollution by other acidic gases such as oxides of sulfur and nitrogen and by particulates.

Although a large amount of this energy is used in direct heat generation in buildings and industrial processes, the majority is used to power machines, primarily as transport fuel and in electricity generation. Most of these machines use some form of lubricant to reduce frictional losses and ensure efficient conversion of energy input into useful work. As will be shown in the next section, correct lubricant selection can lead to improvements in energy efficiency of up to 10%. The efficiency of utilisation of the enormous flow of energy through our industrial economy is therefore significantly dependent on lubricant performance.

A further purpose of lubricants is to reduce wear. Minimising wear by efficient lubrication prolongs the useful life of machines, thereby minimising the consumption of non-renewable resources such as fossil energy and metal ores required for manufacture and disposal of the machinery itself. Wear of mechanical elements can also cause machinery to operate less efficiently, so wear reduction has a secondary benefit in terms of overall reduced energy consumption throughout the operating lifetime of the equipment.

A third key performance measure of lubricants affecting the environmental impact is the stability or lifetime of the lubricant itself. For applications where lubricant is regularly replaced, there is an inverse relationship between lubricant stability and consumption. If a lubricant can be made to last twice as long, only half as much lubricant will be required, with corresponding reductions in the energy and material requirements for lubricant manufacture, and in the environmental impact of lubricant disposal. Increased sophistication of lubricant technology is already leading to an overall reduction in volume of demand for lubricants globally, for example, through use of high stability automotive engine lubricants offering extended drain intervals. Fig. 3 shows how lubricant demand during the period 1989–99 decreased by approximately 5%, despite an increase in world GNP of 48.5% over the same period.[73] Fig. 4 shows lubricant consumption per unit of GNP in 1990 and 1997 for the major economic regions. All regions show a significant decrease over the period. Lubricant consumption per unit GNP is significantly lower in the most developed economies such as Europe, which lead in their adoption of high performance lubricant technologies, such as synthetic basefluids (Fig. 5).[71]

Therefore, in summary, optimisation of three lubricant performance parameters; friction reduction, wear reduction and lubricant stability, will lead to a positive environmental impact

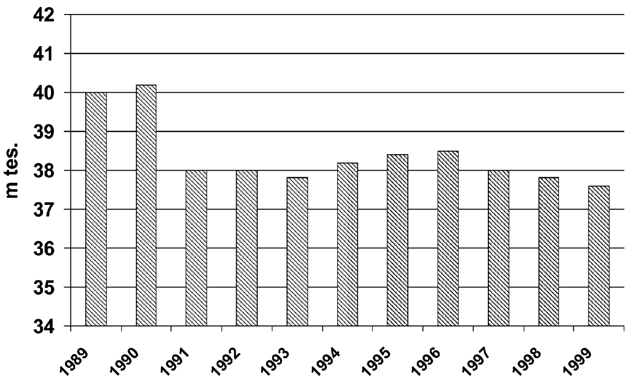


Fig. 3 Global lubricants demand (mtes) 1989–99 (ref. 73).

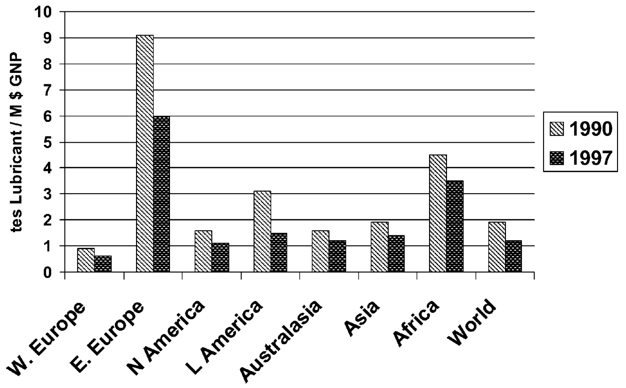


Fig. 4 Lubricant demand per unit of GNP (ref. 73).

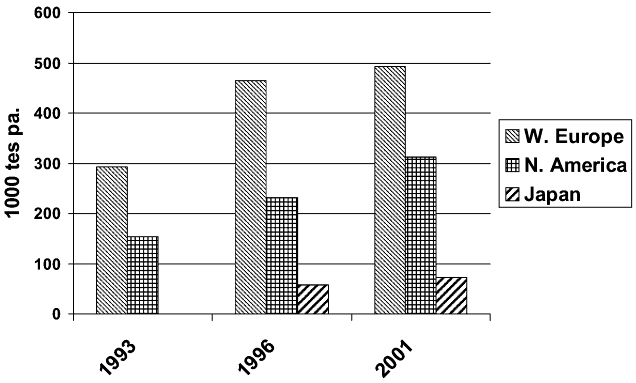


Fig. 5 Consumption of synthetic lubricants (ref. 71).

in use. The next section presents practical examples of how innovative product development is being used to improve lubricant performance in these key areas.

3 Practical examples

This section provides some examples of current technical developments which are leading to reduction of the environmental burden of lubricants and lubrication technology.

3.1 Refrigeration compressor lubricants. Reducing electrical energy consumption through lubricant basefluid design

5–10% of the UK's domestic electricity consumption is used to power refrigerators and freezers. Industrial and commercial refrigeration and air conditioning represents a similar proportion of non-domestic power consumption. With the growing recognition of the importance of energy conservation, refrigeration engineers are exploring all options for increased efficiency, including optimisation of lubricant performance.[74]

A domestic refrigerator or freezer contains a small reciprocating or rotary compressor directly coupled to an electric motor. Both the compressor and the motor bearings require lubrication, and the system imposes some very specific performance requirements on the lubricant. Since the motor and compressor are hermetically sealed inside the refrigeration circuit, the lubricant cannot be changed, and must be stable for the lifetime of the appliance, typically 10–20 years. Since the lubricant is not exposed to atmospheric oxygen and water, oxidative and hydrolytic stability are of less importance than thermal stability. Because of the contact with the electric motor, refrigeration lubricants must have very good electrical insulation properties and must be stable to electrically induced decomposition. They must also have very good low temperature fluidity characteristics, with no tendency to deposition of waxes.[75]

Most importantly, a refrigeration lubricant must be miscible with the refrigerant gas so that any lubricant transported into the refrigeration circuit is returned to the sump and does not foul heat exchanger surfaces or restrict pipework, which would lead to reduced energy efficiency. Hydrofluorocarbon (HFC) gases are currently the most widely used non-flammable, zero ozone depletion potential refrigerants. HFCs are relatively polar and are not miscible with mineral oils. Polyol esters (POEs), which are esters of monoacids with neopentyl polyol alcohols, have become the lubricant of choice for use with HFC gases for reasons of miscibility and also because of their inherently good lubricity[75]

Esters also represent a very versatile chemistry for assembly of synthetic basefluids because a wide range of organic acid and alcohol raw materials are available, derived both from oleochemical and petrochemical sources. By appropriate selection of raw materials so as to control molecular properties such as molecular weight, polarity, linearity and structural diversity, ester fluids having a very wide range of physical and chemical properties can be produced.[33,36] Some of the relevant structure–property relationships are illustrated in Fig. 6.

As described in Section 1, for any given lubricated system, the coefficient of friction depends on the lubricant viscosity, the relative velocities of the surfaces and on the load to be supported.[3,4] Lowest friction, and greatest energy efficiency, is obtained by operation at the minimum of the curve shown in Fig. 1. Small appliance refrigeration compressors are designed to operate under conditions of hydrodynamic lubrication, where metal to metal contact is avoided by ensuring that a full fluid film separates the surfaces. The energy required for shearing the entrained hydrodynamic film increases with the viscosity of the lubricant. Therefore, the energy requirement of an appliance compressor can be reduced by reducing the lubricant viscosity.

However, if the lubricant viscosity is reduced too far, it is no longer high enough to ensure that a full fluid film is entrained, and the system will move into the boundary lubrication regime.

Property	Molecular Weight	No. of ester groups	Branches	Longest linear chain	Structural diversity
Viscosity	+	+	+	+	
VI	+		-	+	
Flash point	+	+	-	+	-
Low temp fluidity	-	+	+	-	+
Solvency	-	+	-	-	+
Biodeg-radability.	-	+	-		

Fig. 6 Structure–property relationships for ester basefluids. + indicates positive correlation, − indicates negative correlation (ref. 38).

Here, metal to metal contact occurs, so some wear is unavoidable. Wear reduces efficiency of operation, and eventually limits the lifetime of the appliance. Also, friction coefficients in mixed and boundary lubrication are much higher than in the hydrodynamic regime, leading to increased frictional losses. Friction converts mechanical energy to thermal energy, so higher friction also leads to overheating of the fluid and the contacting surfaces, which further reduces the expected lifetime of the appliance.

Loss of full fluid film lubrication will also occur if the load increases, or if the relative velocity decreases, in particular at startup and shutdown conditions. Therefore, in order to exploit the energy efficiency benefits of operation at the minimum friction point, the lubricant must be designed to have not only the correct viscosity under operating conditions, but also good inherent antiwear capabilities to prevent wear occurring during excursions to non hydrodynamic lubrication regimes.

Structure–property relationships such as those shown in Fig. 6 have been used to develop a range of POEs optimised for energy efficiency in refrigeration lubrication applications. These optimised POEs have permitted a progressive reduction in the industry standard lubricant viscosity, from 18 cSt at 40 °C when polyol ester lubricants were first introduced, to a typical value of 10 cSt today. This has delivered real benefits in energy efficiency, as shown in Fig. 7, which illustrates the dependence of energy consumption on lubricant viscosity for a standard domestic refrigerator. Reductions of energy consumption of approximately 10% as compared to the 18 cSt benchmark are achievable.[74]

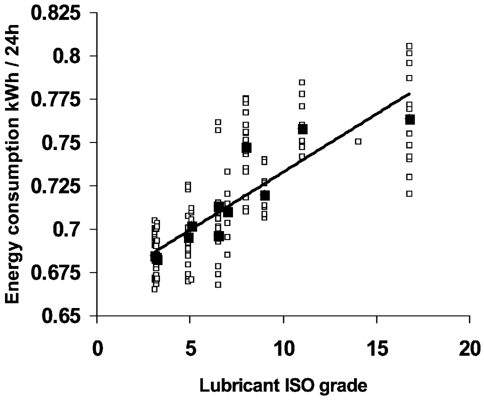


Fig. 7 Dependence of refrigerator energy consumption on lubricant viscosity, ref. 74.

The annual energy saving for a single appliance attributable to the viscosity reduction from 18 to 10 cSt is approximately 60 MJ. This is significantly higher than the process energy requirement for manufacture of the lubricant. Since the lifetime of a typical refrigerator is approximately 10 years, it is apparent that the lifetime energy saving greatly outweighs the total energy requirement for lubricant manufacture. A secondary benefit has been that the new generation optimised POE lubricants have been designed to be readily biodegradable and to use a significant proportion of raw materials derived, or potentially derivable, from renewable resources (Fig. 8).

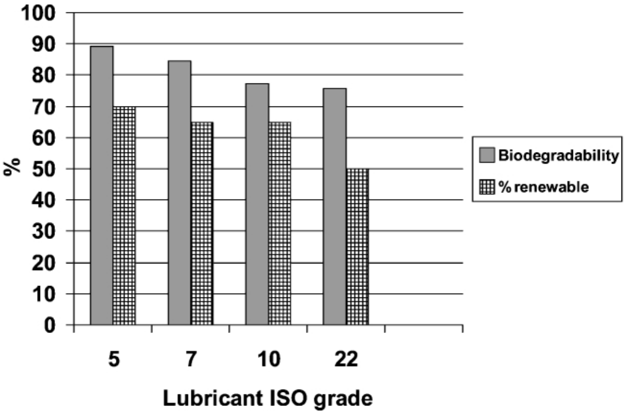


Fig. 8 Biodegradability by OECD 301B and percentage of renewable raw materials for a range of polyol ester refrigeration lubricant basefluids.

3.2 Hydraulic fluids. Reducing resource consumption through extended lubricant lifetime

Hydraulic fluids are used to transmit power. Typically, the fluid is pumped in a circuit from a central pumping unit *via* pipework to remote motors or actuators where the fluid energy is converted back to mechanical motion. Although lubrication is not their primary purpose, hydraulic fluids are regarded as a class of industrial lubricant because they must provide adequate lubrication to prevent wear of the pump and actuators, which would impair efficiency. For efficient power transmission, without high viscous losses or internal leakage, the viscosity of hydraulic fluids should normally be in the range 22–46 cSt at 40 °C. High thermal and oxidative stability, so as to maintain viscosity and prevent formation of sludge and varnish, is therefore a critical performance requirement.

Hydraulics are a very flexible, lightweight and efficient method for power transmission, and their use is particularly widespread in mobile equipment used in transportation, construction and agriculture. In such mobile hydraulic equipment, the pressurised hydraulic fluid is contained in flexible hoses, which are vulnerable to puncture or rupture. Any failure of containment leads to accidental discharge of hydraulic fluid to the environment. Consequently, where hydraulic equipment is used in environmentally sensitive applications such as watercourse maintenance and forestry, the fluids are increasingly required to be biodegradable.[27,76]

In some applications, the requirement for biodegradable hydraulic fluids can be met by use of natural oils. However, the applicability of natural oils is limited by their relatively low thermo-oxidative stability which restricts their useful lifetime. Also, their poor low temperature fluidity makes them unsuitable for use in low ambient temperature. Consequently, there is a developing requirement for high performance fluids, with thermo-oxidative stability equivalent or superior to that of mineral oil-based fluids, good low temperature fluidity and acceptable biodegradability characteristics. Synthetic esters are well suited to meet this requirement.

Consideration of the mechanisms of chemical decomposition of natural oils can be used to guide the molecular design of synthetic esters having improved stability. The structure of a typical vegetable oil is shown schematically in Fig. 9. Under high temperature oxidation conditions there are two distinct modes of reaction leading to decomposition, namely thermolysis and autoxidation.

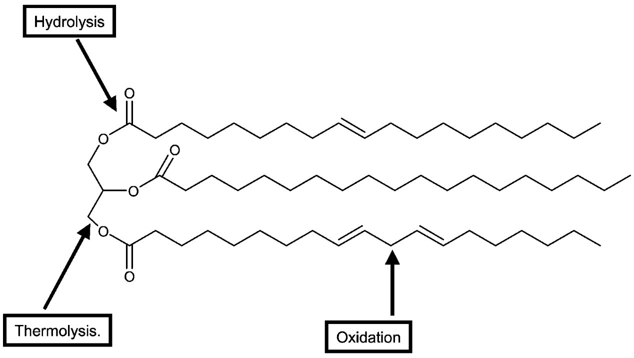


Fig. 9 Schematic structure of triglyceride natural oil, showing positions vulnerable to chemical degradation.

Thermolysis occurs by β-elimination at the ester group. The thermolysis pathway can therefore be prevented by transesterification to substitute the glycerol moiety in the original vegetable oil by a neopentyl polyol such as trimethylolpropane. The resulting ester contains no beta hydrogen atoms and therefore cannot undergo thermal decomposition by β-elimination.

Autoxidation is initiated by hydrogen abstraction from the carbon atoms vicinal to the olefinic bonds in the fatty acid residues. The rate of autoxidation is greatly reduced in compounds containing no olefinic unsaturation. Olefinic unsaturation can be removed by hydrogenation. However, hydrogenated vegetable oils are typically solid at ambient temperature and therefore not suitable for lubricant applications. Fatty acid isomerisation to introduce branching prior to hydrogenation gives good low temperature fluidity, but increases viscosity too much for the application. To substantially improve oxidative stability it is necessary to look to alternative basic structures, such as diesters or polyol esters of short chain saturated fatty acids. The structure–property relationships illustrated in Fig. 6 can be used to design materials having the appropriate properties for the application.

These principles have been used to develop high performance biodegradable hydraulic fluids based on synthetic esters. Biodegradability was assessed according to the OECD 301B protocol.[60] Thermo-oxidative stability was measured by determination of the oxidation induction time using high pressure differential scanning calorimetry (HP-DSC).[77] The HP-DSC induction time correlates with the expected oxidation–limited service lifetime for the lubricant.

Fig. 10 compares HP-DSC induction time for a series of oils including commercial formulated hydraulic oils based on vegetable and mineral oil basefluids, a formulation based on a trimethyolpropane ester of natural fatty acids, and a petrochemically derived fully saturated diester. At 150 °C, the induction time for the trimethyolpropane ester is higher than that for the vegetable oil formulation. The induction time for the saturated diester is shown to be equivalent to that of the mineral oil formulation, and approximately 10 times longer than that of the vegetable oil formulation. This illustrates that the autoxidation pathway is more significant than the thermolysis pathway under these conditions.

However, the thermolysis pathway still makes a significant contribution to overall decomposition, and thermo-oxidative stability can be further improved by combining the two approaches and designing synthetic esters based on neopentyl polyols with fully saturated acid groups. In saturated polyol esters of this type, both oxidative stability and biodegradability can be additionally improved by increasing the average number of ester groups per molecule and reducing the amount of tertiary branching. Operating within these constraints increases the manufacturing cost of the products, but can give significantly enhanced performance.

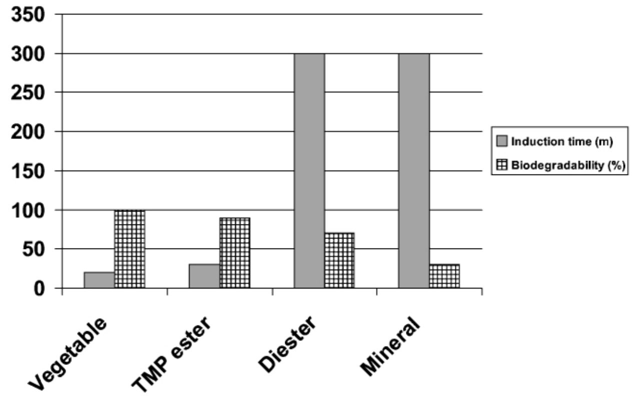


Fig. 10 Comparative HP-DSC induction time at 150 °C and biodegradabilities for formulated hydraulic fluids based on vegetable oil, trimethyolpropane ester of natural fatty acids, petrochemical diester and mineral oil.

Fig. 11 shows HP-DSC induction time under higher severity conditions for an optimised example of this type of saturated polyol ester, compared with the diester and mineral oil based formulations. At this higher test temperature, the diester can be seen to have significantly higher induction time than the mineral oil, but the optimised saturated polyol ester shows an induction time approximately five times greater than that of the mineral oil formulation, while retaining biodegradability equivalent to that of the vegetable-based formulation.

Products based on both types of synthetic ester have already been commercialised as basefluids for biodegradable hydraulic fluid formulations. Field experience has confirmed that the products deliver the predicted high stability and extended lifetime in practice.

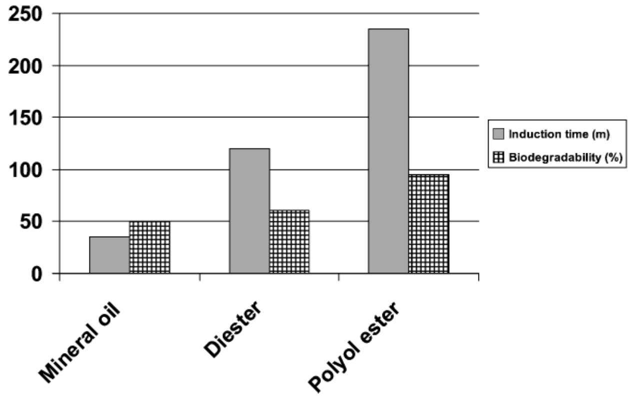


Fig. 11 Comparative HP-DSC induction time at 200 °C and biodegradabilities for formulated hydraulic fluids based on mineral oil, petrochemical diester and saturated short chain polyol ester.

3.3 Automotive lubricants. Improving fuel efficiency through additive technology

A very large proportion of overall fossil fuel consumption is used as transport fuel in internal combustion engines. Improving the fuel efficiency of these engines has long been a key objective of the automotive industry and it is generally recognised that the crankcase and transmission lubricants can contribute to improving energy efficiency in many ways.[78]

In a typical car engine, only around 20–35% of the chemical energy of combustion is converted to useful mechanical work. The remainder is lost as heat through the exhaust and through the engine cooling system, or as frictional or pumping losses in the engine and transmission.[79] Potentially the greatest gains in fuel efficiency would come by reducing the amount of energy lost as heat. Exploitation of this in so-called low heat rejection engines, coupled with other trends, such as cooling on demand, suggests that in future, lubricants will be required to operate at higher sump temperatures than at present.[78] This will obviously increase the thermo-oxidative stress and favour use of synthetic fluids having inherently good oxidative stability, as illustrated above for hydraulic fluids.

A further contribution to energy efficiency will come from the more widespread use of lower viscosity fluids. Ford Motor Company have recently announced a change from 5W-30 to lower viscosity 5W-20 lubricants for factory-fill for the majority of their vehicles. This is expected to deliver a net average 0.6% fuel economy saving across the product range. Ford believes the switch to lower viscosity oils in the USA alone will reduce carbon dioxide emissions by 190,000 metric tons a year and reduce fuel consumption by over 21 million US gallons a year.

The continuation of this trend will also lead to greater application of synthetic fluids. Lower viscosity generally implies lower molecular weight and consequently higher volatility. The combination of higher sump temperatures with lower viscosity fluids will be a major driver towards more widespread use of polar fluids such as esters, which have lower volatility than hydrocarbons of the same viscosity. High stability synthetics can also reduce the viscosity increase associated with oxidative degradation. This will give better retention of energy efficiency through the lifetime of the lubricant charge, and allow extension of drain intervals, which will reduce overall consumption of lubricant.

Thus, the same lubricant design considerations as outlined above in the hydraulic fluid and refrigeration lubricant examples will also contribute to energy conservation in internal combustion engines. However, for the internal combustion engine there is an further contribution to be made by friction modifier additives.

Unlike a domestic refrigeration compressor, a significant contribution to overall frictional losses in an internal combustion engine arises from contacts which operate under boundary lubrication conditions.[80,81] Under boundary conditions, the friction coefficient is essentially independent of lubricant viscosity, and becomes dependent on the nature of the contacting metal surfaces. Surface-acting additives can be used to modify the surface chemistry and reduce friction.

Inorganic friction modifiers based on molybdenum dithiocarbamate complexes act by chemical reaction to give *in situ* deposition of MoS_2, which is an effective solid lubricant because it has a lamellar structure with low interatomic forces between the planes.[82] Since this reaction is irreversible, soluble Mo concentration decreases over time and activity decreases with fluid ageing.[83] Furthermore, the molybdenum dithiocarbamates contribute to emissions of heavy metals and sulfur compounds. There is therefore growing interest in organic friction modifiers based on derivatives of natural long chain fatty acids. These are believed to act by reversible formation of mono- or multilayer surface films having low surface energy, which reduce friction through minimising adhesive forces between the opposing surfaces.[84]

Boundary friction coefficients can be measured using a pin on disk tribometer, which measures the friction force between metal test pieces under controlled load, relative velocity and temperature. Fig. 12 shows the variation of friction coefficient with sliding velocity at constant load and temperature for lubricants formulated with and without organic friction modifier. At high speeds the system is in the hydrodynamic lubrication regime and the test pieces are separated by a lubricant film. The friction force measured is due only to the viscosity of the bulk fluid and the additive has no effect. At low speeds the system is in the boundary lubrication regime, there is metal–metal contact and the presence of the additive reduces the friction coefficient by approximately 20%.

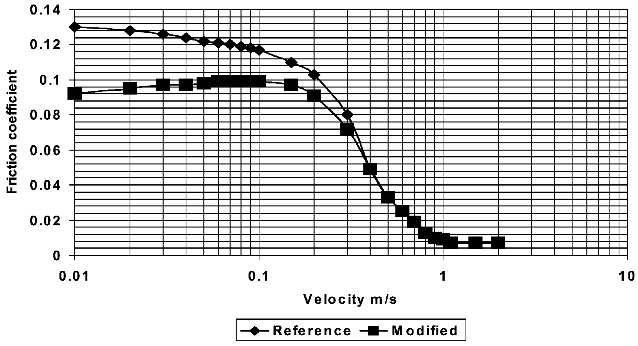


Fig. 12 Effect on boundary friction coefficient of friction modifier additive in reference lubricant, using a pin on disk tribometer.

Approximately 5% of the overall fuel energy in a typical internal combustion is dissipated in overcoming boundary friction,[79,80] so this translates in practice to a potential for approximately 1% reduction in fuel consumption . At present, both inorganic and organic friction modifier additives systems lose activity during the lifetime of a lubricant charge, due to oxidative instability. Development of improved additive systems offering higher activity and improved oxidative stability is an active area of research.

4 Discussion. What makes a lubricant 'green'?

This final section offers provisional conclusions as to how the principles of Green Chemistry should be applied to support future development of more sustainable lubricant technologies.

4.1 The importance of performance in use

The previous sections have developed the theme that lubricants have a unique capability to deliver environmental benefits in use, mainly through their role in reducing friction in machinery, which improves energy efficiency, thereby conserving fuel resources and reducing emissions of CO_2 and acid gases.

For car engine oils, the difference in fuel consumption between an optimised low friction oil and a standard oil can be as much as 5%.[85] In mobile hydraulics, fuel consumption savings of up to 3% may be obtainable through optimising the hydraulic fluid properties.[29] Even greater reductions in power consumption of domestic refrigerators have been demonstrated[74] and the same principles may be exploited to reduce power losses in hydro-electricity generation.[86]

These energy efficiencies potentially accessible through lubricant optimisation are significantly greater than the energy requirements for lubricant manufacture.[27,31]

The other key role of lubricants is reducing wear. This obviously serves to extend the useful life of machinery and thus also contributes to resource conservation. At the same time, consumption of the lubricants themselves, and of the resources involved in their manufacture, can be minimised by optimisation of the stability of the lubricant basefluids. Therefore, the most important issues to consider in assessing the environmental impact of lubricants are the performance parameters; friction reduction, wear reduction and lubricant stability.

Although these broad principles are applicable to lubricant optimisation in general, their implementation across many widely different lubricant applications, each having very different performance criteria, will require a very wide range of optimised lubricant solutions. To continue to develop this range of increasingly specialised products, lubricant developers will need to draw on the full range of available raw materials, and will make increasing use of synthetic basefluids and functional additives which permit optimisation of application performance through chemical design at the molecular level.

These conclusions are important in the context of the growing recognition of the necessity to make a transition to more sustainable technologies. Governments, industry and pressure groups are seeking to accelerate this transition by use of economic incentives to promote more sustainable technologies and by harnessing the power of consumer choice through ecolabelling schemes. It is essential that these measures are correctly targeted, or their effects will be counter-productive.

4.2 The role of renewable raw materials

The current focus on sustainable development has led to increasing interest in lubricants derived from renewable resources. In particular, the use of vegetable oils in lubricant and hydraulic fluid applications is being promoted.[87–90] Vegetable oils are renewable, biodegradable, have relatively low manufacturing process energy requirements and show some good lubricant properties. However they also have performance deficiencies which mean that their use is not necessarily an environmentally preferable option. The poor thermo-oxidative stability of vegetable oils reduces operational lifetime and increases the amount of lubricant required to be manufactured and disposed of.[27,36] Also, in applications where a closely specified viscosity is required for optimum energy efficiency, the narrow range of viscosities available from natural oils may not be optimal, with consequent energy inefficiencies.

Because of their particular combination of properties, natural oils are a good option for total loss, once-through applications like chainsaw lubricants and railroad greases, where stability is not an issue and ready biodegradability is a requirement. Vegetable oils such as rapeseed, canola and soybean oils are already widely used in such applications.

Considerable effort is being applied to modifying the properties of vegetable oils in order to make them more suitable for use in other applications. Conventional plant breeding and genetic modification of oil producing crops has been undertaken in order to alter the composition of the oils that they produce, for example by controlling polyunsaturation in order to improve oxidative stability,[91] and introducing branching to improve low temperature flow properties or increase viscosity.[92] However, the performance improvements achieved so far are marginal when compared to mineral oil or synthetic lubricant formulations.

The issue of operational lifetime is particularly significant in this context, in view of the very large volumes of lubricants currently consumed. Agricultural yields of vegetable oils from oilseed crops such as rape are typically in the range 1–2 tes ha^{-1},[93] so to produce enough vegetable oil to meet current European demand for around 5 Mtes pa of lubricants would require approximately 5 Mha (or around twice the area of Wales) to be cultivated for the purpose. However, because the lifetime of the vegetable oil derived products is shorter than that of the mineral oil formulations they would to replace, as in the hydraulic fluid example shown in Fig. 10, then a greater volume of vegetable oil would be required, and the land requirement would increase further.

Clearly, if renewable resources are to make a significant contribution, it must be in the form of raw materials for high performance synthetic lubricants and effect additives that will have extended lifetimes and therefore reduced material requirements, as compared to mineral oil based formulations. As described in Section 2.3.2 above, natural fatty acids and their derivatives are already used in the manufacture of high performance synthetic ester lubricants, and this use can be expected to increase. However, at present, synthetic lubricants having optimised performance cannot be manufactured from renewable resources alone. Petrochemically derived materials, such as the neopentyl polyols, are also essential components. Although these components could in principle be derived from biomass it is presently not economic to do so. Therefore, in the medium term there will continue to be an essential role for petrochemically derived components in lubricants.

The simplistic assumption that renewable resources are necessarily sustainable must also be questioned. True sustainability requires economic and social, as well as environmental sustainability. The exploitation of renewable resources is not necessarily sustainable in this broader sense. For example, the debate around the environmental impact and land use requirements for production of biodiesel (methyl esters of vegetable fatty acids)[93] has highlighted the fact that contemporary Western agriculture requires very high inputs of energy in the form of fertilisers and fuel for agricultural machinery and crop processing. The sustainability of these agricultural practices has been widely questioned, and the social implications in terms of land and labour requirements to deliver the same outputs without use of fossil fuel inputs have yet to be addressed.

In summary, exclusive use of renewable resources is not a sufficient condition for a sustainable technology, and may not be the most appropriate first step on the way. At present, legislation or economic incentives to restrict options for lubricant raw materials to those currently derived from renewables would lead to use of inappropriate or inferior products and would have a net detrimental effect on overall environmental burden. In a fossil-fuel powered society, where 95% of crude oil is consumed as fuel, it is both rational and responsible to divert some of that material for use as raw materials for lubricants, in order to ensure that our utilisation of the remainder is as efficient as possible.

4.3 Recycling or re-use as fuel

Another area where there is potential for legislative or economic incentivisation to have counterproductive effects arises at end of life, in the debate over whether it is preferable to recycle used lubricants by re-refining, or to re-use them for fuel value by combustion.

The European Waste Oil Directive is currently under review. The European Commission favours increased incentivisation of recycling and has considered a mandatory requirement for incorporation of a minimum percentage of recycled fluids into all new lubricant products. This prospect is of obvious concern to lubricant users and their suppliers, since it would constrain the development of products tailored to the requirements of particular applications, such as the examples given in Section 3. The composition of basefluids from recycling processes as currently practised is similar to that of lightly processed mineral oils, which have low biodegradability and relatively low thermal and oxidative stability. Incorporation of significant levels of this material would preclude development of biodegradable lubricants for use in environmentally sensitive areas, or high stability fluids with extended service lifetimes. Consequently, the lubricant industry, and most national governments generally regard fuel use as a more practical and equally acceptable option.

This debate over the extent to which recycling into the same application should be incentivised by legislation is common to many other product groups where recycling is becoming significant *e.g.* polymers and paper products. Recycling processes are greatly facilitated by standardisation, and reduction of the number of different materials used. However, enforced standardisation of materials, or requiring a minimum recycled component, can lead to inappropriate use of materials which may compromise economic or environmental performance and even safety. Well-intended legislation to require a predetermined arbitrary level of recycling can be a blunt instrument having unintended adverse consequences.

A recent article outlined the arguments for and against the recycling and combustion options, concluding that highest priority should be given to encouraging collection of used oil for disposal by whichever route.[85] It can also be argued that the issue would be best addressed by promoting the use of lubricants having improved stability and extended drain intervals, in order to reduce at source the amount of waste oil requiring disposal.

4.4 Ecolabelling schemes

In addition to legislative requirements, labelling schemes are increasingly being developed in order to promote the use of more environmentally acceptable materials. Recent articles have reviewed the current status of labelling schemes and environmental legislation for lubricants.[21,94,95] Particularly influential developments in Europe have included the German Blue Angel labelling scheme for hydraulic fluids, saw lubricants and metal working fluids,[96] and the voluntary section on environmental properties included in the Swedish Standard for hydraulic fluids.[97] These initiatives set criteria for all components of a lubricant formulation and have prompted considerable effort in the industry to develop products meeting the requirements.

Ecolabels have played a valuable role in aiding decision making and influencing market activities. However it must be understood that they represent an attempt to compress all of the potential environmental impacts of a product or process into a single criterion for decision making. This necessarily involves judgements about the relative importance of the various potential impacts, which will reflect the needs of a particular application and the values of the organisation responsible. Thus, whereas LCA or Eco-profiles provide objective and quantitative information, ecolabels represent subjective interpretation. Ecolabels should therefore only be used in the context for which they were originally developed and are potentially misleading if conclusions are taken out of context.[98] In particular, existing ecolabelling schemes have focussed on toxicity, ecotoxicity and biodegradability and do not recognise the potential environmental benefits of optimised performance in use.

A further criticism of current labelling schemes is that they are based on the properties of unused lubricants and do not take account of the significant changes in toxicology or ecotoxicity which may result from ageing of oils in use.[99,100] However, given the range of potential operating conditions there is currently no consensus on what would constitute a meaningful standardised oil ageing protocol in order to generate reproducible and representative samples of aged oils.

5 Conclusions. Towards sustainability

A recent OECD workshop considered the contribution of chemistry to sustainable development, and concluded that 'We should strive to maximise resource efficiency through activities such as energy and non-renewable resource conservation, risk minimisation, pollution prevention, minimisation of waste at all stages of a product life cycle and the development of products that are durable and can be re-used and recycled'.[101]

There is scope for development of lubricant technology in all of these areas, but lubricants have a particularly important contribution to make in relation to energy conservation, minimisation of waste and development of durable products. While material recycling and use of renewable raw materials are undoubtedly requirements of a future sustainable technology, they are not necessarily the first issues to address. Truly green lubricants are those that optimise energy efficiency and minimise wear in the machinery which they lubricate, and which have maximised service lifetimes in order to reduce the amount of lubricant required. These principles are expected to lead to increasing use of high performance synthetic basefluids and effect additives. Green Chemists will have an important role to play in the design and manufacture of the novel materials which will be required.

Acknowledgements

Thanks are due to my many colleagues in Uniqema Lubricants who have assisted in preparation of this paper, in particular Steve Randles, Thomas Bunemann and Hans Ridderikhoff, and to Uniqema for permission to publish.

References

1 *Chemistry and Technology of Lubricants*, ed. R. M. Mortier and S. T. Orzulik, Blackie Academic and Professional, London, 2nd edn., 1997.
2 D. Klamann, *Lubricants and related products*, Verlag Chemie, Hamburg, 1984.
3 A. Dorinson and K. C. Ludema, *Mechanics and Chemistry in Lubrication*, Elsevier, Amsterdam, 1985.
4 *Industrial Tribology*, ed. M. H. Jones and D. Scott, Elsevier, Amsterdam, 1983.
5 *Industrial Liquid Lubricants, ISO Viscosity Classification*, International Organisation for Standardisation. ISO 3448, 1992.
6 *SAE viscosity grades for engine oils*, Society of Automotive Engineers, SAE J300, Dec. 1999.
7 H. A. Spikes, *Boundary lubrication and boundary films*, in *Thin Films in Tribology*, ed. D. Dowson , Elsevier, Amsterdam, 1993, p. 331.
8 J. Briant, J. Denis and G. Parc, *Rheological Properties of Lubricants*, Editions Tecnip, Paris, 1989.
9 S. Bair, *Recent developments in high pressure rheology of lubricants*, in *Lubricants and Lubrication. Proc 20th Leeds – Lyon Symposium on Tribology*, 1994, ed. D. Dowson *et al.*, Elsevier, Amsterdam, 1995, p. 169.
10 *Pressure – Viscosity Report*, ASME Research Committee on Lubrication, American Society of Mechanical Engineers, New York, 1953.
11 A. R. Lansdown, *High Temperature Lubrication*, MEP, London, 1994.
12 *New Directions in Tribology*, ed. I. M. Hutchings, IMechE, London, 1997.
13 C. Kajdas, *Tribochemistry*, in *Tribology 2001*, ed. F. Franek *et al.*, OTG, Vienna, 2001, p. 39.
14 F. Gunstone, *Fatty Acid and Lipid Chemistry*, Blackie Academic and Professional, London, 1996.
15 L. Archbutt and R. M. Deeley, *Lubrication and Lubricants*, Charles Griffin & Co., London, 5th edn., 1927.
16 D. Soul, *Lubricant Additives*, in ref. 4, p. 242.
17 *Synthetic Lubricants and High Performance Functional Fluids*, ed. L. R. Rudnick and R. L. Shubkin, Marcel Dekker Inc., New York, 1999.
18 S. Boyde, S. J. Randles and P. Gibb, *The effect of molecular structure on boundary and mixed lubrication by synthetic fluids – an overview*, in *Lubrication at the Frontier*, ed. D. Dowson *et al.*, Elsevier, Amsterdam, 1999, p. 799.
19 *Lubricating Oil Additives*, SRI International, *Chemical Economics Handbook*, Menlo Park, CA, December 1999.
20 *Strategy for a future chemicals policy*, Commission of the European Communities, White Paper, Brussels, 27/2/2001.
21 W. J. Bartz, *Lubricants and the Environment*, in ref. 12, p. 103.
22 *Lubricants for the Future and Environment. Proceedings of the 6th International LFE congress*, Brussels, 1999.
23 (*a*) *Ecological and Economic Aspects of Tribology. Proceedings of 9th International Conference, Technische Akademie Esslingen*, ed. W. J. Bartz, 1994; (*b*) *Solving Friction and Wear Problems, Proceedings of the 10th International Symposium, Technische Akademie Esslingen*, ed. W. J. Bartz, 1996; (*c*) *Industrial and Automotive Lubrication. Proceedings of 11th International Conference, Technische Akademie Esslingen*, ed. W. J. Bartz, 1998; (*d*) *Tribology 200 – Plus. Proceedings of 12th International Conference, Technische Akademie Esslingen*, ed. W. J. Bartz, 2000; (*e*) *Lubricants, Materials and Lubrication Engineering. Proceedings of 13th International Conference, Technische Akademie Esslingen*, ed. W. J. Bartz, 2002.
24 *Environmental Management - Life Cycle Assessment - Principles and Framework*, International Organisation for Standardisation., ISO 14040, 1997.
25 M. Stalmans, H. Berenbold, J. L. Berna, L. Cavalli, A. Dillarstone, M. Franke, F. Hirsinger, D. Janzen, K. Kosswig, D. Postlethwaite, Th. Rappert, C. Renta, D. Scharer, K.-P. Schick, W. Schul, H. Thomas and R. van Sloten, *'European Life Cycle Inventory for detergent surfactants production'*, *Tenside Surfactants Deterg.*, 1995, **32**, 84.
26 I. Boustead, *Eco profiles of the European plastics industry*, APME, Brussels, 1999.
27 (*a*) C. R. Burrows, G. P. Hammond and M. C. McManus, *The Sixth Scandinavian International Conference on Fluid Power; SICFP 99; Tampere; Finland*, 1999, p. 1163; (*b*) M. C. McManus, G. P. Hammond and C. R. Burrows, in *Environmental Impact of Fluid Power Systems*, IMechE, 1999; (*c*) M. C. McManus, G. P. Hammond and C. R. Burrows, *Proc. 48th National Conference on Fluid Power*, NFPA, Chicago, 2000, p.21; (*d*) C. R. Burrows, G. P. Hammond and

M. C. McManus, *Fluid Power Systems and Technology, FPST*, ed. S. S. Nair and S. I. Misstry, ASME, New York, 1998, vol. 5, p. 61.

28 C. Ciantar and M. Hadfield, *Investigating the sustainable development of domestic refrigerating systems working in an HFC-134a environment*, in *Recent Developments in Refrigeration and Heat Pump Technologies*, IMechE Semin. Publ. 10, 1999, p. 47.

29 C. Vag, A. Marby, M. Kopp, L. Furberg, T. Norrby, *A comparative life cycle assessment (LCA) of the manufacturing of base fluids for lubricants*, in ref. 23(*d*), p. 2241.

30 Levizzari, M. Voglino and P. Volpi, *Environmental and Economic Impact of re-refined produts: a Life Cycle Analysis*, in ref. 22.

31 M. Voltz, *Ökobilanz fur Schmierstoffe - Grundlagen und Vorgehensweise*, in ref. 23(*e*), p. 1041.

32 *Green chemistry, Theory and Practice*, ed. P. T. Anastas and J. C. Warner, OUP, Oxford, 1998.

33 P. T. Anastas and R. L. Lankey, *'Life Cycle Assessment and green chemistry: the yin and yang of industrial ecology'*, *Green Chem.*, 2000, **2**, 289.

34 A. D. Curzons, D. J. C. Constable, D. N. Mortimer and V. L. Cunningham, *'So you think your process is green'*, *Green Chem.*, 2001, **3**, 1.

35 G. van der Waal, D. Kenbeek, *Environment Protective Ester Base Fluids*, in ref. 23(*a*), 13.3–1.

36 S. Z. Erhan and S. Asadauskas, *'Lubricant basestocks from vegetable oils'*, *Ind. Crops Prod.*, 2000, **11**, 277–282.

37 *Fatty Acids in Industry*, ed. R. W. Johnson and E. Fritz, Marcel Dekker, New York, 1989.

38 S. J. Randles, *Esters*, in ref. 17, p. 63.

39 T. E. Brewer, *Dimer Acid*, in *Kirk Othmer Encyclopaedia of Chemical Technology*, Wiley, New York, 4th edn., 1993, **vol. 8**, p. 223.

40 R. W. Johnson, C. W. Pollock and R. R. Cantrell, *Dicarboxylic Acids*, in *Kirk Othmer Encyclopaedia of Chemical Technology*, Wiley, New York, 4th edn., 1993, **vol. 8**, p. 118.

41 S. Boyde, *'Low temperature characteristics of synthetic fluids'*, *Synth. Lubr.*, 2001, **18**, 99.

42 A. S. Patil, V. A. Pattanshetti and M. C. Diwedi, *'Functional Fluids and Additives based on Vegetable Oils and Natural Products'*, *Synth. Lubr.*, 1998, **15**, 193.

43 W. F. Holderich, L. A. Rios, P. P. Weckes and H. Schuster, *Development of new environmentally acceptable lubricants and pressure media*, in ref. 23(*e*), p. 1759.

44 T. A. Isbell, M. R. Edgcomb and B. A. Lowery, *'Physical properties of estolides and their ester derivatives'*, *Ind. Crops Prod.*, 2001, **13**, 11.

45 Environmental Data Services, *ENDS Rep.*, 2001, **323**, p. 33.

46 *Lubricant Additives and the Environment*, ATC document 49. ATC (The Technical Committee of Petroleum Additive Manufacturers in Europe), CEFIC, Brussels, 1993.

47 *The collection, disposal and regeneration of waste oil and related materials*, Concawe (Oil companies European Organisation for Environmental and Health Protection), Report 85/53, The Hague, 1985.

48 *Economics of Waste Oil Regeneration*, Coopers & Lybrand, The Hague, 1997.

49 *Critical Review of Existing Studies and Life Cycle Analysis on the Regeneration and Incineration of Waste Oils*, Taylor Nelson Sofres Consulting, Final Report, Dec 2001, http://europa.eu.int/comm/environment/waste/waste_oil.htm.

50 A. R. Lansdown, *Consumption and Conservation of Lubricants*, in ref. 4, p. 267.

51 W. D. Phillips and D. I. Sutton, *'Improved maintenance and life extension of phosphate esters using ion-exchange treatment'*, *Synth. Lubr.*, 1996, **13**, 225.

52 D. de Winter, *Rerefining in Europe today*, in ref. 22.

53 C. I. Betton, *Lubricants and their Environmental Impact*, in ref. 1, p. 13.

54 G. Glasgow and R. J. Bruns, *Reclamation of synthetic turbine engine oil mixtures*, USAF Report AFAPL-TR-78-50, MRC-DA-780, 1979, from *Gov. Rep. Announce. Index*, 1979, **79**, 167 (*Chem. Abstr.*, 1980, **92**, 200605n).

55 D. Gourgouillon, S. Sarrade and L. Schrive, *Refining treatment of oils*, *PCT Pat. Appl.*, WO-200052118 A, 2000.

56 B. R. Bond, A. G. Gorneau, C. W. Harrison and R. M. Steinberg, *Reclaiming used lubricating oil*, *US Pat. Appl.*, US-5306419 A, 1994.

57 R. Deutsch, *Separation and recovery of synthetic oils from used motor sump oils*, *Eur. Pat. Appl.*, EP-1028158 A, 2000.

58 R. B. Cain, *Biodegradation of Lubricants*, in *Biodegradation and Biodeterioration 8*, ed. H. W. Rossmore, Elsevier, Amsterdam, 1991.

59 *Test method for the biodegradability of two-stroke cycle outboard engine oils in water*, CEC (Coordinating European Council for the development of performance tests for lubricants and engine fuels), CEC L-33-T-93, 1993.

60 *OECD guideline for the testing of chemicals. Ready Biodegradability*, OECD (Organisation for Economic Cooperation and Development.) OECD 301, 17/7/92.

61 S. J. Randles, *Synthetic Lubricants applied to Air Compressors*, in ref. 22.

62 N. S. Battersby, *Application of the Concawe Biodegradability test for oil products*, *Synth. Lubr.*, 2000, **17**, 136.

63 N. S. Battersby, *The Concawe biodegradability test for oil products*, in ref. 23(*d*), p. 113.

64 *Microbial Degradation of Organic Compounds*, ed. D. T. Gibson, Marcel Dekker, New York, 1984.

65 J. A. Henry, *'Composition and toxicity of petroleum products and their additives'*, *Hum. Exp. Toxicol.*, 1998, **17**, 111.

66 *Health aspects of lubricants*, CONCAWE report 5/87, CONCAWE, October 1987.

67 T. M. Warne and C. A. Halder, *'Toxicity of lubricating oils'*, *Lubr. Eng.*, 1986, **42**, 97.

68 A. R. Eyres, *Health and Safety Aspects of Lubricants*, in ref. 4, p. 275.

69 E. Clonfero, *Mutagenic and carcinogenic agents in new, used and re-refined oils*, in ref. 22.

70 R. K. Hewstone, *Health, Safety and Environmental Aspects of Handling, Re-use and Disposal of Used Crankcase Lubricating Oils*, in ref. 23(*a*), 13.7–1.

71 R. F. Modler, E. Anderson and Y. Ishikawa, *Synthetic Lubricants*, *Speciality Chemical Update Programme*, SRI International, Menlo Park, CA, 1997.

72 *IPCC Special Report on Emissions Scenarios*, IPCC (Intergovernmental Panel on Climate Change), 2001. http://www.grida.no/climate/ipcc/emission/index.htm.

73 M. Fuchs, *The World Lubricants Market - Current Situation and Outlook*, in ref. 23(*d*), p. 9.

74 S. Boyde, P. Gibb, S. J. Randles, S. Corr, P. Dowdle and A. McNicol, *Effect of lubricant properties on efficiency of refrigeration compressors*, *Proc. 2000 Intl. Compressor Engineering Conf. at Purdue*, ed. W. Soedel, 2000, p. 311.

75 S. J. Randles, *Refrigeration Lubes*, in ref. 17, p. 563.

76 T. Norrby and M. Kopp, *Environmentally adapted lubricants in Swedish forest industry*, in ref. 23(*d*), p. 161.

77 *Standard Test Method for Oxidation Induction Time of Lubricating Oils by Pressure Differential Scanning Calorimetry*, American Society for Testing of Materials, ASTM D6186-98, 1998.

78 S. Korcek, J. Sorab, M. D. Johnson and R. K. Jensen, *'Automotive Lubricants for the next millenium'*, *Ind. Lubr. Tribol.*, 2000, **52**, 209.

79 M. T. Benchaita and F. E. Lockwood, *'Reliable model of lubricant related friction in internal combustion engines'*, *Lubr. Sci.*, 1993, **5**, 259.

80 R. I. Taylor, *Engine Friction Lubricant Sensitivities*, in ref. 23(*c*), p. 1289.

81 R. C. Coy, *Practical Applications of Lubrication Models in Engines*, in ref. 12, p. 197.

82 J. Graham and H. Spikes, *The behaviour of molybdenum dialkyldithiocarbamate friction modifier additives*, in *Lubrication at the Frontier*, ed. D. Dowson, M. Priest, C. M. Taylor, P. Ehret, T. H. C. Childs, G. Dalmaz, Y. Berthier, L. Flamand, J.-M. Georges and A. A. Lubrecht, Elsevier, Amsterdam, 1999, p. 759.

83 S. Korcek, *Chemistry of Engine Oil An important design parameter*, in *Tribology for Energy Conservation*, ed. D. Dowson, T. H. C. Childs, C. M. Taylor, Y. Berthier, G. Dalmaz, L. Flamand, J.-M. Georges and A. A. Lubrecht, Elsevier, Amsterdam, 1998, p. 25.

84 J. Crawford, A. Psaila and S. T. Orszulik, *Miscellaneous Additives and Vegetable Oil*, in ref. 1, p. 181.

85 *Disposing of used lubricating oils*, Concawe (Oil companies European Organisation for Environmental and Health Protection), *Concawe Review*, 2000, **vol. 9**, p. 21.

86 S. B. Glavatskikh, *On the hydrodynamic lubrication of tilting pad thrust bearings*, Doctoral Thesis 2000:34, University of Luleå, Sweden, 2000.

87 D. L. Johnson and W. Lambert, *Biodegradable liquid lubricant composition for internal combustion engines*, *US Pat. Appl.*, US 5888947, 1997.

88 L. A. T. Honary, *'Production of soya bean-based hydraulic fluid'*, *Bioresource Technol.*, 1996, **56**, 41.

89 P. De Caro and A. Gaset, *'Lubricants based on renewable resources'*, *Ol., Corps Gras, Lipides*, 1999, **6**, 217.

90 A. Willing, *'Oleochemical esters. Environmentally compatible raw materials for oils and lubricants from renewable resources', Fett/ Lipid*, 1999, **101**, 192.

91 L. R. Debonte, Z. Fan and D. R. Kodali, *New triacylglycerol oils with high 1,3-dierucoyl-2-oleoylglycerol content*, *PCT Pat. Appl.*, WO-200007432 A, 2000.

92 P. Duhot, E. Gontier, M. Menard, D. Thomas and B. Thomasset, *Transgenic plants producing branched fatty acids*, *Fr. Pat. Appl.*, FR-2769320 A, 1999.

93 *Alternative Road Transport Fuels - A Preliminary Life Cycle Study for the UK*, ETSU, HMSO, London, 1996.

94 B. F. Droy and S. J. Randles, *Environmental Impact*, in ref. 17, p. 793.

95 E. M. Stempfel, *'Practical experience with highly biodegradable lubricants, especially hydraulic oils and lubricating greases', NLGI Spokesman*, 1998, **62**, 8.

96 *Basic Criteria for the Award of the Environmental label*; (*a*) RAL-UZ 48, *Rapidly biodegradable chain lubricants for motor saws*; (*b*) RAL-UZ 64, *Rapidly biodegradable lubricants and forming oils*; (*c*) RAL-UZ 79. *Rapidly biodegradable hydraulic fluids*, Umweltbundesamt, Berlin, Jan. 2000.

97 *Hydraulic fluids, Requirements and test methods*, Swedish National Standard, SS 15 54 34, SIS (Swedish Standards Institute), 1997.

98 I. Boustead, B. R. Yaros and S. Papasavva, *Eco-labels and eco-indices. Do they make sense?, Proceedings of the 2000 Total Life Cycle Conference*, 2000, pp. 63–75 (SAE paper 00TLCC-49).

99 R. P. H. Schmitz, P. H. Roland, A. Eisentrager, T. Lindvogt, F. Moller and W. Dott, *'Increase of the toxic potential of synthetic ester lubricant oils by usage', Chemosphere*, 1998, **36**, 1513.

100 R. P. H. Schmitz, P. H. Roland, A. Eisentrager, T. Lindvogt, F. Moller and W. Dott, *'Operation-caused impairment of the environmental compatibility of lubricating oils based on synthetic esters', Tribol. Schmierungstech.*, 1998, **45**, 10.

101 *Proc. OECD Workshop on Sustainable Chemistry*, Series on Risk Mangement No. 10., 1998, OECD, ENV/JM/MONO(99)19. http://www.olis.oecd.org/olis/1999doc.nsf/LinkTo/env-jm-mono(99)19-PART1.

The sustainability of resource utilization

S. Lems, H. J. van der Kooi and J. de Swaan Arons

Laboratory of Applied Thermodynamics and Phase Equilibria, Delft University of Technology, Julianalaan 136, NL-2628 BL Delft, Netherlands. E-mail: s.lems@tnw.tudelft.ul

Received 9th April 2002
First published as an Advance Article on the web 23rd July 2002

There is a need for a method with which the sustainability of technological processes can be described quantitatively, and earlier work by De Wulf *et al.*[1] in cooperation with our laboratory has yielded a useful method based on thermodynamic principles. New insights however have led to a revision of this earlier work, and considerable improvements have been introduced. Most progress is made in quantitatively describing the sustainability of resource utilization. Instead of classifying resources either as renewable or as non-renewable, the new method is based on the depletion rates of resources, which account for many grades of resource renewability and which include also the size of natural reserves of resources. Also, this paper reviews the quantification of other aspects of process sustainability, explains the vital role of exergy, and discusses how the overall sustainability of a process should be determined.

Introduction

Industry is under increasing pressure from governments and environmental groups to improve the sustainability of its processes. However, how this higher level of sustainability should be achieved is not really clear, and even the definition of sustainability is often only qualitative. The most widely accepted description of sustainability is given by Brundlandt[1] as fulfilling the needs of present generations without endangering the possibilities of fulfilling the needs of future generations. However, besides the qualitative description of sustainability by Brundlandt,[2] there is a need for a tangible *quantitative* description that allows the sustainability of technological processes to be systematically evaluated, compared and improved.

Earlier work by De Wulf *et al.*[1] in cooperation with our laboratory had shown that different aspects of process sustainability can be quantified by using thermodynamic principles. Indeed, the thermodynamic concept of exergy is used as the basis for the construction of sustainability parameters, which conveniently express particular aspects of process sustainability on a scale of zero to one. Elements of this work were used at our laboratory to analyze the sustainability of several industrial processes, and new insights have led to some meaningful improvements. In this article, we will briefly discuss the work of De Wulf *et al.*[1] and we will explain how further improvements can be made. First however, we will explain how thermodynamic principles can help to give a proper quantitative expression of process sustainability.

Role of thermodynamics

Thermodynamics can contribute to a method for quantifying process sustainability *via* the concept of exergy. Exergy is defined by Szargut[3] as the amount of work that can *ideally* be performed by a material or amount of energy when it is brought from its actual conditions to the conditions of the natural environment (see Fig. 1). The term ideally in this definition refers to the thermodynamic limit that can theoretically be achieved in a completely reversible process. In essence, exergy views both energy and matter in terms of their ability to perform useful work in a particular natural environment.

All real processes must consume exergy to proceed, and this means that all our technological activities are ultimately limited by our ability to supply exergy to our processes. The only exergy that can be considered as truly sustainable is the exergy supplied by solar radiation, because this solar exergy will be available on a very large timescale and its immaterial nature allows processes using it to operate within closed material cycles on earth.

However, our potential to use solar exergy is limited. Although the total amount of exergy reaching the earth as solar radiation is enormous, this exergy is dispersed over a very large area and its effective harvesting is limited to relatively few sites. These sites are often also the areas needed for agriculture, living space, and industrial activity, and, in addition, too intensive harvesting of solar exergy can be disruptive to the natural

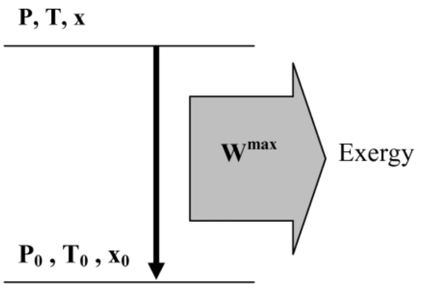


Fig. 1 Exergy is the maximum amount of work (W^{max}) that can be obtained from an amount of energy or matter when it is brought from its actual conditions (P, T, x) to the conditions of the natural environment (P_0, T_0, x_0).

Green Context

Sustainability is a critical issue and the word is often bandied about. However, how can we measure whether a process is genuinely sustainable? This paper relates to the evolution of a model which can be used to help decide on the sustainability of a given practice. Key advances include the quantification of renewability beyond a renewable/not renewable basis. ***DJM***

DOI: 10.1039/b203490p

environment. For instance, large-scale introduction of solar panels can alter the natural heat absorption of the surface and it thereby has the potential to alter local climates.

It is clear that ultimately our only limitation to sustainable production is obtaining the exergy to run the production processes and to drive closed material cycles. In view of this, exergy can be considered the ultimate scarce resource in our technological processes, and exergy flows to or from these processes are therefore vital elements of a method aiming to quantify process sustainability. The first attempts to use exergy flows in the construction of sustainability parameters were made by De Wulf *et al.*[1] in cooperation with our laboratory. This original quantification method is the basis for our newly developed method and will therefore be described first.

Original quantification method by De Wulf *et al.*[1]

De Wulf *et al.*[1] define one sustainability coefficient, which aims to quantitatively express the overall sustainability of a process on a scale of zero to one. This coefficient is based on two sustainability parameters, which are the renewability parameter α^{renew} and the overall efficiency parameter η^{overall}. These two parameters and the construction of the overall sustainability coefficient are discussed in the following sections.

Renewability parameter (α^{renew})

The renewability parameter focuses on the sustainable nature of the resources used in a process. To this end, a distinction is made between renewable resources and non-renewable resources. Resources are considered renewable when their (re)generation rate is at least as high as their consumption rate, while resources are non-renewable when their consumption rate exceeds their regeneration rate. Examples of non-renewable resources are mineral deposits and fossil fuels such as coal, oil, and natural gas; examples of renewable resources are solar-, wind-, hydro- and geothermal energy. In this way, all resources used in a process can be divided into two groups: renewable resources and non-renewable resources.

The renewability parameter then views the extent to which the process uses renewable resources rather than non-renewable ones (see Fig. 2). As discussed earlier, all resources can be expressed thermodynamically in relation to the natural environment by their exergy values, and the renewability parameter is therefore defined as the exergy value of the ingoing renewable resources as a fraction of the exergy value of all resources used in the process:

$$\alpha^{\text{renew}} = \frac{\sum \dot{E}x_{\text{in,renewable}}}{\sum \dot{E}x_{\text{in}}} \tag{1}$$

The renewability parameter expresses the extent to which the exergy input of the process is achieved with renewable resources. More use of renewable resources then leads to higher values of α^{renew}; $\alpha^{\text{renew}} = 1$ is achieved when all exergy required in the process is supplied by renewable resources and none is derived from non-renewable resources.

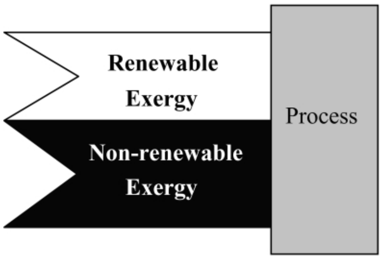


Fig. 2 The renewability parameter represents the fraction of exergy input obtained from renewable resources.

Efficiency parameter (η^{overall})

The efficiency parameters focus on the sustainability of the production process. The first efficiency parameter η_1 relates the exergy required to run the process to the total exergy required to run the process when also abating harmful emissions that are formed either during the production or during the destruction stage of the products:

$$\eta_1 = \frac{\sum \dot{E}x_{\text{in,process}}}{\sum \dot{E}x_{\text{in,process}} + \sum \dot{E}x_{\text{in,I}} + \sum \dot{E}x_{\text{in,II}}} \tag{2}$$

The first exergy term in the numerator of eqn. (2) represents the exergy required to run the production process without considering abatement. The second and third term both represent the exergy required to convert harmful emissions to compounds that are harmless to the natural environment. The second term deals with the emissions occurring during production, while the third term deals with the emissions that occur during the destruction stage of the product.

This efficiency parameter η_1 is also referred to as an environmental parameter because it expresses the extent to which no extra exergy input is required to abate harmful emissions relative to the exergy input of the process without abatement. Indeed, at $\eta_1 = 1$ the second and third exergy terms are zero, and hence no harmful emissions are generated either during the production process or during the destruction of products after their use.

The second efficiency parameter η_2 considers only the efficiency of the process itself (*i.e.* without abatement) and therefore simply relates the exergy input to the exergy output of the process. The parameter is defined as the exergy value of the useful products as a fraction of the exergy value of resources required to run the process:

$$\eta_2 = \frac{\sum \dot{E}x_{\text{out,useful}}}{\sum \dot{E}x_{\text{in,process}}} \tag{3}$$

Both efficiency parameters η_1 and η_2 are combined in the overall efficiency parameter η^{overall}:

$$\eta^{\text{overall}} = \eta_1 \cdot \eta_2 = \frac{\sum \dot{E}x_{\text{out,useful}}}{\sum \dot{E}x_{\text{in,process}} + \sum \dot{E}x_{\text{in,I}} + \sum \dot{E}x_{\text{in,II}}} \tag{4}$$

The overall efficiency parameter η^{overall} relates the exergy value of the useful products to the exergy required to produce the products and to abate harmful emissions that occur either during production or during the destruction stage of the products.

Overall sustainability

De Wulf *et al.*[1] finally define the overall sustainability coefficient S as the average of the two sustainability parameters α^{renew} and η^{overall}:

$$S = \tfrac{1}{2}\cdot(\alpha^{\text{renew}} + \eta^{\text{overall}}) \tag{5}$$

In this definition, both parameters α^{renew} and η^{overall} have equal effect on the overall sustainability coefficient S. Maximum overall sustainability $S = 1$ is obtained when all resources used in the process are renewable, giving $\alpha^{\mathrm{renew}} = 1$, and when also no exergy is lost in the process and no exergy is needed to abate harmful emissions.

Revised quantification method

The revised quantification method expresses the sustainability of technological processes in a set of three independent sustainability parameters. These three parameters deal with the resource utilization, the energy conversion, and the environmental compatibility of the process, respectively. The second and third parameter are revised elements of the work of De Wulf *et al.*,[1] while the definition of the first parameter is entirely different. The parameters are discussed separately in the sections below.

Sustainable resource utilization (α)

One of the major factors undermining the sustainability of a production process is the depletion of the resources it uses. A quantification of process sustainability should therefore include a parameter that deals with the sustainability of resource utilization, and the construction of such a parameter begins with defining a quantitative measure for the depletion of an individual resource. One way of doing this is to classify each resource as either renewable or non-renewable, as was done by De Wulf *et al.*[1] The distinction made between renewable and non-renewable resources is that renewable resources are produced at least as fast as they are consumed, while non-renewable resources are consumed faster than they are produced (see section renewability parameter).

However, there are two major problems with this renewability concept. First, the idea of a resource being either renewable or non-renewable seems somewhat artificial. Even the sun is depleting a finite amount of nuclear fuel, and it is therefore dubious to regard solar energy and derived energy sources such as wind and hydro energy as completely renewable. Also, so-called non-renewable resources such as fossil fuels or mineral deposits are being formed naturally to some extent, and therefore they are not entirely non-renewable. Obviously, the renewability of resources is more gradual than suggested in the black-and-white representation of renewable *vs.* non-renewable, and a parameter expressing the sustainability of resource utilization should account for these more subtle differences in resource renewability.

A second objection that can be made against the renewability concept is that renewability is only a part of sustainable resource utilization, since it does not involve the natural reserves of resources. Although the concept of renewability rightfully views the consumption rate of a resource in relation to its production or regeneration rate, this gap between consumption and regeneration rate should in turn be viewed in relation to the size of the natural reserves of that resource. In fact, a temporary discrepancy between the consumption and the regeneration rate of a resource does not necessarily threaten the sustainability of a process when the resource is plentiful. Of course, not having certain material cycles closed can have a profound effect on the natural environment *e.g. via* harmful emissions, but this is beyond the scope of this particular sustainability parameter, which deals only with resource depletion.

Hence, instead of considering the renewable versus the non-renewable resources in a process, it is preferred to quantitatively combine the consumption rate ($\phi_{\mathrm{m,consumption}}$), the regeneration rate ($\phi_{\mathrm{m,production}}$), and the extent of natural reserves (M_{reserves}) of a resource, as they are known at this time, in a resource depletion time (τ) defined as:

$$\tau = \frac{M_{\mathrm{reserves}}}{\phi_{\mathrm{m,consumption}} - \phi_{\mathrm{m,production}}} \tag{6}$$

Besides taking into account any gap between the consumption and regeneration rate of a resource, the depletion time relates this gap to the extent of the natural reserves. The depletion time is then a measure for the rate at which the currently known reserves of a resource are being depleted. For example, a depletion time of a hundred years means that currently one percent of the known reserves is being depleted yearly; likewise, a depletion time of a thousand years means that yearly one tenth of a percent is being depleted. It should be stressed that the depletion time as defined in eqn. (1) does not attempt to predict resource depletion in the future; it merely indicates how fast a known supply of a resource is *currently* being depleted.

This definition means that the depletion time of a resource is time-dependent. The consumption rate of a resource may increase over time as a result of increased industrial production, or it may decrease if alternative resources are increasingly being used. Likewise, the regeneration rate may increase when more resources are recycled, and reserves may shrink after prolonged utilization or expand when new natural deposits are found. In addition, more accurate data may become available for example on the extent of currently known reserves or on the natural formation rates of certain deposits. In any case, the depletion time t is variable, and it reflects the rate of resource depletion only in the present situation.

The depletion time of a resource obtained with eqn. (6) can not be used directly in the construction of the sustainability parameter and, therefore, it is first converted to a factor that can be viewed as an expression of resource abundance on a scale of zero to one (see Fig. 3). For a resource i with a depletion time τ_i the abundance factor a_i is defined as:

$$a_i = \left(\frac{\tau_i}{\tau_i + \tau_0} \right) \tag{7}$$

The reference time τ_0 in eqn. (7) represents the resource depletion time at which the abundance factor a_i is at the value of exactly one half (*i.e.* 50%). This reference time τ_0 must be given an appropriate value at which the factors a_i adequately reflect the differences in the abundance of real resources. For example, a reference time τ_0 of one thousand years will give fossil fuels abundance factors roughly ranging from 0.1 to 0.5, while sunlight, probably available for billions of years, will have an abundance factor approaching unity.

Important to notice is the non-linear behavior of eqn. (7), which is clearly seen in Fig. 3. This non-linearity causes the abundance factor a_i to be more sensitive at small depletion times and less sensitive at large depletion times, which is in accordance to our intuitive judgment. When comparing two different natural resources, the difference between 100 and

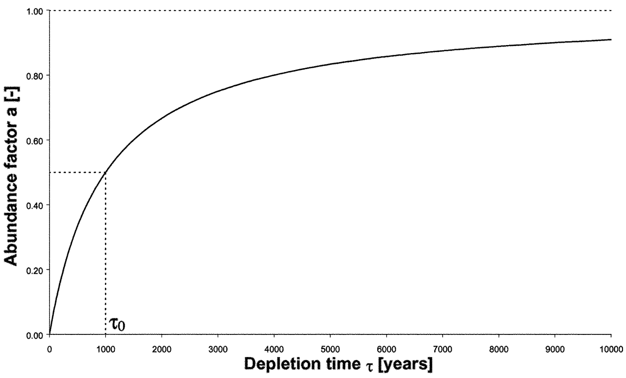


Fig. 3 The depletion-time τ_i of a resource i is converted to an abundance factor a_i with a non-linear function.

1000 years of depletion time is much more important than the difference between 1 billion and 10 billion years. The latter timescales are both so large that it is almost equally unlikely that the depletion of either one of these resources will cause a process using them to become unsustainable. Hence, the non-linear behavior of eqn. (7) brings some common sense to the quantification method.

With the abundance factors as quantitative measures for the abundance of individual resources, focus can now be on expressing the sustainability of multiple-resource utilization in a particular technological process. The first step is to determine how available are, on average, all the resources used in the process. This average abundance (a^{average}) is obtained by averaging the abundance factors (a_i) of the individual resources while using their exergy flows (Ex_i) to the process as averaging weights (see Fig. 4):

$$a^{\text{average}} = \frac{\sum_i a_i \cdot \dot{E}x_{\text{in},i}}{\sum_i \dot{E}x_{\text{in},i}} \qquad (8)$$

Eqn. (8) uses the exergy flows of the resources because these values express the minimum amount of work required to (artificially) produce these resources from compounds that are thermodynamically in equilibrium with the natural environment. As ultimately only exergy is scarce (see Introduction), the exergy flows of resources are better indicators of relative importance than their mass or volume flows.

Although very useful, the average abundance of resources (a^{average}) alone is not capable of adequately expressing the sustainability of resource utilization. As a result of the averaging procedure, small abundance factors, which come from resources that are rapidly being depleted, can be (partly) compensated by large abundance factors, which come from resources that are depleted relatively slowly. In this way, the weakest link in the chain, *i.e.* the resource that is being depleted at the highest rate, does not act as a barrier to the sustainability of the resource utilization in a process. This opposes common sense because a process already becomes unsustainable when only one of the resources it requires is depleted.

This problem can be solved by not only looking at the *average* resource abundance, but also at *minimum* resource abundance. Minimum resource abundance (a^{min}) can be defined simply as the smallest of the resource abundance factors a_i relevant in the process:

$$a^{\text{min}} = \underset{i}{\underline{\min}}\left[a_i\right] \qquad (9)$$

With a^{min} we have identified the weakest link in the chain of resources used in the process, and this can be used to limit the effect of the average abundance factor (a^{average}). Hence, the parameter for sustainable resource utilization (α) can then be defined as the product of the average (a^{average}) and the minimum (a^{min}) abundance of resources:

$$\alpha = a^{\text{average}} \cdot a^{\text{min}} \qquad (10)$$

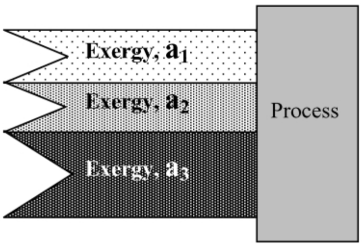


Fig. 4 The sustainability parameter α is based on the average abundance factor a^{average}, which considers all the abundance factors a_i and exergy flows Ex_i of the individual resources used in the process.

In this way, the sustainability parameter α includes the depletion rates of all resources used in the process (*via* a^{average}), while, at the same time, it is directly limited by the resource with the highest depletion rate.

The proposed method for quantitatively describing the sustainability of resource utilization in a process *via* eqn. (10) has several advantages over the renewable *vs.* non-renewable method of eqn. (1). First, the proposed method considers the *degree* of resource renewability, which allows even subtle differences in the depletion of different resources to be accounted for. Secondly, the proposed method includes also the (natural) reserves of resources, making the quantification method yet more refined. Finally, the concept of depletion times and their translation to abundance factors allow the resource sustainability parameter α of a process to be limited by its most rapidly depleting resource, which is quite realistic.

Example. To illustrate the quantification method described above, the following hypothetical process is considered. Suppose a process using no other resources can be driven by three different sources of exergy: oil, coal, and solar energy. Using their current consumption rate, regeneration rate, and extent of natural deposits, the depletion times of oil and coal are calculated with eqn. (6) *e.g.* at 150 and 1000 years, respectively. For solar energy the depletion time equals the lifetime of the sun, which is approximately 5 billion years (Table 1).

Taking the reference depletion time τ_0 at 1000 years, the depletions times of oil and coal yield abundance factors of 0.13 and 0.50, respectively; the very large depletion time of nuclear fuel in the sun leads to an abundance factor for solar energy that approaches unity (note that the abundance factor is less sensitive at high depletion times and that this is convenient because higher depletion times can usually be determined less accurately).

With eqns. (8), (9) and (10), and with the abundance factors for oil, coal and solar energy as determined above, it is possible to determine the parameter for sustainable resource utilization for a process that uses solely one or more of these three resources. Table 2 lists the relevant data for several such processes, each extracting different percentages of the total required exergy from oil, coal, and solar energy.

First of all, Table 2 lists three processes that each extract their exergy entirely from one of the three resources (process 1, 2 and 3). In these situations, there is only one relevant abundance factor, and its value then solely determines the values of the average and minimum abundance factor. Also, the sustainability parameter is then simply this value squared. The results show that the process using only oil (process 1) is the least

Table 1 Depletion times and abundance factors of oil, coal and solar energy

Exergy source	Depletion time/years	Abundance factor
Oil	150	0.13
Coal	1000	0.50
Solar energy	5 billion	~ 1

Table 2 Relevant data on sustainability of resource utilization in processes using oil, coal, and solar energy

Process	Oil (%)	Coal (%)	Solar (%)	a^{average}	a^{min}	α
1	100	0	0	0.13	0.13	0.02
2	0	100	0	0.50	0.50	0.25
3	0	0	100	~ 1	~ 1	~ 1
4	50	50	0	0.32	0.13	0.04
5	20	50	30	0.58	0.13	0.07
6	10	0	90	0.91	0.13	0.12
7	0	10	90	0.95	0.50	0.48

sustainable in its utilization of resources, the process using only coal (process 2) is more sustainable, and the process extracting all exergy from solar energy (process 3) is practically entirely sustainable in terms of resource utilization.

Table 2 also lists three processes (process 4, 5, and 6) that extract a decreasing percentage of the total required exergy from the least durable resource oil, and an increasing percentage from the more durable resources coal and solar energy. Correspondingly, the average abundance factor increases, causing also the value of the sustainability parameter to raise. However, the minimum abundance factor remains the same since all three processes use oil to some extent, which has a relatively small depletion time of only 150 years. The values of the parameter rightfully indicate that using more durable resources helps to increase the sustainability parameter, but that its effect is limited, because the weakest link, *i.e.* the least durable resource, is not completely replaced. In fact, process 7 in Table 2 illustrates that when the use of oil in process 6 is replaced by coal, the sustainability parameter indicates a much more sustainable use of resources.

The effect of the minimum abundance factor $a^{\min}$ on the sustainability factor α may seem counter-intuitive. However, it must be realized that the sustainability parameter a only expresses that part of process sustainability that involves the availability of the resources used. The fact that process 6 in Table 2 may be more sustainable than for example process 2 in terms of environmental impact, is not relevant to this particular aspect of process sustainability. Purely in terms of resource utilization, process 2 is more sustainable than process 6, because process 2 does not depend on a rapidly depleting resource like oil.

Notes on determining depletion times and abundance factors. A special situation in the determination of depletion times and abundance factors occurs when a resource used in a process is actually a half-product; for example, iron metal is not a naturally occurring resource but is produced from iron ore in a blast furnace. The abundance factor of such a half-product must then be derived from the smallest depletion time among the resources used during its production. Since the abundance of *e.g.* iron metal is limited by the abundance of heavy oil fractions, which are used to convert coal into cokes, the abundance factor of iron metal can be based on the depletion time of oil.

Another special situation arises when one resource has its origin in two different processes. For instance, when a process uses the electricity provided by an energy company, it is possible that this electricity is generated partly by burning coal and partly by burning natural gas. In this case, the process should be considered to use two different types of electricity: electricity from coal and electricity from natural gas. Both types of electricity then have their own derived depletion time and, based on how much they contribute to the total amount of electricity supplied, their own exergy flow.

Finally, the concept of depletion times, as is used in the construction of the sustainability parameter, is also suitable to include the sustainability of production of facilities needed to harvest resources. For instance, solar energy may in principle have a depletion time of billions of years, but the production of photovoltaic cells usually requires some very scarce elements for which the depletion times are much smaller. The sustainability of using solar energy harvested with photovoltaic cells should then be based on these latter depletion times and not on the depletion time of solar energy itself.

Exergy efficiency (η)

The efficiency parameter focuses on the conversion of energy in the process itself (see Fig. 5). Since exergy rather than any other resource is the ultimate limiting factor to production activities, a process is most sustainable when it uses the exergy of its ingoing resources most efficiently. For this reason, the exergy efficiency of the process is important enough to be considered as a separate sustainability parameter:

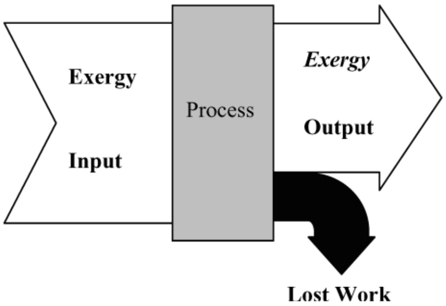


Fig. 5 The sustainability parameter η is the efficiency with which the exergy of resources is transferred to the products of the process.

$$\eta = \frac{\sum \dot{E}x_{\text{out,useful}}}{\sum \dot{E}x_{\text{in,process}}} \tag{11}$$

Eqn. (11) explicitly mentions the *useful* exergy flows coming out of the process because exergy can be lost in two different ways. First, exergy is lost in any real process as a result of irreversibility in the process itself, and such losses are called internal exergy losses. Secondly, exergy can be lost *via* waste streams that are not yet at equilibrium with the natural environment. Examples of such external exergy losses are the release of hot flue gasses or high pressure gas to the atmosphere. Both the internal and the external exergy losses are in principle inefficiencies, and the exergy used efficiently in the process is therefore only the exergy of products and the exergy of waste products when they are made useful in other processes.

Environmental compatibility (ξ)

A third main aspect of process sustainability is not damaging the natural environment, and the environmental parameter ξ_i as defined by De Wulf *et al.*[1] elegantly quantifies this part of process sustainability. Even if it is possible to define adequate quantitative measures expressing how damaging for example certain emissions are to the natural environment, the definition of the environmental parameter avoids all these difficulties. Its basic idea is that negative effects of a process on the environment must be abated before they can do damage to the natural environment. The extra exergy required to achieve this abatement then reflects the environmental incompatibility of a process to the natural environment (see Fig. 6).

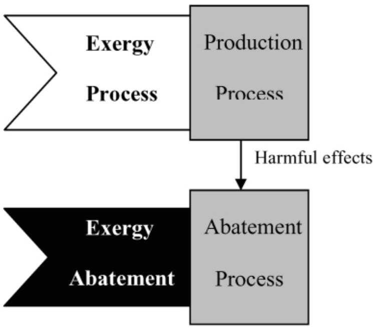


Fig. 6 The sustainability parameter ξ views the exergy required to abate all the effects of the process that are harmful to the natural environment.

It should be noted that abating negative effects is a very broad concept. Abatement not only applies to emissions, as considered by De Wulf *et al.*,[1] but it can apply to all kinds of negative effects, including also thermal pollution or even extraction of resources from the environment. Examples of harmful effects of resource extractions are erosion of soil after cutting down forests or subsidence of ground after extraction of natural gas or oil from underground deposits. Abatement is required for all effects considered harmful to the environment that occur either during the process or during the eventual destruction of the products after their use.

Based on the exergy required for abatement, the sustainability parameter expressing the ecological compatibility of a process is defined as given in eqn. (12):

$$\xi = \frac{\dot{E}x^{\text{total}}_{\text{in,process}}}{\dot{E}x^{\text{total}}_{\text{in,process}} + \dot{E}x^{\text{total}}_{\text{in,abatement}}} \qquad (12)$$

The parameter ξ relates the exergy required to run the process to the exergy required to run the process in an environmentally sound way, which includes the extra exergy required for abating the harmful effects on the environment. A large exergy demand for abatement leads to a small value for the environmental parameter ξ, indicating that the process has a small compatibility with the natural environment. Only if a process requires no exergy for abatement, the environmental parameter $\xi = 1$ and the process is considered completely compatible with the natural environment.

Determining overall sustainability

De Wulf *et al.*[1] combine individual sustainability parameters to form one overall sustainability coefficient S. However, although a single expression for the sustainability of a technological process may seem appealing, it has some serious disadvantages.

First of all, one sustainability coefficient falsely suggests that sustainability is one-dimensional, and this undermines the idea that there are different aspects to a complex concept as sustainability. Secondly, a lot of valuable information is lost when merging the individual parameters into one overall coefficient; the combination basically means that concrete and meaningful expressions are merged into an overall expression without a tangible meaning. The overall coefficient merely expresses something vague as the overall sustainability of a process. Thirdly, the method used to combine the three individual parameters is highly subjective. Many methods of combining parameters may be applied such as several different averaging techniques or a least squared method, but every method unavoidably involves a value judgment on the relative importance of the different aspects of sustainability.

Hence, to keep the quantitative expression of process sustainability as meaningful as possible, separate sustainability parameters should not be combined into one overall sustainability coefficient. Expressing the sustainability of a process quantitatively is always a tradeoff between completeness and surveyability; one aims to loose as little valuable information as possible, but at the same time the expression of process sustainability must be concise and well-organized. It is felt that the three sustainability parameters as defined in this article do exactly that, and that the sustainability of a process is therefore best evaluated by considering independently these quantifications of three fundamentally different aspects of process sustainability.

Conclusions

Thermodynamic principles are essential elements of a quantitative description of the sustainability of technological processes. This is because the proceedings of all processes and the availability of all resources ultimately come down to the availability of exergy, which by definition views energy and matter relative to the natural environment.

The earlier work of De Wulf *et al.*[1] already contains the basic elements required to quantify process sustainability with exergy values of process streams. However, the quantification method can be significantly improved by a number of meaningful adjustments.

First of all, the sustainability of the resource utilization in a process can be quantified more accurately by considering the *depletion rates* of the resources used. In this way many grades of resource renewability can be distinguished and the size of natural reserves of resources are also taken into account. In addition, the use of depletion rates allows the sustainability parameter on resource utilization to be limited by the least available resource used in the process, which makes the parameter even more realistic.

Secondly, the exergy efficiency of the process is important enough to be considered as a separate sustainability parameter; more efficient use of exergy is a major enhancement of the sustainability of the process, since production can then be realized with less input of exergy and material resources.

Thirdly, the environmental parameter should not only involve abatement of emissions, but should account for abatement in a much broader sense. The requirement for abatement should apply to *all* negative effects related to the process itself or to the destruction of its products. In this way, the compatibility of a process with the environment is truly determined.

Finally, individual sustainability parameters should not be merged into one overall sustainability coefficient, because this destroys the meaningfulness and the objectiveness of the quantification method. The parameters address fundamentally different aspects of process sustainability, and their interpretation should therefore be independent from each other.

References

1 J. De Wulf, H. Van Langenhove, J. Mulder, M. M. D. Van den Berg, H. J. Van der Kooi and J. D. Arons, *Green Chem.*, 2000, **2**, 108–114.

2 Our Common Future, *The World Commission on Environmental and Development*, Oxford University Press, New York, 1987.

3 J. Szargut, D. R. Morris and F. R. Steward, *Exergy analysis of thermal, chemical and metallurgical processes*, Hemisphere Publ. Corp., New York, 1988.

High atomic yield bromine-less benzylic bromination

Ramon Mestres* and Jesús Palenzuela

Departament de Química Orgànica, Universitat de València, 46100 Burjassot, València, Spain. E-mail: ramon.mestres@uv.es

Received 27th April 2002
First published as an Advance Article on the web 27th June 2002

A two-phase mixture (sodium bromide, aqueous hydrogen peroxide/carbon tetrachloride or chloroform) under visible light provides a simple and convenient system for benzylic bromination of toluenes. A high atomic yield for bromine atoms is attained. Substitution of the chlorinated solvents by other more environmentally benign organic solvents has been attempted and good results are obtained for methyl pivalate.

Introduction

Molecular bromine in preparative chemistry is a serious cause of concern, due to its toxicity and corroding properties. In order to circumvent this drawback, generation of bromine *in situ* by oxidation of hydrogen bromide or an alkali-metal bromide by potassium permanganate, sodium bromate, hydrogen peroxide, or other reagents has been performed as far back as in the 19th century, although these methods have not found general application.[1–3]

Further, some of the most significant synthetic reactions of molecular bromine, namely the bromination of aromatic nuclei, ketones, carboxylic acids or allylic or benzylic sites occur under low atomic yield for bromine. Indeed, only one out of two bromine atoms of molecular bromine becomes part of the product, the other atom becomes the corroding hydrogen bromide, a substance which must be neutralized before it is discarded.[4] Brominations may thus be qualified as environmentally unfriendly reactions.[5]

The Wohl–Ziegler method of bromination with the easy to handle NBS has become for many years the reagent of choice for allylic and benzylic brominations.[6,7] Direct use of molecular bromine in the laboratory is avoided and no hydrogen bromide is generated. However, the atomic yield is still poor and succinimide is obtained as a concomitant product which, although not harmful, must be either disposed or recycled to NBS, and very frequently complicates cristallizations for isolation and purification of products.

Combined bromide–hydrogen peroxide systems have been used recently for addition to unsaturated double or triple bonds,[8–10] aromatic electrophilic substitution,[8,9,11] synthesis of amine tribromides,[12] or for oxidation of alcohols, aldehydes,[9] or sulfides.[13–15] Aromatic side-chain halogenations in the presence of metal oxide catalysts have been reported as well.[16,17] Interestingly, significant improvements of both electrophilic aromatic and photochemical side-chain brominations by bromine in the presence of zeolites have been recently described.[18]

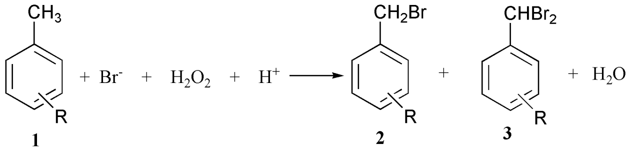
In the course of our studies for the synthesis of some benzyl ether dendritic and polymeric structures,[19] we wished to improve the benzylic bromination of protected methylphenols. Although bromination of 4-methylbenzoyloxybenzene **1a** with NBS occurred satisfactorily in general terms, we needed a procedure more suitable for a multigram scale. On the other hand, the urgent need for development of safe and environmentally benign methods encouraged us to search for the possibility of a convenient benzylic bromination through oxidative generation of bromine *in situ*. Use of hydrogen peroxide seemed very convenient in the view of the above precedents and because water is the only concomitant product (eqn. (1)–(3)).

$$2\ \mathrm{Br}^- + \mathrm{H_2O_2} + 2\ \mathrm{H}^+ = \mathrm{Br_2} + 2\ \mathrm{H_2O} \qquad (1)$$

$$\mathrm{ArCH_3} + \mathrm{Br_2} = \mathrm{ArCH_2Br} + \mathrm{Br}^- + \mathrm{H}^+ \qquad (2)$$

$$\mathrm{ArCH_3} + \mathrm{Br}^- + \mathrm{H_2O_2} + \mathrm{H}^+ = \mathrm{ArCH_2Br} + 2\ \mathrm{H_2O} \qquad (3)$$

Further, when the substitution reaction is taken into account, the whole conversion should be possible by consuming a single mole of bromide and one mole of acid. The photochemical bromination of a number of substituted toluenes by a bromide–hydrogen peroxide reagent under acidic conditions was thus studied (Scheme 1). The reactions were carried out initially in carbon tetrachloride, the solvent commonly used up now for molecular bromine or NBS brominations. Other chlorinated solvents and other non-chlorinated solvents were then assayed.



1a: R = p-$C_6H_5CO_2$;
1b: R = p-Cl; **1c**: R = m-Cl; **1d**: R = H; **1e**: R = p-NO_2;
1f: R = p-MeO_2C; **1g**: R = p-HO

Scheme 1

Green Context

The use of bromine is fraught with problems of handling and the low atom efficiency of substitution reactions (50% maximum with bromide by-poduct). For these reasons work has been carried out using bromide and an oxidant to generate bromine (or electrophilic Br species) for electrophilic aromatic brominations. Here, bromide is used in conjunction with light to carry out side-chain brominations of benzylic systems, extending the concept to radical-type reactions. Importantly, a non-halogenated solvent has also been found for these reactions which typically use CCl_4 or $CHCl_3$. ***DJM***

DOI: 10.1039/b203055a

Results and discussion

For comparison purposes, brominations of 4-benzoyloxytoluene **1a** with NBS and with molecular bromine in carbon tetrachloride were carried out first. Thus, bromination with one equivalent of NBS in the presence of benzoyl peroxide, ilumination with visible light and heating under reflux, according to the typical procedure, gave a 84:16 mixture of mono- and di-bromination compounds, **2a** and **3a**, with the starting material left as a trace amount. With a slight excess (1.1 molar equivalents) of bromine relative to the substituted toluene **1a**, the red colour of the solution faded in less than 10 min and the resulting mixture (91% isolated crude yield) contained compounds **2a** (72%) and **3a** (25%), and a very small amount of the starting toluene **1a** (3%). When the bromination was carried out with slightly more than half an equivalent (0.55) of bromine in the presence of hydrogen peroxide (1.5 equivalents), progress of the reaction was much slower, a red to orange colour change being observed after 8 h. Quenching of the reaction after 20 h gave a crude mixture (85%) of compounds **1a**, **2a** and **3a** in a ratio 18, 74 and 8%, respectively. The introduction of a second atom of bromine is in keeping with the results of Smith *et al.* on the bromination of ethyl 4-methylbenzoate,[18] and is probably due to the rate constants for the dissociation of the C–H bonds of the starting toluene and of the monobromo derivative **1** being of a similar order.

Brominations with the bromide–hydrogen peroxide system were carried out at room temperature in an open vessel provided with a cooling condenser and under illumination with an incandescent light bulb. Sodium (occasionally potassium) bromide, hydrochloric or sulfuric acid and 30% aqueous hydrogen peroxide, the concentration of which was determined volumetrically with $KMnO_4$, were employed. On mixing of the reagents and the toluene **1**, a red colour developed, which slowly faded in *ca.* 4–6 h. However, no systematic control of the reaction time was conducted, as most experiments were carried out overnight (20 h). The simple work-up procedure for most toluenes **1** consisted in thorough removal of peroxides from the organic layer by aqueous sodium hydrogensulfite and evaporation of the solvent to give a crude material, whose composition was established by ^1H NMR spectroscopy. Work-up for bromination of toluene **1d** differed in that evaporation of the solvent was not carried out, as remaining unreacted toluene might be partly evaporated along with the solvent. Only the starting material **1**, and the mono- and di-bromo compounds **2** and **3** (Scheme 1) were found in the crude mixtures.

Study of the effect of conditions were carried out with 4-benzoyloxytoluene **1a** as substrate, due to the easy isolation of the resulting reaction mixture. It had been ascertained previously that no substitution reaction took place in the absence of photochemical activation and that the alkali-metal bromide could be added either as a solid or previously dissolved in the aqueous acid with no significant change in the results. Similarly, changes in the concentration or nature of the acid, the cation (Na or K) of the bromide salt, or the order of addition of reagents had no effect.

A rough estimation of the efficiency of the bromination is given by the bromination yield (Table 1). This is obtained here by summing the amounts of bromine found in the reaction mixture, as given by the product ratios for the mono- and di-brominated compounds **2** and **3**, corrected by the crude yield. Good bromination yields were obtained with only a slight excess (1.1) of bromide salt. According to eqns. (1)–(3) bromination could be complete with one molar equivalent of acid, but the reaction became slower and afforded much lower halogenation (Table 1, entry 5) on use of 1.1 equivalents of acid. A large excess of acid seems thus to have a beneficial effect and most brominations were carried out in the presence of 3 equivalents of acid. The amount of hydrogen peroxide could be reduced to 1.1 equivalents without a significant detriment on bromination yields. However, most experiments were carried out with a larger excess of hydrogen peroxide.

Chloroform as solvent gave a satisfactory result (Table 1, entry 10), but poor bromination yields were obtained with methylene dichloride (entry 9).

The general applicability of this procedure was confirmed when bromination of other substituted toluenes **1b**–**g** was assayed (Table 2). No significant differences were observed in proportions of the mixtures resulting as function of the electron-donating or electron-withdrawing character of the substituents in toluenes **1b**–**f**, although crude yields for the chloro compounds **1b** and **1c** were lower and thus, bromination yields were also low. For *p*-cresol **1g** side-chain bromination did not occur to a significant extent, electrophilic aromatic substitution instead being observed. This finding is in keeping with earlier results of oxybromination of strongly activated benzenes.[8–10] Methylene dichloride and chloroform were also assayed for *p*-nitro- and *p*-methoxycarbonyl toluenes **1e** and **1f**.

Non-chlorinated solvents were examined with substrate **1a** in the hope of improving the environmental aspects of the procedure (Table 3). Hexane was not convenient due to the low solubility of the substrate **1a**. Benzene gave fairly good results, but esters, namely ethyl and isopropyl acetate or methyl isobutyrate, or *tert*-butyl methyl ether gave poor conversions. Methyl pivalate gave a satisfactory bromination yield, although halogenation products were accompanied by 4-benzoyloxybenzoic acid, which might result from substitution and oxidation of monobrominated **2a** or from hydrolysis of **3a** and oxidation of the resulting benzaldehyde. Higher solubility of water in this solvent is probably the origin of this exceptional behaviour. A similar very small amount of carboxylic acid was observed in the halogenation of *p*-nitrotoluene **1e** in carbon tetrachloride.

In conclusion, we have found a very simple method for side-chain bromination of methylbenzenes which should be easily scaled-up.

Table 1 Conditions and results (^1H NMR) for bromide/hydrogen peroxide benzylic bromination of toluene **1a** (0.25 M) in chlorinated solvents

	Reagents[a]					Product ratio			
Run	H_2O_2	NaBr	H^+	Solvent	Crude yield	**1**	**2**	**3**	Bromination yield[b]
1	3	1.5	3[c]	CCl_4	95	2.5	80.5	17	108.7
2	3	1.1[d]	3	CCl_4	94	6	84	10	97.7
3	3	1.1	2	CCl_4	91	16	76	8	83.7
4	3	1.1	1.5	CCl_4	89	15	77	8	81.9
5	3	1.1	1.1[c]	CCl_4	87	29	71	tr	61.8
6	2	1.1	3	CCl_4	89	16.5	78	5.5	79.2
7	1.5	1.1	3	CCl_4	91	20.2	74.3	5.5	77.6
8	1.1	1.1	3	CCl_4	88	16	76	8	81
9	1.5	1.1	3	CH_2Cl_2	86	37	63	tr.	54.2
10	1.5	1.1	3	$CHCl_3$	93	15.5	79.5	5	83.2

[a] Molar ratio relative to **1**. [b] Bromination yield; estimated: (crude yield/100)[ratio **2** + (2 × ratio **3**)]. [c] 2 M HCl; other runs, conc. H_2SO_4. [d] KBr.

Table 2 Bromide/hydrogen peroxide benzylic bromination of toluenes **1b**–**f** (0.25 M) in chlorinated solvents[a]

Run	**1**	Solvent	Crude yield	Product ratio **1**	**2**	**3**	Bromination yield[b]
1	**1b**	CCl_4	62	13.5	79.5	7	58
2	**1c**	CCl_4	60	16	74.5	9.5	56
3	**1d**	CCl_4		14.5	79.5	5	
4	**1e**	CCl_4	82	14	79	7	76.2
5	**1e**	CH_2Cl_2	92	12.5	80.5	7	86.9
6	**1e**	$CHCl_3$	93	13	78	8.7	88.7
7	**1f**	CCl_4	63	15	78	7	57.9
8	**1f**	CH_2Cl_2	76	57	43	tr.	32.7
9	**1f**	$CHCl_3$	99	13	87	tr.	86.1

[a] Conditions for all runs: 3 equivalents of 30% H_2O_2, 1.1 equivalent of NaBr, 3 equivalents of conc. H_2SO_4. [b] Bromination yield; estimated: (crude yield/100)[ratio **2** + (2 × ratio **3**)].

Table 3 Conditions and results (^{1}H NMR) for bromide/hydrogen peroxide benzylic bromination of toluene **1a** (0.25 M) in non-halogenated solvents

Run[a]	Solvent	Crude yield	Product ratio **1**	**2**	**3**	Bromination yield
1	Hexane–ethyl acetate	85	63	37	—	31.5
2	Benzene	91	21	74	5	76.5
3	Ethyl acetate	76	66.5	33.5	—	25.5
4	Isopropyl acetate	84	20.4	79.6	tr	66.8
5	Methyl isobutyrate	97	67	33	—	32
6	Methyl pivalate	84	11	84	5	79
7	Methyl pivalate	78	5.7	85.7	8.6	80
8	*tert*-Butyl methyl ether	89	58	42	tr.	30

[a] Conditions for all runs: 3 equivalents of 30% H_2O_2, 1.1 equivalent of NaBr, 3 equivalents of conc. H_2SO_4.

Experimental

4-Benzoyloxybenzyl bromide 1a

A mixture of 4-benzoyloxytoluene (2.12 g; 10 mmol), sodium bromide (1.13 g; 11 mmol), 30 % hydrogen peroxide (1.70 mL; 15 mmol), conc. sulfuric acid (1 mL; 15 mmol) and chloroform (40 mL) was stirred in a 100 mL round bottomed flask provided with a reflux condenser and under illumination with a 100 W incandescent lamp. The mixture became red and the colour slowly faded in 2.25 h. The mixture was washed with 40% sodium hydrogensulfite (2 × 10 mL), until a negative starch-iodide test for peroxides, and water and dried. Evaporation of the solvent gave a crude mixture as an oil which solidified (2.71 g; 93%). The ^{1}H NMR spectrum of a sample was run. Crystallization from hexane–benzene gave the title compound as colourless prisms (2.11 g; 73%), mp 110–111 °C (lit.,[20] 108–111 °C).

Acknowledgements

The present work has been financed by Ministerio de Ciencia y Tecnología (Project PPQ2000-0816).

References

1 Eugen Müller, *Methoden der Organischen Chemie (Houben-Weyl)*, Band V/4, Georg Thieme Verlag, Stuttgart, 1960, p. 13.

2 A. R. Katritzky, O. Meth-Cohn and C. W. Rees, *Comprehensive Organic Functional Group Transformations*, Pergamon, Oxford, 1995, vol. 2, p. 3.

3 B. M. Trost and I. Fleming, *Comprehensive Organic Synthesis*, Pergamon, Oxford, 1991, vol. 7, p. 15.

4 J. Clark, *Green Chem.*, 1999, **1**, 1.

5 P. T. Anastas and J. C. Warner, *Green Chemistry, Theory and Practice*, Oxford University Press, Oxford, 1998, p. 105.

6 Eugen Müller, *Methoden der Organischen Chemie (Houben-Weyl)*, Band V/4, Georg Thieme Verlag, Stuttgart, 1960, pp. 221, 341.

7 A. R. Katritzky, O. Meth-Cohn and C. W. Rees, *Comprehensive Organic Functional Group Transformations*, Pergamon, Oxford, 1995, vol. 2, p. 3.

8 N. B. Barhate, A. S. Gajare, R. D. Wakharkar and A. V. Bedekar, *Tetrahedron*, 1999, **55**, 11127.

9 J. H. Espenson, Z. Zhu and T. H. Zauche, *J. Org. Chem.*, 1999, **64**, 1191.

10 B. F. Sels, D. E. DeVos and P. A. Jacobs, *J. Am. Chem. Soc.*, 2001, **123**, 8350.

11 G. Rothenberg and J. C. Clark, *Green Chem.*, 2000, **2**, 248.

12 M. K. Chaudhuri, A. T. Khan, B. K. Patel, D. Dey, W. Kharmawophlang, T. R. Lakshmiprabha and G. C. Mandal, *Tetrahedron Lett.*, 1998, **39**, 8163.

13 A. Bravo, B. Dordi, F. Fontana and F. Minisci, *J. Org. Chem.*, 2001, **66**, 3232.

14 E. Mondal, G. Bose, P. R. Sahu and A. T. Khan, *Chem. Lett.*, 2001, 1158.

15 A. T. Khan, J. Boruwa, E. Mondal and G. Bose, *Indian J. Chem. B*, 2001, **40**, 1039.

16 E. Baciocchi and M. Creszenzi, *Tetrahedron*, 1988, **45**, 6525.

17 J. Nakayama, T. Kawamura, K. Kuroda and A. Fujita, *Tetrahedron Lett.*, 1993, **34**, 5725.

18 K. Smith, G. A. El-Hiti, M. E. W. Hammond, D. Bahzad, Z. Li and C. Siquet, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2745.

19 A. K. Maiti, R. Martínez, R. Mestres and A. Tortajada, *Tetrahedron*, 2001, **57**, 3397.

20 J. H. Barnes, J. Elks, F. F. Stephens and G. J. Waller, *J. Chem. Soc.*, 1953, 764.

Communication

Facile synthesis of homoallylic alcohols from aldehyde acetals in water

Dmitry E. Gremyachinskiy, Lori L. Smith, Paul H. Gross and Vyacheslav V. Samoshin*

Department of Chemistry, University of the Pacific, Stockton, CA 95211, USA.
E-mail: vsamoshi@uop.edu

Received 20th May 2002
First published as an Advance Article on the web 22nd July 2002

Homoallylic and bis-homoallylic alcohols, which are widely used in organic synthesis, were prepared in good yields by a facile allylation of aldehyde acetals with allyl bromide, tin(II) chloride and potassium iodide in water.

Homoallylic alcohols are widely used in organic synthesis.[1] They have been prepared by a variety of methods, in particular by allylation of carbonyl compounds, mostly aldehydes.[1] However, some aldehydes, especially dialdehydes are unstable (*e.g.* malonaldehyde[2]), and are commercially available only in water solutions or as acetals.

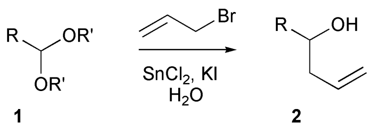
To the best of our knowledge, there have been four publications describing a direct synthesis of homoallylic alcohols from acetals. Homoallylic alcohols were prepared by allylation of carbonyl compounds and some non-aromatic aldehyde acetals in water with allyldibutyltin chloride,[3a] and in cyclohexane/aq. $LiClO_4$ with allyl halide and Zn/Bu_2SnCl_2.[3b] A treatment with either trifluoroacetic acid or silica gel followed by tetraallyltin has been used for one-pot transformation of acetals into homoallylic alcohols.[4] A synthesis of homoallylic alcohols by indium mediated allylation of benzaldehyde and cinnamaldehyde dimethylacetals with allylic bromides in aqueous THF has been described recently.[5] Aliphatic acetals appeared to be unreactive.[5] Under similar conditions, *gem*-diacetates produced homoallylic acetates.[6] Other Lewis acid promoted reactions of acetal allylation afforded homoallylic ethers.[7]

We report here a mild, simple and inexpensive general synthesis of homoallylic alcohols from aldehyde acetals by treatment with allyl bromide, $SnCl_2$ and KI in water (Scheme 1, Table 1). Apparently, a hydrolysis of acetal in a weakly acidic medium preceded the allylation. These reaction conditions have been used for allylation of aldehydes,[8] but have never been applied to acetals.

Experimental

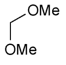
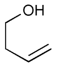
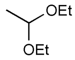
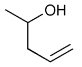
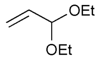
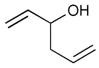
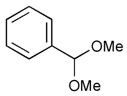
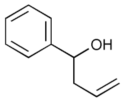
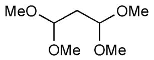
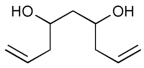
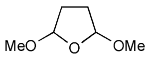
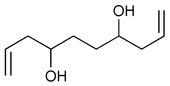
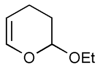
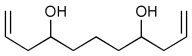
Typical procedure for acetal allylation

Allyl bromide (0.15 mol) was added to a mixture of $SnCl_2{\cdot}2H_2O$ (0.15 mol) and KI (0.15 mol) in water (200 ml). A solution of acetal **1** (0.1 mol) in THF (20 ml) was added during 1 h. The stirring was continued for several hours (up to 48 h in case of **1f**); the acetal conversion was monitored by TLC. The resulting



Scheme 1

Table 1 Synthesis of homoallylic alcohols **2**

Starting acetal **1**	Homoallylic alcohol **2**[a]	Yield (%)
 **1a**	 **2a**	91
 **1b**	 **2b**	89
 **1c**	 **2c**	78
 **1d**	 **2d**	89
 **1e**	 **2e**	77
 **1f**	 **2f**	66
 **1g**	 **2g**	80

[a] All the products were characterized by ^1H NMR, ^{13}C NMR, mass-spectrometry, and comparison with literature values: **2a**,[9,10] **2b**,[11] **2c**,[12] **2d**,[4,8,11,13,14] **2e**,[15] **2f**,[16] **2g**.[17]

Green Context

The use of water has many advantages, it is non-toxic, easy to handle, is non-inflammable and does not contribute to VOC emissions. Here, work is discussed which relates to the elaboration of aldehyde derivatives under very mild conditions. Yields are good, and the method works directly from the acetals, avoiding the often labile aldehydes themselves.
DJM

DOI: 10.1039/b204856f

mixture was neutralized with Na_2CO_3 and was extracted with CH_2Cl_2 or ether. The organic phase was washed with 5% aq. $Na_2S_2O_3$, and was dried and evaporated to yield a yellowish oil. The essentially pure product **2** was additionally purified by flash chromatography (silica gel; ether–hexane). In the case of **2a** and **2b**, the ether solution was concentrated on a rotary evaporator at room temperature, and the product was purified by distillation.

The amount of reagents was doubled for dialdehyde bis-acetals **1e–g**. According to NMR data, the products **2e–g** were mixtures of approximately equal amounts of diastereomers.

1,8-Nonadien-4,6-diol (2e). ^{1}H NMR (300 MHz, $CDCl_3$), δ 1.55–1.65 (m, 2H, CH_2), 2.25 (m, 4H, $CH_2C{=}C$), 3.2 (br.s, 2H, OH), 3.90, 4.00 (m, 2H, CHO), 5.1–5.2 (m, 4H, $C{=}CH_2$), 5.80 (m, 2H, –CH=C). ^{13}C NMR (75 MHz, $CDCl_3$), δ 41.2, 41.4 (CH_2), 41.9, 42.2 (CH_2), 67.9, 71.5 (CHO), 117.4, 117.5 (=CH_2), 134.1, 134.5 (–CH=).

1,9-Decadien-4,7-diol (2f). ^{1}H NMR (300 MHz, $CDCl_3$), δ 1.45–1.75 (m, 4H, CH_2), 2.23 (m, 4H, $CH_2C{=}C$), 3.68 (m, 2H, CHO), 4.0 (s, 2H, OH), 5.05–5.15 (m, 4H, $C{=}CH_2$), 5.82 (m, 2H, –CH=C). ^{13}C NMR (75 MHz, $CDCl_3$), δ 32.3, 33.4 (CH_2), 41.7, 42.0 (CH_2), 70.8, 71.3 (CHO), 117.7 (=CH_2), 134.9 (–CH=).

1,10-Undecadien-4,8-diol (2g). ^{1}H NMR (300 MHz, $CDCl_3$), δ 1.35–1.65 (m, 6H, CH_2), 2.2 (m, 4H, $CH_2C{=}C$), 2.7 (br.s, 2H, OH), 3.63 (m, 2H, CHO), 5.0–5.15 (m, 4H, $C{=}CH_2$), 5.80 (m, 2H, –CH=C). ^{13}C NMR (75 MHz, $CDCl_3$), δ 21.7, 21.8 (CH_2), 36.4, 36.6 (CH_2), 42.0, 42.1 (CH_2), 70.5, 70.7 (CHO), 117.6 (=CH_2), 134.9 (–CH=).

This approach allows a synthesis of homoallylic and bis-homoallylic alcohols in water from readily available, stable precursors using inexpensive reagents.

Acknowledgement

The Eberhardt Research Fellowship from the University of the Pacific is gratefully acknowledged by V. V. S.

References

1 (*a*) D. Seebach, B. Weidmann and L. Widler, in *Modern Synthetic Methods*, ed. R. Scheffold, John Wiley & Sons, New York, 1983, **vol. 3**, pp. 217–353; (*b*) C. J. Li, *Chem. Rev.*, 1993, **93**, 2023–2035; (*c*) Y. Yamamoto and N. Asao, *Chem. Rev.*, 1993, **93**, 2207–2293; (*d*) J. A. Marshall, *Chem. Rev.*, 1996, **96**, 31–47; (*e*) C. J. Li and T. H. Chan, *Organic Reactions in Aqueous Media*, John Wiley & Sons, New York, 1997; (*f*) A. Fürstner, *Chem. Rev.*, 1999, **99**, 991–1045; (*g*) M. C. Law, K. Y. Wong and T. H. Chan, *Green Chem.*, 2002, **4**, 161–164; (*h*) P. V. Ramachandran, *Aldrichim. Acta*, 2002, **35**, 23–35.

2 A. Gómez-Sánchez, I. Hermosin, J. M. Lassaletta and I. Maya, *Tetrahedron*, 1993, **49**, 1237–1250.

3 (*a*) D. Furlani, D. Marton, G. Tagliavini and M. Zordan, *J. Organomet. Chem.*, 1988, **341**, 345–356; (*b*) D. Marton, D. Stivanello and G. Tagliavini, *J. Org. Chem.*, 1996, **61**, 2731–2737.

4 A. McCluskey, D. M. Mayer and D. J. Young, *Tetrahedron Lett.*, 1997, **38**, 5217–5218.

5 J. S. Kwon, A. N. Pae, K. I. Choi, H. Y. Koh, Y. Kim and Y. S. Cho, *Tetrahedron Lett.*, 2001, **42**, 1957–1959.

6 J. S. Yadav, B. V. Subba Reddy and G. S. Kiran Kumar Reddy, *Tetrahedron Lett.*, 2000, **41**, 2695–2697.

7 (*a*) A. Hosomi, H. Hashimoto and H. Sakurai, *Tetrahedron Lett.*, 1980, **21**, 951–954; (*b*) H. Sakurai, K. Sasaki and A. Hosomi, *Tetrahedron Lett.*, 1981, **22**, 745–748; (*c*) R. Hunter and G. D. Tomlinson, *Tetrahedron Lett.*, 1989, **30**, 2013–2016; (*d*) J. S. Panek and M. Yang, *J. Am. Chem. Soc.*, 1991, **113**, 9868–9870; (*e*) T. K. Hollis, N. P. Robinson, J. Whelan and B. Bosnich, *Tetrahedron Lett.*, 1993, **34**, 4309–4312; (*f*) D. Sames, Y. Liu, L. DeYoung and R. Polt, *J. Org. Chem.*, 1995, **60**, 2153–2159; (*g*) N. Thery, J. Szymoniak and C. Moise, *Tetrahedron Lett.*, 1999, **40**, 3155–3158; (*h*) V. S. Enev, H. Kaehlig and J. Mulzer, *J. Am. Chem. Soc.*, 2001, **123**, 10764–10765; (*i*) L. C. Wieland, H. M. Zerth and R. S. Mohan, *Tetrahedron Lett.*, 2002, **43**, 4597–4600.

8 D. Houllemare, F. Outurquin and C. Paulmier, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1629–1632.

9 N. O. Brace, *J. Am. Chem. Soc.*, 1955, **77**, 4666–4668.

10 G. Crank and F. W. Eastwood, *Aust. J. Chem.*, 1964, **17**, 1392–1398.

11 P. K. Jadhav, K. S. Bhat, P. T. Perumal and H. C. Brown, *J. Org. Chem.*, 1986, **51**, 432–439.

12 R. H. Newman–Evans, R. J. Simon and B. K. Carpenter, *J. Org. Chem.*, 1990, **55**, 695–711.

13 M. Kira, K. Sato and H. Sakurai, *J. Am. Chem. Soc.*, 1988, **110**, 4599–4602.

14 H. Schumann, J. Kaufmann, S. Dechert and H. G. Schmalz, *Tetrahedron Lett.*, 2002, **43**, 3507–3511.

15 S. D. Rychnovsky, G. Griesgraber, S. Zeller and D. J. Skalitzky, *J. Org. Chem.*, 1991, **56**, 5161–5169.

16 C. Baylon, M. P. Heck and C. Mioskowski, *J. Org. Chem.*, 1999, **64**, 3354–3360.

17 A. Yanagisawa, H. Inoue, M. Morodome and H. Yamamoto, *J. Am. Chem. Soc.*, 1993, **115**, 10356–10357.

Increased catalytic productivity for nanofiltration-coupled Heck reactions using highly stable catalyst systems†

Dinesh Nair,[a] Justin T. Scarpello,[a] Ivo F. J. Vankelecom,[b] Luisa M. Freitas Dos Santos,[c] Lloyd S. White,[d] Ralf J. Kloetzing,[e] Thomas Welton[e] and Andrew G. Livingston*[a]

[a] *Department of Chemical Engineering and Chemical Technology, Imperial College of Science, Technology and Medicine, London, UK SW7 2BY. E-mail: a.livingston@ic.ac.uk*
[b] *Centre for Surface Chemistry and Catalysis, Katholieke Universiteit Leuven, Kasteelpark Arenberg 23, 3001 Leuven, Belgium*
[c] *GlaxoSmithKline Pharmaceuticals, New Frontiers Science Park, Harlow, Essex, UK CM19 5AW*
[d] *W. R. Grace & Co.-Conn, 7500 Grace Drive, Columbia, MD 21044, USA*
[e] *Department of Chemistry, Imperial College of Science, Technology and Medicine, London, UK SW7 2AY*

Received 2nd April 2002
First published as an Advance Article on the web 6th June 2002

The recycle of homogeneous Heck catalysts from post-reaction mixtures using solvent resistant nanofiltration (SRNF) membranes is known to increase catalytic productivity. However, the technique is sensitive to catalyst stability when applied to conventional catalysts: catalyst deactivation will cause declining reaction rates and higher reactor occupancy with an increasing number of catalyst recycles. In this study, a conventional Heck catalyst {bis(acetato)bis(triphenylphosphine)palladium(II)}, was recycled six times, before the reaction rate dropped below 20% of the original value. A cumulative turnover number (TON) of 690 in 120 h was obtained, whilst providing a product substantially lowered in organometallic impurities. Significant improvements in system performance were realised by employing, at identical Pd loading, state-of-the-art catalysts with greater chemical stability. An imidazolylidene catalyst, bis(1,3-dibenzylimidazoline-2-ylidene)diiodopalladium(II), yielded an equal TON for six recycles in 40 h with substantially less reaction rate decline. Palladium(II) acetate stabilised by the quaternary phosphonium salt (quat) tetraphenylphosphonium bromide even gave six recycles in under 30 h after careful solvent selection. In all cases, the membrane showed good selectivity against the catalyst (up to 96% Pd rejection), while allowing the reaction product to permeate completely. Through the sustainable high reaction rates, reactor occupancy can be minimised, and waste generated by downstream processing reduced. Indeed, the imidazolylidene and the quat-stabilised catalyst systems surpassed 10 catalyst recycles with TONs >1000 within 60 and 45 h, respectively.

Introduction

The use of organometallic complexes as homogeneous catalysts in high value added organic synthesis promises higher atom economy than routes involving stoichiometric reagents.[1–5] A major drawback, however, is that the catalyst can be difficult to separate from the reaction products. Extensive downstream processing (work-up) is usually necessary to remove the catalyst from the products, and these work-ups generate metal-rich sludges. In the best case, these are returned to catalyst suppliers for metal reclamation.[2] Substantial waste and poor economics are often associated with work-up due to high solvent volumes and energy requirements,[6,7] as well as permanent loss of high value ligands stabilising the metal catalyst centres.

The Heck reaction is an important homogeneous reaction in organic chemistry, enabling the palladium-catalysed single step coupling of an aryl halide to an olefin.[3,8,9] The inherent instability of the Heck catalyst has prompted much research into affording catalytic stability without reducing reactivity.[10] The conventional approach to increase the productivity of a given catalyst system in Heck chemistry has thus far mostly been through use of adapted ligands or additives.[10]

Spencer showed that the arylation could be a low catalyst loading, high activity process if carried out in a polar aprotic solvent in the presence of phosphine ligands.[11] Phosphine-assisted Heck catalysis was further advanced by the develop-

Green Context

Solvent resistant nanofiltration membranes have been shown to be effective in increasing the productivity of organometallic catalysts in organic reactions. A good example of this is the industrially important C–C bond forming Heck reaction using palladium catalysis but the method was limited by low catalyst stability leading to the formation of palladium black. In the detailed paper significant improvements in the performance of the membrane system are achieved through the use of palladium catalysts designed to have greater chemical stability. Good selectivities for catalyst capture are observed along with high turnover numbers. These results effectively progress the commercial potential for using nanofiltration reaction in the synthesis of speciality chemicals. ***JHC***

---

† Electronic supplementary information (ESI) available: Tables S1–4. See http://www.rsc.org/suppdata/gc/b2/b203232p/

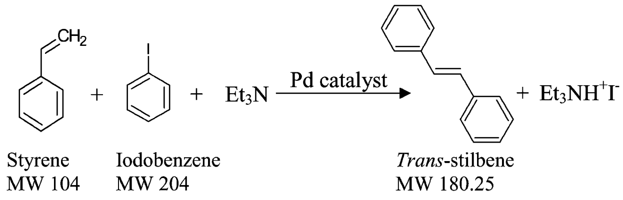
DOI: 10.1039/b203232p

ment of coordinatively unsaturated single-phosphine catalysts, due to the discovery of the unique catalytic activity of a dimeric complex containing bidentate ligands known as Herrmann's Palladacycle.[12] Herrmann *et al.* demonstrated that stable imidazolylidenes are excellent Heck catalyst ligands,[13] forming a wide range of complexes with increased catalytic reactivity and improved stability.[14–16] Compared to the usually applied phosphine ligands these complexes have advantages: they are more stable under the harsh conditions of the Heck coupling reaction, where Pd–phosphine complexes suffer degradation of the catalyst by cleavage of the P–C bond; the addition of an excess of the ligand can be avoided; and it is possible to apply them at very high reaction temperatures, which are necessary for the activation of industrially interesting chloroarenes.

The use of quaternary ammonium or phosphonium salts (quats) as additives has also been shown to be reaction enhancing for Heck coupling.[17–19] Most recently the influence of phosphines, additives, bases and solvents on the Heck coupling of an activated aryl chloride with styrene was reported.[20] The outcome of the possible combinations of phosphine/quat/base was shown to be difficult to predict, and small changes in the latter two caused a dramatic decrease in catalyst productivity. Further, the optimisation of a reaction for a particular coupling pair would not be automatically optimal for other coupling partners; every combination of aryl halide and olefin required its own optimisation procedure. The use of enhancing ligands or additives is clearly not a well understood and generally applicable technology.

An easier and more generic alternative to increase activities of Heck catalysts would be a recyclable system, where an active catalyst could be easily separated from the products and recycled for multiple catalyst reuses. Heterogeneous recyclable Heck systems have been built in liquid–liquid and solid–liquid modes.[10] Only two homogeneous systems have been reported thus far,[21,22] utilising solvent resistant nanofiltration (SRNF) membranes in a continuous or semi-continuous mode, respectively. Applied to the Heck reaction,[22] increased catalytic productivity and reduced metal contamination of the product were obtained. Although multiple catalyst recycles and increased TONs were achieved, the major problem was the limited catalyst stability reflected in the formation of Pd black. The need for more stable homogeneous catalyst recycle systems to maximise catalyst productivity was thus apparent.

In this paper, the combination of SRNF with more stable homogeneous catalytic systems is reported for the Heck coupling of iodobenzene and styrene to form *trans*-stilbene (Scheme 1). The higher stability is realised in two ways: either by using the recently developed, stable, Pd–imidazolylidene catalyst, or by a better selection of solvents to enhance the stability of the more traditional Pd–phosphine catalysts with quats. Even though the current availability of SRNF membranes is limited, they are sufficiently versatile to allow such solvent optimisation. The study demonstrates the potential of SRNF to recycle stable catalytic systems, thus increasing the catalytic productivity above that expected from either a single pass of a stable catalyst or from recycling less stable catalysts. Moreover, in contrast with the single pass approach, the catalyst is recycled and cleaner products are obtained with reduced metal and quat contamination. Compared with the previously described SRNF/Heck systems suffering from deactivation, similar product yields can be reached with less total Pd fed to the system.



Scheme 1 Heck coupling of iodobenzene with styrene to form *trans*-stilbene.

Experimental

Catalysts and stabilisers

{Bis(acetato)bis(triphenylphosphine)palladium(II)} (**1**, 98%), and tri-*o*-tolylphosphine (P(*o*-tol)$_3$, 97%), were obtained from Aldrich UK. Bis(1,3-dibenzylimidazoline-2-ylidene)diiodopalladium(II) **2** was synthesised from a 1,3-dibenzylimidazolium iodide precursor. The preparation of 1,3-dibenzylimidazolium chloride has been reported previously.[23] All preparations were carried out using standard Schlenk techniques in a dry nitrogen atmosphere and under exclusion of moisture. Solvents were dried by standard methods. All other starting materials were used as supplied.

1,3-Dibenzylimidazolium iodide. 1,3-Dibenzylimidazolium chloride (854 mg, 3.00 mmol) and sodium iodide (2.25 g, 15.0 mmol) were suspended in 15 mL acetone and heated under reflux for 40 h. The solvent was evaporated *in vacuo* and the remaining solid was treated three times with 15 mL DCM and filtered. The combined solutions were evaporated and dried, giving a yellow powder. The product was dissolved in 1 mL hot dry MeCN and crystallized by the addition of approx. 1.3 mL dry toluene. The white crystals were washed with dry toluene and light petroleum (bp 30–60 °C) and dried *in vacuo*. Yield: 842 mg, (75%). Mp 108 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 9.41 (t, 1H, ^4J 1.6 Hz, Im H^2), 7.48 (d, 2H, ^4J 1.6 Hz, Im H^{4,5}), 7.43 (m, 10H, Ph), 5.44 (s, 4H, CH$_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 52.1 (CH$_2$), 122.9 (Im C^{4,5}H), 128.4 (Ph CH), 128.8 (Ph CH), 129.1 (Ph CH), 134.8 (Ph C^q), 136.3 (Im C^{2}H). FAB(+)-MS: 625 ((M$^+$)$_2$I$^-$), 249 (M$^+$), 91 (CH$_2$C$_6$H$_5$$^+$); FAB(−)-MS: 503 ((M$^+$)(I$^-$)$_2$), 127 (I$^-$). Elemental analysis. Calc.: C, 54.27; H, 4.55; N, 7.45. Found: C, 54.21; H, 4.63: N, 7.39%.

Bis(1,3-dibenzylimidazoline-2-ylidene)diiodopalladium(II). 1,3-Dibenzylimidazolium iodide (2.00 g, 5.32 mmol) and palladium(II) acetate (0.561 g, 2.50 mmol) were heated in 40 mL dry THF under reflux for 2 h. The solvent was evaporated *in vacuo* and the obtained brown residue was washed three times with 5 mL diethyl ether. **2** was isolated on a short (10 cm, diameter: 19 mm) column (SiO$_2$, eluent: DCM, *n*-hexane 2 : 1). The eluent was removed *in vacuo* and the residue dissolved in 80 mL DCM and the solution was filtered. When the obtained yellow solution was layered with 480 mL *n*-pentane, a yellow crystalline precipitate formed, which was isolated by filtration and dried *in vacuo*.. Yield: 1.10 g (52%). Mp 258 °C. ^{1}H NMR (270 MHz, CDCl$_3$): δ 7.5 (m, 8H, Ph), 7.3 (m, 12H, Ph), 6.62 (s, 4H, Im′ H^{4,5}), 5.57 (s, 8H, CH$_2$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 55.1 (CH$_2$), 121.1 (Im′ CH), 128.2 (Ph CH), 128.8 (Ph CH), 129.2 (Ph CH), 135.6 (Ph C$_q$), 168.2 (Im′ C$_q$). FAB(+)-MS: 729 (M$^+$ − I). Elemental analysis: Calc.: C, 47.66; H, 3.76; N, 6.54. Found: C, 47.48; H, 3.59: N, 6.60%.

Palladium(II) acetate and tetraphenylphosphonium bromide ([PPh$_4$]Br, 98%) **3** combined to form a quat-stabilised catalyst *in situ*, were obtained from Aldrich UK.

Catalysts **1**, **2** and **3** are illustrated in Fig. 1.

Other chemicals

Styrene (STY, 99+%), iodobenzene (IB, 98%) *trans*-stilbene (TSB, 96%) and acetonitrile (MeCN, HPLC grade) were obtained from Aldrich UK. Triethylamine (Et$_3$N, 99%) and

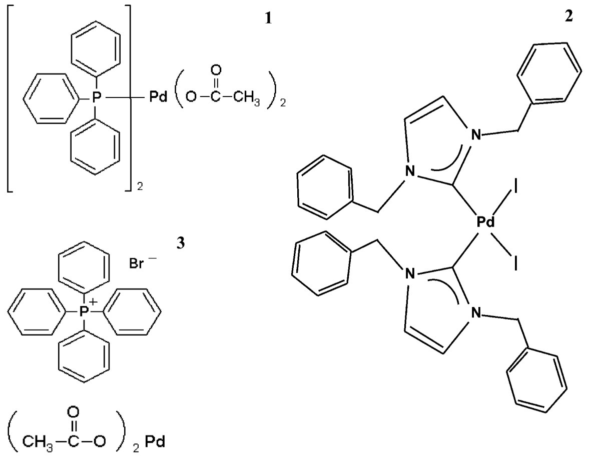
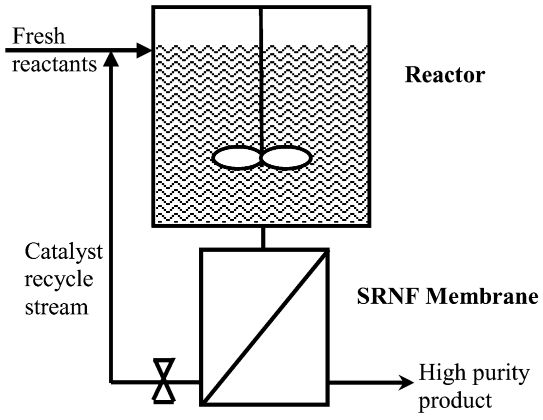


Fig. 1 Catalysts used in Heck reactions: **1** ‘Pd–phosphine’, stabilised with tri-*o*-tolylphosphine in system I; **2** ‘Pd–imidazolylidene’ in system II; **3** ‘Pd–quat’, palladium(II) acetate with $[PPh_4]Br$ in systems III and IV.



Scheme 2 Coupled reaction–separation scheme for catalyst recycle.

tetrahydrofuran (THF, 99+%) were obtained from Sigma UK. Water was deionised with a conductivity of < 1 μS cm^{-1}.

Catalyst recycle procedure

The coupled reaction-separation procedure for performing the reaction (Scheme 2) was the same for all systems. 50 mL screw-cap stainless steel reactors were placed in a stirred oil bath controlled within 1 °C of the desired reaction temperature. Samples were taken for immediate GC assay using a 1 μL syringe. When between 95 and 100% conversion of IB was attained and the reaction was quenched under cold water. The reaction solution was transferred to the SRNF cell and filtered until 85% of the initial volume had permeated using an SRNF membrane. The retained, catalyst-rich solution was then diluted with fresh reactant solution, transferred back to the reactor and the reaction re-initiated. This reaction–filtration procedure was repeated multiple times to achieve successively higher catalyst productivity. Recycling was stopped arbitrarily when the reaction rate fell significantly.

Detailed reaction compositions

System I ‘Pd–phosphine’. IB (0.168 mL, 1.2 equiv.) STY (0.138 mL, 1.0 equiv.), Et_3N (0.167 mL, 1.0 equiv.), H_2O (6.31 mL), **1** (0.0072 g, 0.01 equiv.) and P(*o*-tol)$_3$ (0.0117 g, 0.04 equiv.) were dissolved in 32.2 mL THF and heated to 60 °C

System II ‘Pd–imidazolylidene’. IB (0.168 mL, 1.2 equiv.), STY (0.137 mL, 1.0 equiv.), Et_3N (0.166 mL, 1.0 equiv.), H_2O (6 mL), **2** (0.005 g, 0.01 equiv.) and P(*o*-tol)$_3$ (0.0146 g, 0.04 equiv.) were dissolved in 33.5 mL THF and heated to 160 °C.

System III ‘Pd-quat’. IB (0.168 mL, 1.2 equiv.), STY (0.137 mL, 1.0 equiv.), Et_3N (0.166 mL, 1.0 equiv.), H_2O (6 mL), palladium(II) acetate (0.002 g, 0.01 equiv.) and $[PPh_4]Br$ (0.020 g, 0.06 equiv.), to form **3**, dissolved in 33.7 mL THF and heated to 160 °C.

System IV ‘Pd–quat–MeCN’. IB (0.168 mL, 1.2 equiv.), STY (0.137 mL, 1.0 equiv.), Et_3N (0.166 mL, 1.0 equiv.), palladium(II) acetate (0.002 g, 0.01 equiv.) and $[PPh_4]Br$ (0.020 g, 0.06 equiv.) to form **3** dissolved in 39.5 mL MeCN and heated to 160 °C.

Membranes

Samples of an integral asymmetric SRNF membrane, STARMEM 122 (STARMEM is a trademark of W.R.Grace), with an active surface manufactured from polyimides were kindly supplied by W. R. Grace, Columbia, MD, USA. These membranes are similar to those described in a previous report.[24] In THF/H_2O systems, the membrane separation performance deteriorated with multiple uses, so a new membrane disk was used for each filtration in systems I–III.

A composite SRNF membrane, MPF60, was purchased from Koch Membrane Systems. This membrane showed long-term stability in MeCN and was consequently the preferred membrane for this solvent. The same MPF60 membrane disc was reused for all MeCN separations in system IV.

Filtration details

Nanofiltration was performed in a Sepa ST pressure cell (Osmonics, USA) at a transmembrane pressure, ΔP, of 3.0 MPa. The stainless steel cell was fitted with a removable Teflon magnetic stirrer. Membrane disks of 49 mm diameter were mounted in the pressure cell using a Teflon-coated ring-seal. When fixed in the cell, the available active membrane area for filtration, A_m, was measured as 1.69×10^{-3} m^2. The cell was immersed in a water-bath controlled at a temperature of 20 ± 0.1 °C and mounted on a magnetic stirrer effecting stirring of the cell contents at 900 rpm.

The time, t, to collect the permeate volume, V_p, was recorded. For all systems the reaction solution volume in the cell was 40 mL, which was pumped into the cell directly from the reaction vessel; 6 mL of the solution was retained.

Following filtration and sampling of the permeate and retentate, the retentate was diluted *in situ* with the necessary solvent–reactant solution to make it up to 40 mL and then pumped back to the reactor. The conversion in a subsequent reaction was calculated by subtracting the amount of product that was still present in the 6 mL left from the previous reaction.

Analytical techniques

Gas chromatography. Concentrations of STY, IB, TSB and P(*o*-tol)$_3$ were determined using a Shimadzu GC-14A Gas Chromatograph with a flame ionisation detector (FID) and a Megabore column (length 25 m with 0.23 mm i.d.) with BP1 (SGE, Australia) as the stationary phase. The programme ran from 50 to 280 °C at a rate of 40 °C min^{-1} following being held at initial temperature for 2.5 min.

NMR. ^{1}H NMR Spectra were obtained on a JEOL JNM-EX 270 FT NMR System, ^{13}C NMR spectra were obtained on a Bruker DRX-400 Spectrometer. IR spectra (4000–650 cm^{-1}) were recorded as KBR disks on a Perkin Elmer FT-IR 1725 X Spectrometer. Mass spectra were obtained from the Imperial College Chemistry department service. Melting points were obtained on a Gallenkamp Sanyo MPD 350 apparatus. The given melting points are uncorrected. Elemental analyses were obtained from the University of North London service.

AAS. Atomic Absorption Spectrophotometry analysis was obtained for Pd on a Perkin-Elmer 1100B using an oxy–acetylene flame at 2000 °C.

Calculation of reaction parameters

Reaction conversion. Conversion, Conv(t), was calculated on the basis of disappearance of IB, with no visible side reactions occurring. Initial IB concentration was 20% in excess of the concentration of STY to avoid excessive Pd black formation, which occurred rapidly on complete disappearance of IB from the reaction solution. Therefore, an 83% conversion of fed IB corresponded to a 100% conversion of STY. Thus, conversion at time t was calculated using eqn. (1):

$$\mathrm{Conv}(t) = ((C_{\mathrm{IB},0} - C_{\mathrm{IB},t})/(0.83 \times C_{\mathrm{IB},0})) \times 100\% \tag{1}$$

where $C_{\mathrm{IB},0}$ is initial IB concentration and $C_{\mathrm{IB,t}}$ is IB concentration at time t during the reaction.

Turnover number (TON). Turnover number, a measure of catalyst efficiency, was calculated using eqn. (2):

$$\text{TON} = \text{moles IB converted/moles Pd initially fed} \tag{2}$$

Cumulative TON for a set of recycle sequences at any given time was calculated by adding values of TON for all reactions performed across the cumulative reaction time taken up to that given time.

Mean turnover frequency. Mean turnover frequency (TOF), describing the rate of change of TON for a reaction in any given recycle sequence (reflecting reaction rate for fixed Pd loading), was calculated from eqn. (3):

$$\text{cumulative TON/time taken to achieve cumulative TON} \quad (\text{TON h}^{-1}) \tag{3}$$

Calculation of membrane parameters

The membrane performance was assessed in terms of flux and rejection.

Solvent flux. Solvent flux, J_s, was calculated using eqn. (4):

$$J_{\mathrm{s}} = V_{\mathrm{p}}/A_{\mathrm{m}}t \tag{4}$$

which represents the volume permeated per unit area over a time period (l m^{-2} h^{-1}) at a transmembrane pressure of 30 bar.

Rejection. The rejection, R, of the membrane is a measure of the membrane separation performance with respect to a solute, and is defined by eqn. (5):

$$R = (1 - (C_{\mathrm{p},x}/C_{\mathrm{r},x})) \times 100\% \tag{5}$$

where $C_{\mathrm{p},x}$ is the concentration of solute x in the permeate and $C_{\mathrm{r},x}$ is the concentration of solute x in the retentate. A rejection of 100% corresponds to perfect retention of the species and 0% to no separation. Molecular weight cut-off (MWCO) is defined as the molecular weight of solute for which a 90% rejection is observed. MWCO for the STARMEM 122 and MPF60 membranes, as reported by the respective manufacturers, were 220 and 400 Da, respectively.

Results and discussion

Figs. 2–5 show the conversion of IB and cumulative TON as a function of time for Pd–phosphine, Pd–imidazolylidene, Pd–quat and Pd–quat–MeCN (systems I–IV, respectively). The abrupt discontinuity between conversion lines is attributable to the filtration, addition of new reagents and the re-initiation of

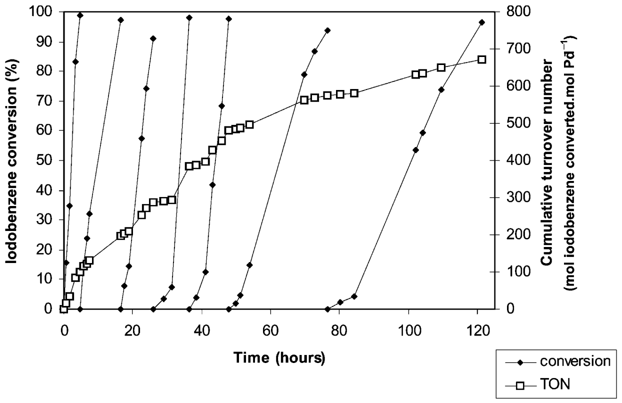


Fig. 2 IB conversion and cumulative TON *versus* reaction time for system I 'Pd–phosphine'.

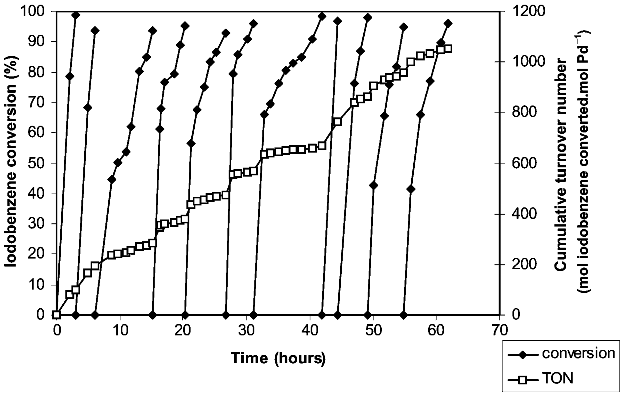


Fig. 3 IB conversion and cumulative TON *versus* time for system II 'Pd–imidazolylidene'.

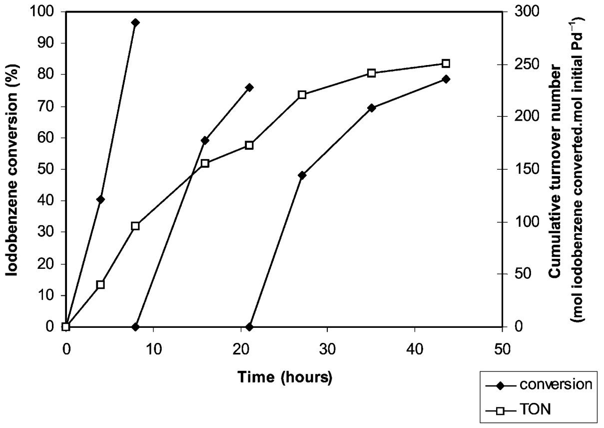


Fig. 4 IB conversion and cumulative TON *versus* time for system III 'Pd–quat'.

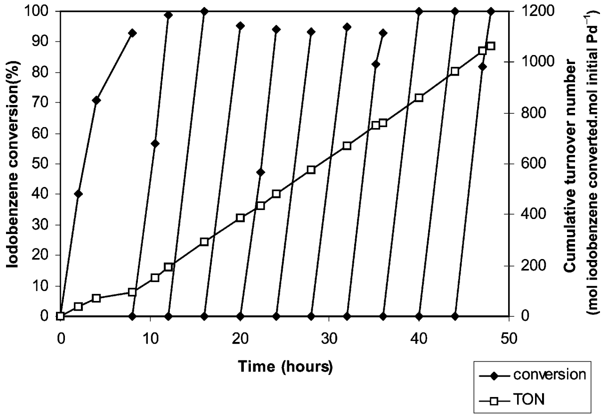


Fig. 5 IB conversion and culutative TON *versus* time for system IV 'Pd–quat–MeCN'.

the reaction at zero conversion of IB at the start of the following cycle.

As shown in Fig. 2, SRNF-assisted catalyst recycle can substantially increase TON in a reaction system based on the conventional catalyst **1** stabilised by 4 molar equivalents of P(*o*-tol)$_3$. The first batch of system I achieved near complete conversion in less than 4 h. Substantial deposits of Pd black accompanied this reaction. In the subsequent filtration, 96% Pd rejection was realised. A decline in reaction rate, coupled with further Pd black deposition, allowed only six catalyst recycles in 120 h before activity dropped to below 20% of the initial level. System I was operated at 60 °C, while the other systems were operated at 160 °C. Use of identical temperatures was unfeasible: screening experiments showed that **1** suffered significant decomposition at 160 °C, to such an extent that not even one catalyst recycle was possible. Conversely, the other catalyst systems were inactive at 60 °C.

The problem of Pd black formation and reaction rate decline was tackled by using and recycling two state-of-the-art, more robust catalysts; a Pd–imidazolylidene, **2** (in system II) and a Pd–quat catalyst, **3**, formed by stabilising palladium(II) acetate with [PPh$_4$]Br (in systems III and IV). System II showed no sign of an induction period during the first reaction, which reached near complete conversion in less than 3 h (Fig. 3). A small amount of Pd black was observed after this reaction, but this was not the case for the remaining reactions. Apart from deviant behaviour during the seventh run, only a minor reaction rate decline was observed during 11 runs, with the final reaction taking 5 h. These results confirm the excellent stability of the Pd–imidazolylidene system, allowing 10 catalyst recycles leading to a cumulative TON of 1050 in less than 60 h. This proves the potential of the SRNF-coupled catalysis system to increase the productivity of existing stable catalytic systems without any extra additives or chemical modifications.

System III was conducted in the THF/H$_2$O solvent as used in the previous systems. No induction period but significant Pd black deposition suggested that an active but unstable quat-derived complex was forming. The first reaction attained near complete conversion of IB after 8 h (Fig. 4). Significant reaction rate decline and further Pd dropout were observed in the 2 subsequent reactions.

Further screening of reaction solvents for a more stable Pd–quat system revealed MeCN was an excellent solvent choice, leading to its use in system IV. The first reaction started very quickly, with some reaction rate decline towards the end, requiring 8 h to reach 93% conversion (Fig. 5). This suggested either the slow formation of a quat-derived complex or Pd becoming inactive over the reaction duration. As no Pd black was observed (under conditions where uncomplexed **3** would completely degrade) and no reaction rate decline occurred for each of the subsequent 4 h reactions, the former explanation appeared more plausible. Indeed, this suggested that not only was the catalyst complex stable, but also highly active—the most active stable Heck catalyst recycle system reported to date, with 10 catalyst recycles completed within 45 h. Comparison of systems III and IV highlighted the importance of solvent choice for building a stable catalyst system and the impact this can have on the recyclability of the catalyst. Polar aprotic solvents have often proven better facilitators for Heck reactions, and may also be beneficial for formation of stable quat-derived Pd complexes. It should be noted that the quat has a key role in this reaction, since an experiment following system IV but with no added quat took 13 h to give 94.4% conversion, but with substantial Pd black formation. After filtration and catalyst recycle, the reaction stalled completely at 62 % conversion after 13 h.

Table 1 presents membrane performance (mean flux, Pd rejection and P(*o*-tol)$_3$ rejection) and overall reaction performance (calculated mean TOF) for each system. Average solvent flux across the membranes was reasonable and ranged between 24 and 41 L m^{-2} h^{-1}. The membranes proved selective against Pd (> 92% rejection) and P(*o*-tol)$_3$ (present in systems I and II > 94% rejection), while transmitting the product completely (0% rejection). The slightly lower mean Pd rejection values obtained in system IV were consistent with the higher MWCO of the MPF60 membrane. The compromise of lower membrane selectivity (leading to lower catalyst rejection) but increased stability of MPF-60 in MeCN enabled reuse of the same membrane disk for all filtrations in this solvent.

Mean TOF is presented as an indicator of averaged reaction rate over the duration of multiple catalyst recycles. It is clear that highly stable catalyst recycle systems are able to achieve more catalyst recycles and higher cumulative TONs due to increased active catalyst lifetime. However, the increased stability also allowed high reaction rates to be sustained for much longer periods. Consequently, high TONs were achieved more quickly than in conventional unstable catalyst systems, minimising reactor occupancy. The resulting mean TOF values show that, despite running for several more catalyst recycles than other systems, the stable catalyst recycle systems (II and IV) still generate an average reaction rate 3–4 times higher than the unstable systems. Tables S1–4 provide supplementary information for each particular system (see ESI†).

The SRNF-coupled catalysis technology indicates potential not only for efficient catalyst recycle (with substantial catalyst cost reduction), but also for significantly lowered metal levels in the product stream and waste minimisation in the associated

Table 1 System performance for multiple catalyst recycles

System	Mean flux/ l m^{-2} h^{-1}	Mean R_{Pd} and $R_{\mathrm{P}(o\text{-tol})_3}$ (%)	Number of catalyst recycles	Cumulative TON/ mol IB converted (mol initial Pd)$^{-1}$	Cumulative time/h	Mean TOF/TON h^{-1}
I 'Pd–phosphine'	41.0	96, 94	6	689	120	5.74
II 'Pd–imidazolylidene'	24.3	95, 95	10	1053	60	17.6
III 'Pd–quat'	34.7	95, n/a	2	251	42	5.97
IV 'Pd–quat–MeCN'	38.1	92, n/a	10	1062	46	23.1

downstream processing. To see this, consider that without catalyst recycle the molar ratio of Pd/product at the end of a 100% conversion reaction will be at the starting ratio of Pd/STY, *i.e.* 0.01 for all systems. With catalyst recycle and a catalyst rejection of 96%, and a volume ratio of permeate/retentate from the filtration of 4, the molar ratio Pd/product in the permeate (product) stream at the end of a 100% conversion reaction is 0.0014. The potential for generic applicability of coupled reaction–separation is clear for any system where a catalyst molecule can be separated from permeating product molecules. The use of more stable catalytic systems is crucial in this respect.

Acknowledgements

Financial support from the EPSRC Grant No. GR/M50911/01 and support in kind from W. R. Grace, Columbia, MD, USA and GlaxoSmithKline, Harlow, UK, is gratefully acknowledged.

References

1 P. T. Anastas and T. C. Williamson, *Green Chemistry: Frontiers in Benign Chemical Synthesis and Processes*, Oxford University Press, Oxford, 1998.
2 G. Jödicke, O. Zenklusen, A. Weidenhaupt and K. Hungerbühler, *J. Cleaner Prod.*, 1999, **7**, 159.
3 R. F. Heck, *Org. React.*, 1982, **27**, 345.
4 S. Akutagawa, *Appl. Catal. A: Gen.*, 1995, **128**, 171.
5 R. A. Sheldon, *CHEMTECH*, 1994, 38.
6 B. M. Trost, *Science*, 1991, **254**, 1471.
7 A. D. Curzons, D. J. C. Constable, D. N. Mortimer and V. L. Cunningham, *Green Chem.*, 2001, **3**, 1.
8 G. T. Crisp, *Chem. Soc. Rev.*, 1998, **27**, 427.
9 R. F. Heck, *Palladium Reagents in Organic Syntheses*, Academic Press, New York, 1985.
10 I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009.
11 A. Spencer, *J. Organomet. Chem.*, 1983, **258**, 101.
12 W. A. Hermann, C. Brossmer, K. Öfele, C. P. Reisinger, T. Priermeier, M. Beller and H. Fischer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1844.
13 W. A. Herrmann, M. Elison, J. Fischer, C. Koecher and G. R. J. Artus, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2371.
14 W. A. Herrmann, C.-P. Reisinger and M. J. Spiegler, *J. Organomet. Chem.*, 1998, **557**, 93.
15 M. G. Gardiner, W. A. Herrmann, C.-P. Reisinger, J. Schwarz and M. J. Spiegler, *J. Organomet. Chem.*, 1999, **572**, 239.
16 W. A. Herrmann, J. Schwarz, M. G. Gardiner and M. J. Spiegler, *J. Organomet. Chem.*, 1999, **575**, 80.
17 M. T. Reetz, G. Lohmer and R. Schwickardi, *Angew. Chem., Int. Ed.*, 1998, **37**, 481.
18 R. S. Varma, K. P. Naicker and P. J. Liesen, *Tetrahedron Lett.*, 1999, **40**, 6427.
19 T. Jeffery, *Tetrahedron Lett.*, 2000, **41**, 8445.
20 A. Zapf and M. Beller, *Chem. Eur. J.*, 2001, **7**, 2908.
21 K. de Smet, S. Aerts, E. Ceulemans, I. F. J. Vankelecom and P. A. Jacobs, *Chem. Commun.*, 2001, 597.
22 D. Nair, J. T. Scarpello, L. M. Freitas dos Santos, L. S. White, I. F. J. Vankelecom and A. G. Livingston, *Tetrahedron Lett.*, 2001, **42**, 8219.
23 K. J. Harlow, A. F. Hill and T. Welton, *Synthesis*, 1996, 697.
24 L. S. White and A. R. Nitsch, *J. Membr. Sci.*, 2000, **179**, 267.

EPZ-10 catalyzed regioselective transformation of alkenes into β-iodo ethers, iodohydrins and 2-iodomethyl-2,3-dihydrobenzofurans

Vishal A. Mahajan, Popat D. Shinde, Anil S. Gajare, M. Karthikeyan and Radhika D. Wakharkar*

Division of Organic Chemistry, Technology, National Chemical Laboratory, Pune-411008, India. E-mail: rdw@dalton.ncl.res.in

Received 18th March 2002
First published as an Advance Article on the web 5th June 2002

An efficient method for the regioselective synthesis of β-iodo ethers and iodohydrines from styrene, indene and dihydronaphthalene in presence of EPZ-10^R has been presented wherein only 0.5 equivalent iodine (I_2) has been used. Similarly, *o*-allylphenols are converted to 2-iodomethyl-2,3-dihydrobenzofurans in high yields. This demonstrates a clean green chemical transformation with significant atom economy.

Introduction

Development of newer and environmentally preferred synthetic methodologies in organic chemistry has been an important area of current research. Functionalization of alkenes finds applications in various important transformations. β-Iodo ethers are useful intermediates for stereoselective radical reaction[1] and for synthesis of *E*- or *Z*-alkenes with good to moderate distereoselectivity.[2] Treatment of alkenes with iodine in presence of certain nucleophilic species leads to the formation of 2-functionalised iodo compounds such as 1,2-iodoisocynates,[3] 1,2-halohydrins[4] and 1,2-haloacetoxy[5] compounds. The *trans*-2-functionalised iodo compounds are useful intermediates for the synthesis of epoxides[6] *cis*-diols[7] episulfides,[8] aziridines[9] *etc.* Vicinal iodo alkoxy alkanes in particular have been prepared by reaction of alkene with iodine and the corresponding alcohol in the presence of sulfolane.[10] Applications of these compounds are well documented in the literature.[11–14]

Several reagents have been used for vicinal iodo fictionalization of alkenes such as bis(pyridine)iodine(I) tetrafluoroborate,[15] mixture of iodine and $CuO\cdot HBF_4$,[16] copper(II) acetate,[17] silver(I) carboxylates,[18] tetramethylene sulfone,[19] and lead(II) acetate.[20] Some of the reagents listed above are expensive and not easy to prepare, or give by products after completion of reaction, which are difficult to separate from the reaction mixture. Iodo functionalization using two equivalents of iodine *via* triiodide ion formation has also been reported.[21]

Considerably growing interest in the catalysis of organic reactions by inorganic reagents supported on high surface area inorganic material[22] has led to a new family of supported reagents *viz* Envirocat^R, which represents a breakthrough in environmentally friendly chemistry.[23] Envirocat EPZ-10^R is a commercial form of clayzic which is prepared by the treatment of montmorillonite clay with $ZnCl_2$ and exhibits both Brönsted and Lewis acid characteristics.[24] EPZ-10^R is used in industry for Friedel–Crafts reactions including those of aromatic substrates with alkyl halides, aldehydes and alcohols.[24] Other applications include olefination of benzaldehyde and preparation of benzothiophenes by cyclisation of phenylthioacetals.

In this communication, we wish to report an EPZ-10^R mediated highly efficient and convenient protocol for regioselective synthesis of β-halo alkyl ethers from olefins and direct conversion of *o*-allylphenols into the corresponding 2-iodomethyl-2,3-dihydrobenzofurans in a single step. Comparative data using $ZnCl_2$ as a homogenous catalyst is also presented.

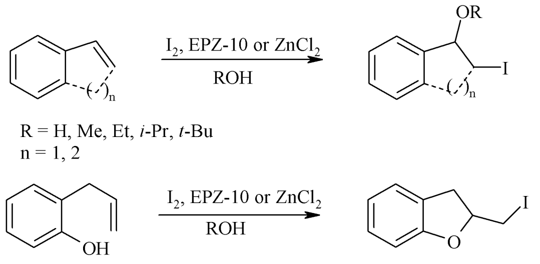
Results and discussion

Initially we studied β-halo alkyl ether formation from activated alkenes such as styrene in the presence of $ZnCl_2$ and only 0.5 equivalent iodine in alcoholic solvents, which resulted into complete conversion to the corresponding β-halo alkyl ether (Scheme 1). Similar experiments using EPZ-10^R instead of $ZnCl_2$ gave efficient transformation to the expected products in excellent yields. We further performed this transformation on indene and 1,2-dihydronaphthalene to get the corresponding addition products. Table 1 exhibits the general applicability of the reaction using various alcohols including primary, secondary and tertiary alcohols. Styrene (Table 1, entries 1–4), indene (entries 6–8) and 1,2-dihydronaphthalene (entries 10–12) on treatment with iodine (0.5 mol) and EPZ-10 (20% w/w) in alcohol (MeOH, EtOH, *i*-PrOH, *t*-BuOH) as solvent gave the corresponding 2-iodo-1-alkoxyethylbenzene in almost quantitative yields (Table 1, 92–98%). When reaction was carried out in dioxane with water olefins *viz.* styrene, indene and 1,2-dihy-

Green Context

The successful application of heterogeneous catalysts in liquid phase organic reactions has been one of the most fruitful areas of green chemistry. Such easy-to-separate and generally renewable catalysts replace soluble and often hazardous traditional reagents and catalysts, thus simplifying important organic processes as well as offering potential economic and health and safety advantages. EPZ10 is a commercial 'green catalyst' developed in ground-breaking applied research some 10 years ago. Since then it has been applied to numerous useful organic reactions with the associated advantages indicated above. Here its first use in the regioselective conversion of alkenes into β-iodo ethers is described. This one-pot conversion is also atom-efficient in the halogen—an important feature of a genuinely green chemistry process. *JHC*

DOI: 10.1039/b202725a



Scheme 1

dronaphthalene gave the corresponding iodohydrins (Table 1, entries 5, 9 and 13) in excellent yield. These representative examples clearly showed the efficacy of EPZ-10, which was comparable with that of $ZnCl_2$.

The Markonikov addition of iodine to the olefin is probably *via* the stepwise formation of iodonium ion that is opened by regioselective nucleophilic attack (ROH or H_2O) leading to the β-iodo ethers and iodohydrins, respectively. Such metal salt supported decomposition is known in the literature. The atom economy (of iodine) exhibited in this reaction can be explained by oxidative regeneration of iodine and hydrogen due to the dissociation of the hydroiodic acid formed during the addition reaction. The regiospecificity for this reaction is in accordance with metal complex based addition reported for styrene, which was confirmed by NMR spectroscopy, and the addition was found to occur in a Markownikov manner. The study of the addition of alkoxide ions on the iodonium ion revealed that the rate of reaction is faster if conducted in methanol and ethanol than in 2-propanol (Table 1: MeOH < EtOH < *i*-PrOH < *t*-BuOH).

In order to explore the scope of this reaction we selected *o*-allylphenols to perform this reaction. Iodo-cyclization of 2-allylphenol or 2-allylcyclohexanol is reported in literature in the presence of $SnCl_4$[25] or $Pb(OAc)_4$ and NaI,[26] respectively. When *o*-allylphenol (Table 1, entry 14) was treated with iodine (0.5 equiv. in methanol) in presence of EPZ-10 2-iodomethyl-2,3-dihydrobenzofuran was obtained exclusively in high yield arising from intramolecular nucleophilic attack on the iodonium intermediate. The generality of this transformation was substantiated by the reaction on substituted phenols and a naphthol derivative (Table 1, entries 15–17).

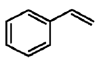
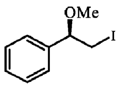
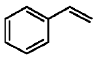
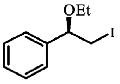
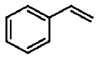
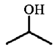
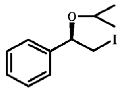
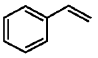
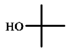
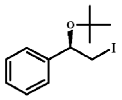
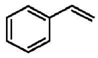
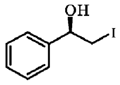
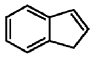
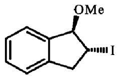
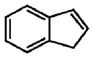
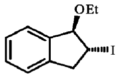
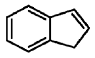
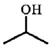
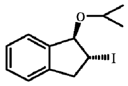
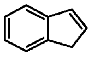
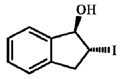
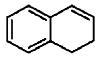
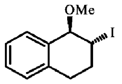
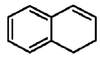
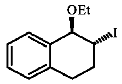
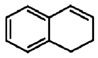
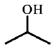
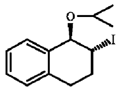
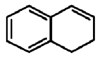
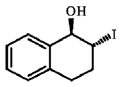
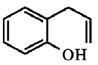
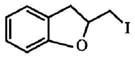
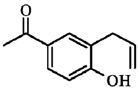
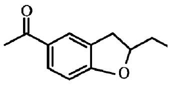
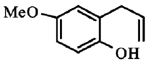
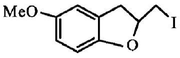
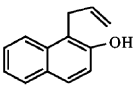
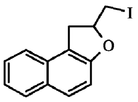
Experimental

Envirocat EPZ-10^{R} was procured from Contract Chemicals Ltd., Merseyside, UK, and activated prior to use by azeotropic drying overnight for removal of loosely bound water. Solvents were purified and dried by standard procedures before use. Infrared spectra were recorded on an ATI MATTSON RS-1 FT-IR spectrometer. ^1H NMR spectra were recorded on a Bruker AC-200 spectrometer.

General procedure

Typical procedure for the preparation of 2-iodo-1-methoxy-2,3-dihydro-1*H*-indene 6 using EPZ-10. A mixture of EPZ-10 (20% w/w) and indene (0.5 g) was stirred in anhydrous methanol (10 mL). This was heated to reflux under an argon atmosphere for 10 min, cooled to room temperature and iodine (0.547 g, 0.5 equiv.) added. The reaction mixture was further refluxed for 30 min. The solution was allowed to cool to room temperature, the catalyst EPZ-10 was filtered off and solvent was removed under reduced pressure. Chromatographic purification of the crude product over silica gel gave 2-iodo-1-methoxy-2,3-dihydro-1*H*-indene as a colorless liquid (97%).

Table 1 $ZnCl_2$ or EPZ-10^{R} catalysed one-pot regioselective transformation of alkenes into β-iodo ethers and iodohydrins

Entry No.	Substrate	Alcohol	Product	Time/ min	Yield[a] (%) ZnCl$_2$	Yield[a] (%) EPZ-10
1		MeOH		30	98	97
2		EtOH		40	98	98
3				50	92	95
4				60	93	96
5		H_2O		45	90	93
6		MeOH		30	98	98
7		EtOH		40	95	97
8				55	93	95
9		H_2O		45	98	97
10		MeOH		30	98	97
11		EtOH		30	92	94
12				55	87	91
13		H_2O		45	95	94
14		MeOH		35	80	85
15		MeOH		30	85	86
16		MeOH		30	75	84
17		MeOH		30	70	80

[a] Isolated yield and characterized by usual spectral analysis. All compounds are racemic and only one form is shown for clarity.

Typical procedure for the preparation of 2-iodo-1-methoxy-2,3-dihydro-1*H*-indene 6 using $ZnCl_2$. A mixture of anhydrous $ZnCl_2$ (0.293 g, 0.5 equiv.) and indene (0.5 g) was stirred in anhydrous methanol (10 mL). This was heated to reflux under an argon atmosphere for 10 min, cooled to room temperature and iodine (0.547 g, 0.5 equiv.) added. The reaction mixture was further refluxed for 30 min. The solution was allowed to cool to room temperature and poured into ice-cold water and extracted with diethyl ether. The organic layer was separated and washed twice with water and dried over $MgSO_4$. Solvent was removed under reduced pressure and chromatographic purification over silica gel gave 2-iodo-1-methoxy-2,3-dihydro-1*H*-indene as a colorless liquid (98%).

^1H NMR ($CDCl_3$), δ 7.50 (m, 1H), 7.25 (m, 3H), 5.10 (d, J = 3.65 Hz, 1H), 4.50 (m, 1H), 3.50 (dd, J = 17.07, 1H), 3.60 (s, 3H), 3.25 (dd, J_1 = 17.07, J_2 = 7.0 Hz, 1H). ^{13}C NMR ($CDCl_3$), δ 141.39, 140.23, 129.09, 127.15, 125.18, 124.70, 93.39, 57.58, 43.57, 25.61. MS, *m*/*z* (%): 274 (M^+, 8.5), 147 (93.6), 127 (19.1), 115 (100), 103 (17), 89 (13), 77 (14), 63 (21).

The same procedure was followed for the preparation of all 1,2-iodo ethers and 2-iodomethyl-2,3-dihydrobenzofuran using EPZ-10^R and $ZnCl_2$ as listed in Table 1

Typical procedure for the preparation of iodohydrins. Same as above, a solution of dioxane–water (11 mL : 4 mL) was used instead of the alcohols.

Conclusion

In conclusion, we have described that EPZ-10^R serves as an efficient catalyst for β-iodo ethers and iodohydrin formation in excellent yields. The potential for intramolecular nucleophilic attack leading to formation of 2-iodomethyl-2,3-dihydrobenzofuran derivatives demonstrated herein is noteworthy. The conversion is fast and the advantages of heterogeneous catalyst in terms of easy work up procedures coupled with simple operation and recyclability (7–8 times after reactivation) of the catalyst are obvious. Although the rate of reaction was more-or-less the same using EPZ-10 and $ZnCl_2$ the quantity of EPZ-10 required (20% w/w) is much less than that of $ZnCl_2$ (0.5 equiv.). Moreover, since iodine is completely consumed the reaction represents an example of atom economy, which is of current interest to ‘Green Chemistry’.

Acknowledgements

We wish to thank CSIR, New Delhi for the award of Research Associate ship to A. S. G., SRF to P. D. S. and to the trustees of Lady Tata Memorial Trust, Mumbai for a research fellowship to V. A. M.

References

1 Y. Guinodon, B. Guerin, H. Chabot, H. Mackintosh and W. W. Olgivie, *Synlett.*, 1995, 449; V. H. Rinderknecht and V. Ma, *Helv. Chim Acta.*, 1964, **47**, 162.

2 K. Maeda, H. Shinokubo and K. Oshima, *J. Org. Chem.*, 1996, **61**, 6770.

3 J. S. Pizey, in *Synthetic Reagents*, Wiley, New York, 1977, vol. 3, p. 227.

4 A. Hassner, *Acc. Chem. Res.*, 1971, **4**, 9.

5 P. D. Woodgate, S. J. Janseen, P. S. Rutledge, S. D. Woodgate and R. C. Cambie, *Synthesis*, 1984, 1017.

6 R. C. Cambie, R. C. Hayword, J. C. Robers and P. S. Rutledge, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1858.

7 C. A. Horiuchi and J. Y. Satoh, *Chem Lett.*, 1988, 1209.

8 J. C. Hinshaw, *Tetrahedron Lett.*, 1972, **34**, 3567.

9 C. Georgoulis and J. M. Valery, *Bull. Soc. Chim. Fr.*, 1975, 2361.

10 J. Barluenga, M. A. Rodriguez and P. J. Campos, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2807.

11 I. Urasaki, *Numazu Kogyo Koto Senmon Gakko Kenky, Hokoku*, 1984, **19**, 73; I. Urasaki, *Chem. Abstr.*, 1985, **103**, 53456.

12 J. Barluenga, J. M. Martinez, J. M. Gallo, C. Najera and M. Yus, *J. Chem. Res. (S)*, 1986, 274; J. Barluenga, J. M. Martinez, J. M. Gallo, C. Najera and M. Yus, *J. Chem. Res. (M)*, 1986, 2416.

13 A. Karnail, *US Pat.*, 5401848, 1995.

14 J. Teulon, *US Pat.*, 4182896, 1998.

15 J. Barluenga, J. M. Gonzalez, P. J. Campos and G. Asensio, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 319.

16 J. Barluenga, M. A. Rodriguez and P. J. Campos, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2807.

17 C. A. Horiuchi and J. Y. Satoh, *J. Chem. Soc., Chem. Commun.*, 1982, 671.

18 C. V. Wilson, *Org. Reactions*, 1957, **9**, 332; F. D. Gunstone, in *Advances in Organic Chemistry: Methods and Rsults*, ed. R. A. Raphael, E. C. Taylor and H. Wynberg, Interscience, New York, 1960, vol. 1, p. 103.

19 R. C. Cambia, W. I. Noall, G. J. Potter, P. S. Rutedge and P. D. Woodgate, *J. Chem. Soc., Perkin Trans. 1*, 1977, 226.

20 A. V. Bedekar, K. B. Nair and R. Soman, *Synth. Commun.*, 1994, **24**, 2299.

21 A. M. Sanseverino and M. C. S. de Mattos, *Synthesis*, 1998, 1584.

22 J. H. Clark, A. P. Kybett and D. J. Macquarrie, *Supported Reagents*, VCH, New York, 1992.

23 J. H. Clark and D. J. Macquarrie, *Chem. Soc Rev.*, 1996, 303; production information of Contract Chemicals, UK, 1994; Enveirocat EPZ-10^R was supplied by Contract Chemicals Ltd, Merseyside, UK.

24 A. S. Gajare, M. S. Shingare and B. P. Bandgaer, *J. Chem. Res. (S)*, 1998, 453.

25 O. Kazuhiko, H. Takahiro, T. Mitsuhiro, S. Hiroshi and T. Masao, *Synthesis (Graduate Sch. Eng., Hokkaido Univ., Sapporo 060, Japan)*, 1997, 23.

26 M. Shigeyasu, S. Masakichi F. Yasuo and T. Takashi, *Heterocycles*, 1985, **23**, 2035.

Solvent-free route to ionic liquid precursors using a water-moderated microwave process

Man Chun Law, Kwok-Yin Wong and Tak Hang Chan*

Department of Applied Biology and Chemical Technology and the Open Laboratory for Chiral Technology, Institute of Molecular Technology for Drug Discovery and Synthesis, The Hong Kong Polytechnic University, Hung Hom, Hong Kong SAR, China.
E-mail: bcchanth@polyu.edu.hk

Received 28th March 2002
First published as an Advance Article on the web 29th May 2002

Water moderation has been used for solvent-free microwave assisted reactions which generate over-heating. The method is demonstrated by the large scale preparation of ionic liquid precursors.

Introduction

Recently, there has been a growing interest in the use of room-temperature ionic liquids as environmentally green solvents for a broad range of chemical and industrial processes. Numerous catalytic reactions, including biocatalytic reactions, can be carried out in ionic liquids.[1–4] Room-temperature ionic liquids have also been widely studied as environmentally benign media for electrochemical technologies,[5] chemical extractions[6] and other industrial processes.[7] This is due to a number of intriguing properties of ionic liquids: high thermal and chemical stability, no measurable vapor pressure, non-flammability, friction reduction, anti-wear performance and high loading capacity. In many cases, the ionic liquids can be recycled easily. The conventional method of preparing the most commonly used ionic liquid precursors, 1-alkyl-3-methylimidazolium halides[8] and *N*-alkylpyridinium halides,[9] involves heating of the alkyl halide and the nitrogen nucleophile in a refluxing solvent overnight to give reasonable yield. Recently, an expeditious solvent-free route to these ionic liquid precursors using microwaves has been reported.[10] In our hands, the method did not work well as described even for small scale (1–2 mmol) preparation of the halide. Overheating of the reaction mixture occurred with generation of vapor, leading to decomposition of the reaction mixture and, on occasions, short-circuit of the microwave oven. While the origin of the discrepancy of our experience with the published report[10] was not clear, we noted that different models of microwave ovens were used even though we attempted to approximate the same power output and length of time of irradiation. Overheating and the possibility of runaway reactions are fairly common for solvent-free reactions since there is no effective heat dissipation by solvent.[11,12] Some of these problems can be avoided with the use of focused microwaves which enable a more precise control of both temperature and radiation intensity[13] or by the dispersal of reactants on inert solid supports.[14] In the present case, the problem may be exacerbated by the fact that the product halide salt is more polar and likely to be strongly microwave absorbing, adding to overheating. We report here a simple experimental modification which allows the large scale preparation of the ionic liquid precursors under solvent-free microwave condition[15] using an unmodified household microwave oven.

Results and discussion

Drawing on the analogy of a nuclear reactor reaction where the generated heat is moderated by water, we attempted to moderate the microwave reactions with water. An unmodified household microwave oven equipped with five step power levels was used. The reaction flask containing the reactants, 1-methylimidazole and 1-bromobutane, and capped with a drying tube, was immersed in a beaker containing water at an initial temperature of 60 °C. The effect of microwave power levels and duration of heating was examined to give the optimum reaction conditions (Table 1). Using the 1.0 mol reaction as an example (Table 1, entry 1), after the first irradiation for 1 min at 110 W power level, there was a partial formation of ionic liquid (pale yellow, opaque). The mixture was then mixed by swirling the flask for 10 s and then heated again at 330 W power level for 3 min. This mix and heat step was repeated until a clear liquid phase, indicating complete alkylation, could be observed. At this stage, the excess 1-bromobutane was removed easily by washing with ether and drying under vacuum at 80 °C. The shorter period and lower microwave power level at the first step was quite necessary, otherwise too vigorous a reaction would occur leading to the degradation of the reaction mixture. After this first step, the following stages were relatively straightforward and eventually leading to complete reaction. The temperature of the water bath was measured during the course of the reaction and found to reach 80 °C. Since unreacted 1-methylimidazole was difficult to remove, it was preferable to use a slight excess of the alkyl halide to ensure 100% alkylation. The yield of

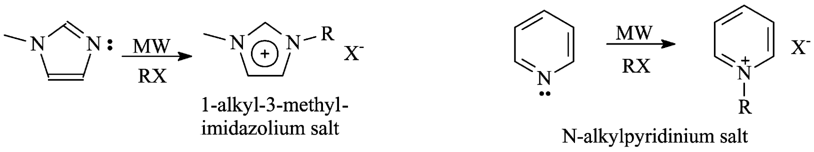
Green Context

Microwave reactors have attracted considerable attention as alternatives to conventional reactors for carrying out synthetic reactions. One particular advantage they can offer is efficiency in solventless reactions thus adding another green chemistry benefit to that of the very short reaction times associated with microwave-assisted processes. However, it can be difficult to control these processes and overheating can cause product decomposition, volatilisation, and possibly dangerous run-aways. Here the use of water as a process moderator is described with particular reference to the preparation of ionic liquids. This is an interesting example of a solventless process developed to make solvents.

DJM

DOI: 10.1039/b203122a

Table 1 Optimum reaction conditions for the synthesis of bmimBr, emimBr and NbupyBr using microwave oven



Entry	Alkyl halide (RX)	RX mol	Substrate (S)	S/mol	Power/W (irradiation time)	Water-bath temperature/°C Start	Water-bath temperature/°C End	Yield (%)
1	1-Bromobutane	1.2	mim	1	110 (1 min) + 330 (3 min) × 3	60	80	100[a]
2	1-Bromobutane	0.55	mim	0.5	110 (1 min) + 330 (2 min) × 4	60	80	100[b]
3	1-Bromoethane	1.5	mim	0.5	110 (3 min) + 330 (2 min) × 9	20 60	50 80	96[b]
4	1-Bromobutane	0.55	Pyridine	0.5	330 (1 min) × 18	70	100	93[b]

[a] Reaction was carried out in a 500 mL round bottom flask immersed in 500 ml of water in a 2 L Pyrex beaker. [b] Reactions were carried out in a 250 mL round bottom flask immersed in 850 ml of water in a 1 L Pyrex beaker.

bmimBr was superior to that obtained by the traditional preparation of heating in a solvent (60–80%). The bmimBr thus prepared had been converted to the corresponding tetrafluoroborate salt and used as reaction media for metal-mediated reactions.[16]

The water moderation approach could also be used for the preparation of 3-ethyl-1-methylimidazolium bromide [emimBr] where the more volatile bromoethane was used (entry 3). An excess of the bromide (3 equivalents) was used. The mixture was irradiated for 3 min with 110 W MW power level. The water temperature at this point was within the range 20–50 °C. Most of the ionic liquid was formed at this stage. An increase of power level to 330 W was applied to complete the reaction, with the water temperature ranging from 50 to 80 °C. Reaction between pyridine and 1-bromobutane (entry 4) was comparatively slower than the previous two cases. A more vigorous reaction condition was required (at MW power level: 330 W) leading to a high yield of the product.

The water-moderated microwave solvent-less synthesis is applicable to small scale preparation as well. Thus, a series of ionic liquid precursors was prepared in mmol scale (Table 2). In those cases involving the preparation of polycation salts (Table 2, entries 5–7), the reactions were extremely fast. The mild conditions used appeared to have yielded a purer product by NMR than in the case where higher MW power level was used.[10] 1,2-Dimethylimidazole (dmim) was also successfully alkylated to the corresponding 1,2,3-trialkylated imidazolium halides (Table 2, entries 1 and 2). On the other hand, the solvent-free route was unsuccessful for the preparation of triphenylphosphonium or trialkylammonium salts with or without water moderation using microwaves (Table 2, entries 10–13).

Conclusion

Water moderation was successfully applied to avoid runaway reactions in the large-scale preparation of a number of ionic liquid precursors under solventless conditions using microwave irradiation. The water functions not only as a heat sink, but also reduces the amount of microwave reaching the reaction mixture. Because of the experimental simplicity, the approach

Table 2 Optimum reaction conditions for the synthesis of ionic liquid precusors[a]

Entry	Alkyl halide (RX)	RX/mmol	Substrate (2 mol equiv.)	Power/W (irradiation time)	Water-bath temperature/°C Start	Water-bath temperature/°C End	Yield (%)
1	1-Bromobutane	2.4	1,2-dmim	110 (40 s) × 2 + 330 (40 s) × 3	70 70	78 82	85
2	1,3-Dibromopropane	1	1,2-dmim	110 (50 s) + 330 (50 s)	50 70	59 83	87
3	1-Bromohexane	2.4	mim	110 (60 s) × 2 + 330 (40 s) × 3	50 70	63 84	100
4	1-Iodooctane	2	mim	110 (30 s) + 330 (30 s) × 3	70 70	76 82	100
5	1,3-Dibromopropane	1	mim	110 (30 s) + 330 (30 s)	50 60	66 70	87
6	1,4-Dibromobutane	1	mim	110 (60 s) + 330 (15 s)	50 70	65 76	82
7	1,6-Dibromohexane	1	mim	110 (60 s) + 330 (15 s)	50 70	66 75	85
8	1-Bromohexane	2.2	Pyridine	330 (60 s) × 10	60	79	100
9	1-Iodooctane	2.2	Pyridine	330 (40 s) × 8	60	73	100
10	1-Bromobutane	2.2	Tripropylamine	330 (40 s) × 5	60	73	0
11	1-Bromobutane	2.2	Triethylamine	330 (40 s) × 5	60	74	0
12	1-Bromobutane	2.2	PPh_3	330 (40 s) × 5	60	73	0
13	1-Bromobutane	2.2	1-Methylpyrrolidine	330 (40 s) × 5	60	73	0

[a] All the reactions were carried out in a test tube immersed in 100 ml of water.

may have applications in other microwave-assisted solventless reactions.

Experimental

An unmodified household microwave oven (SHARP R342D M/OVEN 34L 1100W T; microwave frequency 2450 MHz) was used. According to information provided by the supplier, the power level varied linearly with the microwave power output. Thus, the power output was 1100 W at 100% power level, 550 W at 50% level, 330 W at 30% level and 110 W at 10% level, respectively.

The general preparative procedures are illustrated by two examples.

Preparation of 3-butyl-1-methylimidazolium bromide [bmimBr]

A mixture of 1-bromobutane (164.4 g, 1.2 mol) and mim (82.1 g, 1.0 mol) in a 500 mL round bottom flask equipped with a drying tube was placed in a 2 L beaker containing 500 mL of water. The mixture was heated intermittently according to the schedule listed in Table 1 in the microwave oven until the reaction mixture turned to a clear single phase. The reaction mixture should be mixed properly by swirling between intervals. The temperature of the water bath was in the range 60–80 °C during the course of the reaction. The pale yellow oil was then washed with ether (3 × 50 ml) and dried under vacuum at 80 °C to give bmimBr which was essentially pure. ^{1}H NMR (400 MHz; D_2O): 0.76 (3H, t, J = 7.4 Hz), 1.16 (2H, m), 1.69 (2H, m), 3.73 (3H, s), 4.04 (2H, t, J = 7.2 Hz), 7.27 (1H, s), 7.32 (1H, s), 8.56 (1H, s).

Preparation of *N*-butylpyridinium bromide [NbupyBr]

A mixture of 1-bromobutane (75.37 g, 0.55 mol) and pyridine (39.55 g, 0.50 mmol) was placed in a 250 mL round bottom flask equipped with a drying tube and placed in a 1 L beaker containing 850 mL of water. The mixture was heated intermittently in the MW oven at 330 W power level throughout the preparation until the reaction mixture turned to a clear single phase. The bulk temperature of the water bath was in the range 70–100 °C. The oily yellow liquid was then washed with ether (3 × 50 ml) and dried under vacuum at 80 °C to give the essentially pure product. ^{1}H NMR (400 MHz; D_2O): 0.82 (3H, t, J = 7.4 Hz), 1.24 (2H, m), 1.88 (2H, m), 4.50 (2H, t, J = 7.4 Hz), 7.94 (2H, br t, J = 6.8 Hz), 8.42 (1H, t, J = 7.8 Hz), 8.73 (2H, d, J = 6.2 Hz).

Acknowledgments

This work was supported by the Areas of Excellence Scheme established under the University Grants Committee of the Hong Kong Special Administrative Region, China (Project No. AoE/P-10/01). We thank the Hong Kong Polytechnic University for financial support. T. H. C. acknowledges the support of McGill University for the granting of a leave.

References

1 R. Sheldon, *Chem. Commun.*, 2001, 2399.
2 (*a*) A. J. Carmichael, M. J. Earle, J. D. Holbrey, P. B. McCormac and K. R. Seddon, *Org. Lett.*, 1999, **1**, 997; (*b*) J. Howarth and A. Dallas, *Molecules*, 2000, **5**, 851.
3 T. Kitazume and K. Kasai, *Green Chem.*, 2001, **3**, 30.
4 (*a*) G. S. Owens and M. M. Abu-Omar, *Chem Commun.*, 2000, 1165; (*b*) C. Wheeler, K. N. West, C. L. Liotta and C. A. Eckert, *Chem Commun.*, 2001, 887.
5 (*a*) J. S. Wilkes, J. A. Levinsky, R. A. Wilson and C. L. Hussy, *Inorg. Chem*, 1982, **21**, 1263; (*b*) J. Fuller and R. A. Osteryoung, *J. Electrochem. Soc.*, 1997, **144**, 3881; (*c*) J. Fuller, A. C. Breda and R. T. Carlin, *J. Electroanal. Chem.*, 1998, **459**, 29.
6 (*a*) J. G. Huddleston, H. D. Willauer, R. P. Swatloski, A. E. Visser and R. D. Rogers, *Chem Commun.*, 2001, 1765; (*b*) A. Bosmann, L. Datsevich, A. Jess, A. Lauter, C. Schmitz and P. Wasserscheid, *Chem. Commun.*, 2001, 2494.
7 C. Ye, W. Liu, Y. Chen and L. Yu, *Chem. Commun.*, 2001, 2244.
8 (*a*) P. Bonhote, A. P. Dias, N. Papageorgiou, K. Kalyanasundaram and M. Grätzel, *Inorg. Chem.*, 1996, **35**, 1168; (*b*) P. A. Z. Suarez, J. E. L. Dulius, S. Einloft, R. F. de Souza and J. Dupont, *Polyhedron*, 1996, **15**, 1217; (*c*) M. Koel, *Proc. Estonian Acad. Sci. Chem.*, 2000, **493**, 145; (*d*) J. D. Holbrey, K. R. Seddon and R. Wareing, *Green Chem.*, 2001, **3**, 33.
9 (*a*) K. R. Seddon, *J. Chem. Tech. Biotechnol.*, 1997, **68**, 351; (*b*) K. R. Seddon, A. Stark and M. J. Torres, *Pure Appl. Chem.*, 2000, **72**, 2275.
10 R. S. Varma and V. V. Namboodiri, *Chem Commun.*, 2001, 643.
11 G. W. V. Cave, C. L. Raston and J. L. Scott, *Chem. Commun.*, 2001, 2159.
12 R. Pollington, *Chem. Br.*, January 2001, p. 14.
13 (*a*) R. Commarmot, R. Didenot and J. F. Gardais, *Fr. Pat.*, 25560529, 1985 (*Chem. Abstr.*, 1986, **105**, 17442); (*b*) J. F. Dubreuil, J. R. Cherouvrier and J. P. Bazureau, *Green Chem.*, 2000, **2**, 226; (*c*) B. P. Bandgar, L. S. Uppalla and D. S. Kurule, *Green Chem.*, 1999, **1**, 243; (*d*) N. Kuhnert and T. N. Danks, *Green Chem.*, 2001, **3**, 68.
14 (*a*) For recent reviews, see: S. Caddick, *Tetrahedron*, 1995, **51**, 10403; (*b*) A. K. Bose, B. K. Banik, N. Lavlinskaia, M. Jayaraman and M. S. Manhas, *CHEMTECH*, 1997, **27**, 18; (*c*) R. S. Varma, *Green Chem.*, 1999, **1**, 43.
15 (*a*) H. M. Sampath Kumar, B. V. Subba Reddy, E. J. Reddy and J. S. Yadav, *Green Chem.*, 1999, **1**, 141; (*b*) P. C. Andrews, A. C. Peatt and C. L. Raston, *Green Chem.*, 2001, 313.
16 M. C. Law, K. Y. Wong and T. H. Chan, *Green Chem.*, 2002, **4**, 161.

Optimization of supercritical fluid extraction for the separation of hyperforin and adhyperforin in St. John's wort *(Hypericum perforatum L.)*

Mari Mannila, Hakwon Kim,† Carl Isaacson and Chien M. Wai*

Department of Chemistry, University of Idaho, Moscow 83844 Idaho, USA.
E-mail: cwai@uidaho.edu

Received 6th February 2002
First published as an Advance Article on the web 10th June 2002

Supercritical fluid extraction (SFE) with neat CO_2 was optimized for selective removal of hyperforin and adhyperforin from St. John's wort. High extraction efficiencies were achieved when the fluid density was 0.60 g ml^{-1} or above. The maximum extraction efficiency of hyperforin and adhyperforin could be achieved with a very mild condition such as 30 °C and 80 atm (density = 0.64 g ml^{-1}). Under these conditions, the amount of hyperforin extracted was comparable to the results of conventional solvent-based extractions (ultrasonic or boiling). The maximum quantity of hyperforin extracted from the St. John's wort was around 12 mg/g dry plant and the reproducibility of the SFE method was comparatively good (RSD = 10%). Hyperforin and adhyperforin were isolated from the crude SFE extract (using HPLC) with purities of 98.7 and 93.3%, respectively. The identity of the isolated hyperforins was confirmed by NMR and MS methods.

Introduction

The public interest in using herbal extracts and natural products as health remedies has increased dramatically in recent years. For example, the extract of St. John's wort (*Hypericum perforatum L.*) is widely used today in the USA as a treatment of depression and various psychological and neurologic disorders.[1–3] *Hypericum perforatum* is listed in the pharmacopoeias of many European countries including Germany, Poland, Romania and Russia.[4,5] The active compounds having antidepressant activity in St. John's wort are thought to be hypericin,[6–8] hyperforin,[9–11] and possibly flavonoids.[12]

Hyperforin is a major lipophilic constituent in St. John's wort. The extraction of St. John's wort is traditionally performed using organic solvents such as methanol,[13,14] acetone–ethanol,[15] or hexane.[15,16] Conventional solvent extraction methods have inherited drawbacks including lack of selectivity and generation of liquid wastes. Supercritical fluid extraction (SFE) has gained acceptance in recent years as an alternative to conventional solvent extraction for separation of organic compounds in many analytical and industrial processes. Carbon dioxide is widely used in SFE because of its moderate critical constants (T_c = 31 °C and P_c = 73 atm), nontoxic nature, low price, and readily availability in a relatively pure form.

The solvation power of supercritical CO_2 depends on density, which can be tuned by temperature and pressure. Therefore, by optimizing the SFE temperature and pressure, selective extraction of organic compounds is possible. The extracted organic solutes can be easily separated from CO_2 by reduction of pressure, and the CO_2 gas can be recycled for repeated use. The CO_2 used in SFE can be obtained from industrial fermentation processes, and therefore, it does not contribute to the global warming problem. Due to these benefits, SFE is ideal as a green extraction technology for the isolation of lipophilic compounds from herbs.

Hyperforin, a phytonutraceutical in St. John's wort is highly sensitive to light and oxidation. When exposed to light and air, over 90% of the originally extracted hyperforin (in methanol) can decompose in two hours according to one report.[14] However, when hyperforin was protected from light and air and stored under nitrogen (at −20 °C), it can be stable over eight months.[16] According to the literature, hyperforin can be stabilized by addition of a small amount of ascorbic acid (together with citric acid) or by the formation of an inclusion complex with methyl-β-cyclodextrin.[17] Adhyperforin, a homologue of hyperforin (Fig. 1), differs from hyperforin only by

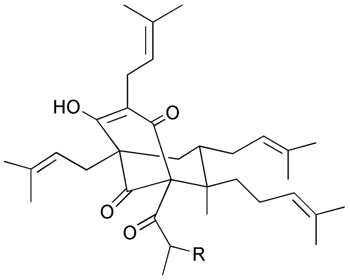


Fig. 1 Structure of hyperforin (R = CH_3) and adhyperforin (R = CH_2CH_3).

Green Context

While we often read of the use of supercritical carbon dioxide as an environmentally benign solvent for organic reactions it is worth remembering that it has a long established use as an extraction medium. This article is an interesting addition to the long list of applications for $scCO_2$. It is used to efficiently and selectively remove some of the active compounds in St John's Wort. Hyperforin, for example, which is believed to have anti-depressant activity is extracted with an efficiency comparable to the best conventional solvent-based extractions. ***JHC***

---

† On leave from Department of Chemistry and Green Nuclear Research Lab., Kyung Hee University, Suwon 449–701, Korea.

DOI: 10.1039/b201363k

having an additional CH_2 group; the isopropyl ketone side chain of hyperforin being replaced by a 2-methyl propyl ketone substituent in adhyperforin.[18] Adhyperforin has shown stability properties similar to hyperforin.[17]

One goal of this study was to optimize the SFE process for the effective and selective separation of hyperforin and adhyperforin from St. John's wort. Other goals were (1) to study the stability of these active compounds, and (2) their isolation as pure products. The effects of temperature, pressure, extraction time and modifier on the efficiency of SFE was studied and the SFE results were compared to the results from solvent-based extraction methods. Hyperforin and adhyperforin were isolated from the crude SFE extract, and the purity and the identification of the isolated compounds were confirmed by chromatographic and spectroscopic techniques.

Results and discussion

Effects of temperature, pressure and density

Using SFE with neat CO_2, hyperforin and adhyperforin were the major compounds in the extract as detected by the HPLC–UV (Fig. 2). The maximum amount of hyperforin extracted by the SFE process from the St. John's wort sample was around 12 mg g^{-1}. Fig. 3 shows the effect of temperature on SFE efficiencies of hyperforin and adhyperforin using neat CO_2 at 100 and at 300 atm. At 100 atm, the extraction efficiency of hyperforin decreased significantly as the temperature was increased over 50 °C, whereas at 300 atm the extraction efficiency was maintained relatively high even at a temperature of 90 °C. This is attributed to the decrease in the fluid density (from 0.64 to 0.27 g ml^{-1}) when the temperature is increased (from 40 to 60 °C) at a low pressure (100 atm). At a higher pressure (300 atm), the fluid density is still high even at 90 °C (0.71 g ml^{-1}) and thus the extraction efficiency was maintained nearly constant. At 100 atm, a high extraction efficiency of hyperforin was achieved even at 30 °C (density 0.79 g ml^{-1}) which was below the critical point of the CO_2. Near the critical point, the property of liquid CO_2 probably is close to that of the supercritical state because the change from liquid to supercritical fluid is known to extend over a small temperature range (several degrees). However 40 °C was chosen for a detail study of pressure effect, since this temperature is still very low and the fluid is in a supercritical state.

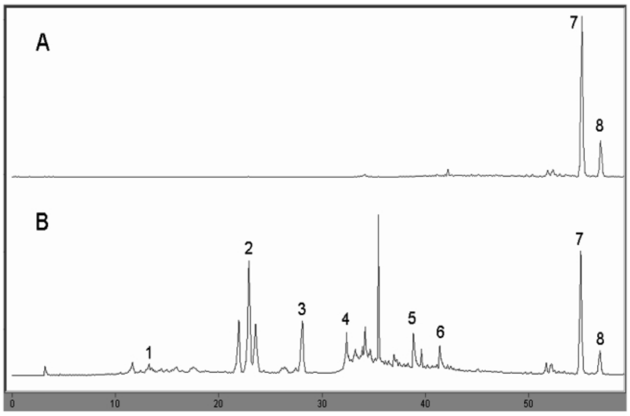


Fig. 2 HPLC chromatograms of extract of St. John's wort by (A) SFE with neat CO_2 (40 °C, 100 atm), and (B) ultrasonic extraction with methanol. Peak 1: chlorogenic acid; 2; rutin; 3: quercitrin; 4: quercetin; 5: pseudohypericin; 6: hypericin; 7: hyperforin; 8: adhyperforin (HPLC conditions are described in the text).

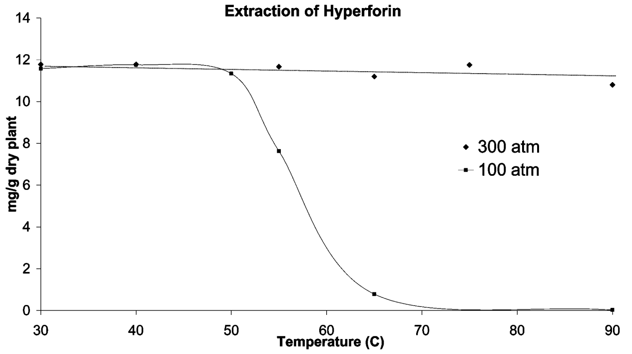


Fig. 3 Effect of temperature and pressure on the SFE efficiency of hyperforin in St. John's wort with neat CO_2 (15 min static and 20 min dynamic mode).

At 40 °C, decreasing the pressure (density) from 100 atm (0.64 g ml^{-1}) to 90 atm (0.51 g ml^{-1}) slightly lowered the extraction efficiency of hyperforin (Fig. 4). Further pressure decrease to 80 atm (lowering the density to 0.30 g ml^{-1}) resulted in less than 50% of the maximum amount of hyperforin extracted from the sample. The results indicate that extraction of hyperforin by SFE depends strongly on the fluid density. The maximum extraction efficiency of hyperforin was achieved when the fluid density was at least 0.60 g ml^{-1} or higher (Fig. 4). At 40 °C, this density was achieved with a pressure of 100 atm.

Increasing the extraction temperature has been reported to improve the SFE efficiency for several organic compounds, including certain natural products from plant matrices.[19,20] However, in the case of SFE of hyperforin from St. John's wort, an increase in extraction temperature (at a fixed density of 0.65 g ml^{-1}) did not show any observable improvement in the extraction efficiency. Maximum extraction was achieved even at as mild conditions as 30 °C and 80 atm. Using mild conditions for extraction of natural products have several advantages including technical convenience, reduced extraction of undesirable products, and minimizing the risk of hyperforin decomposition during extraction.

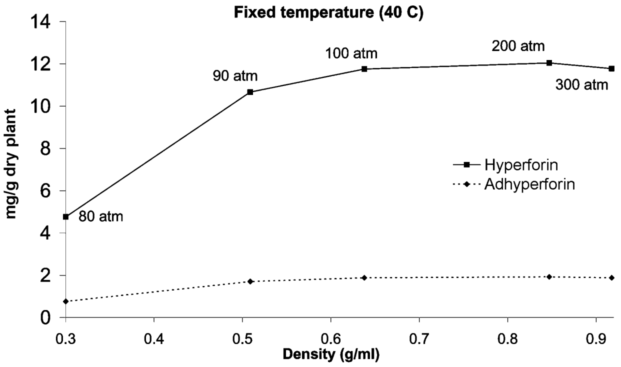


Fig. 4 Effect of pressure and density on the SFE efficiency of hyperforin in St. John's wort at 40 °C with neat CO_2 (15 min static and 20 min dynamic mode).

Extraction time

SFE (at 40 °C and 100 atm) of St. John's wort using a short extraction time (such as 5 min static and 7 min dynamic extraction time, 20 ml CO_2) gave the same result as a longer extraction time (30 min static followed with 20 min dynamic extraction). However, when the same sample was re-extracted, about 10% of the hyperforin detected in the first extraction was detected in the second extraction. Neither extending the extraction time (up to 30 min static) nor increasing the consumption of CO_2 (20 min dynamic time) improved the extraction efficiency towards the retained 10% of the hyperforin. However this retained hyperforin could be removed in a second extraction when the sample was depressurized after first extraction. After the first extraction step (5 min static followed with 7 min dynamic extraction) and depressurization of the sample, only 7 min of dynamic time (10 ml CO_2) was required to remove the remaining hyperforin in the sample.

Depressurization of the plant sample apparently improved the extraction of the remaining hyperforin. It is possible that depressurization breaks or alters the plant cell and thus improves the extraction. If this is the case, the St. John's wort may contain two different bonding sites for hyperforin. In the first bonding site hyperforin is weakly bound in the plant tissue and can be easily extracted by supercritical CO_2. The other bonding site of hyperforin appears to be located in the deeper parts of the tissue. Therefore a pressure change is required to break the plant tissue to comminute the compound to facilitate SFE. Effective SFE of hyperforin from St. John's wort (300 mg dry plant) was achieved with 5 min static extraction, followed by two 7 min dynamic extraction (total of 20 ml CO_2), with a depressurization step between the two dynamic modes.

Effect of modifier

The addition of a modifier to the supercritical CO_2 (at 40 °C and 100 atm) did not improve the extraction efficiency of hyperforin and adhyperforin, but did cause the extraction of some more polar compounds (such as rutin, quercitrin and quercetin) from the plant matrix (Table 1). As the polarity of the modifier was increased, higher concentrations of these polar compounds were detected in the crude extract. When hexane was used as a modifier, only hyperforin and adhyperforin were detected in the crude extract by HPLC, whereas modifiers like 2-propanol, ethanol and methanol resulted in the extraction of more polar compounds. With methanol-modified CO_2, the amount of quercitrin and rutin extracted was ten times higher than that of 2-propanol modified CO_2. However, the very polar compounds identified in this study such as chlorogenic acid and hypericin were not extracted with SFE even when methanol was used as a modifier. These compounds are probably more strongly bound in the plant matrix.[14]

Solvent-based extraction methods

Ultrasound-aided extraction and boiling solvent methods showed similar results to SFE for the extraction of hyperforin and adhyperforin (Table 1). Extraction with hexane showed similar selectivity for hyperforin and adhyperforin as SFE using neat CO_2. Ultrasound-aided extraction at room temperature with methanol or ethanol showed the highest concentrations of co-extracted compounds, especially rutin. Overall, the concentrations of co-extracted polar compounds were significantly higher with solvent-based methods than with modified supercritical CO_2 extraction. The extracted quantities of rutin, queritrin and quercetin were two to five times higher with ultrasonic or boiling solvent methods than with modified SFE. Furthermore, some polar compounds such as chlorogenic acid that were not found in SFE extracts were detected in the solvent-based extracts. Also, hypericin and pseudohypericin were detected in ultrasonic extracts of ethanol and methanol (confirmed by HPLC–UV analysis at 580 nm).

Compared to the solvent-based extraction methods, the SFE with neat CO_2 showed identical separation efficiency and higher selectivity in the extraction of hyperforin and adhyperforin in St. John's wort (Table 1, Fig. 2). To study the reproducibility of the SFE of the hyperforins, the sample extraction was performed as four replicates at 40 °C and 100 atm with neat CO_2. The relative standard deviation for hyperforin was 10% and for adhyperforin 11%.

Isolation and identification of hyperforin and adhyperforin

To evaluate the possibility of developing a SFE method for a larger scale production of hyperforin and adhyperforin, SFE (at 40 °C and 100 atm) of St. John's wort was performed with 10 g of dry plant. The extraction resulted in a 250 mg of yellow oily material, where the amount of hyperforin was about 70 mg and adhyperforin about 25 mg (analyzed by HPLC). All the extracted material was soluble in hexane but in methanol a precipitation of a white solid material occurred.

The ^1H NMR analysis (in deuterated chloroform) of the precipitate (separated from the SFE extract that was dissolved in methanol using a Whatman 1.0 μm filter) showed only a few peaks far on the upfield region (around 0.5–1.5 ppm). Because no peaks were observed in the downfield region, these compounds may be some simple hydrocarbons, such as waxes or cellulose, which have been considered as typical components of the plant matrix. Precipitation of these compounds was observed also in ethanol but in a lower quantity than in methanol. Because the precipitation was increased as the polarity of the solvent was increased, these precipitates were clearly some very unpolar compounds, which are immiscible in polar solvent and were not detectable by HPLC–UV. To achieve the most efficient separation of the co-extracted compounds and purity of hyperforin, methanol was used as a solvent for the crude SFE extract in further experiments.

To investigate the possibility of isolating pure hyperforin and adhyperforin from the crude SFE extract, a small-scale separation was performed by an analytical HPLC instrument. Evaporation of the solvent from the isolated hyperforin and

Table 1 Extracted amounts (mg/g dry weight) of hyperforins, hypericin and some flavonoids in St. John's wort obtained by SFE (40 °C and 100 atm) and solvent based methods (ultrasonic and heating)

Extraction Method	Extracted analyte (mg/g dry plant)							
	Solvent/modifier	Hyperforin	Adhyperforin	Hypericin	Quercetin	Quercitrin	Rutin	Chlorogenic acid
SFE	Neat CO_2	12.4[a]	2.0[a]	—	—	—	—	—
Modified CO_2	Hexane	12.0	1.9	—	—	—	—	—
	2-Propanol	12.7	2.0	—	0.1	0.1	0.5	—
	Ethanol	10.5	1.7	—	0.3	0.4	1.6	—
	Methanol	12.9	2.0	—	0.5	1.0	5.4	—
Boiling	Hexane	9.4	1.5	—	—	—	—	—
	Ethanol	12.6	1.8	0.2	1.0	1.4	6.6	0.7
	Methanol	11.1	1.6	0.2	1.0	3.1	13.2	1.2
Ultrasonic	Hexane	10.0	1.6	—	—	—	—	—
	Ethanol	12.0	1.8	0.2	1.9	4.7	25.8	1.4
	Methanol	11.3	1.8	0.3	1.8	4.8	22.8	1.5

[a] Average of four replicates.

adhyperforin gave in both cases a colorless oily residue, which is the appearance of hyperforin, as well as the oxidation products of hyperforin.[21–23] HPLC analysis of the separated compounds showed a purity of 98.7% for hyperforin and 93.3% for adhyperforin. TLC analysis showed that the R_F of hyperforin was 0.49 in an ethyl acetate–hexane (1 : 5 v/v) eluent, which was identical to that of the hyperforin standard. Adhyperforin's spot was observed slightly above hyperforin and is consistent with a previous publication.[18] In both samples, no additional spots were observed by TLC, which confirmed the purity of the sample.

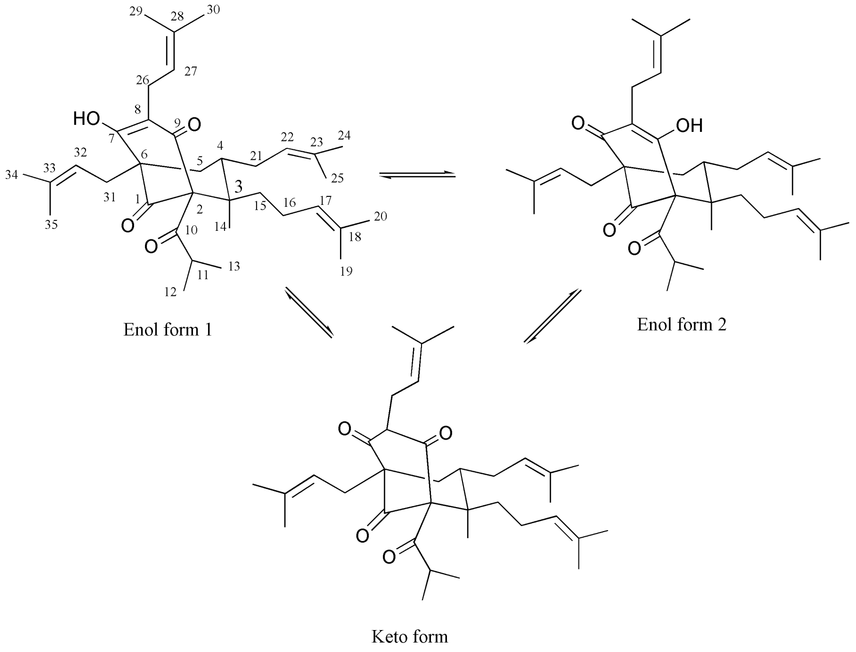
Compound identity was further confirmed by EI-HRMS (high-resolution mass spectrometer with electron ionisation) in comparison with the literature data.[13,18] The observed molecular peak for hyperforin was at *m/z* 536.4 that corresponded well to the calculated molecular weight of hyperforin. Theoretical ion distribution gave the formula of $C_{35}H_{52}O_4$ for hyperforin. The main fractions were 468 ($M - C_5H_9$), 426 ($M - C_5H_9 - C_3H_6$), 357 ($M - C_3H_7 - C_5H_8 - C_5H_8$), 332 ($M - C_5H_9 - C_3H_6$), and 69 ($C_5H_8$). The observed molecular peak for adhyperforin was shown at 550.4, which as well corresponded well to the calculated molecular weight of adhyperforin. The fractions were 482 ($M - C_5H_9$), 426 ($M - C_4H_9 - C_5H_8$), 357 ($M - C_4H_9 - C_5H_8 - C_5H_8$) and 69 ($M - C_5H_9$). The molecular formula obtained from theoretical ion distribution was $C_{36}H_{54}O_4$, showing an additional CH_2 group of adhyperforin compared to hyperforin.

^{1}H NMR studies were performed in chloroform-d, acetone-d_6, and methanol-d_4. In each solvent the observed hyperforin and adhyperforin peaks were identical to the literature data,[16,18,24] but in chloroform some additional peaks (around 7 ppm) were observed that have not been reported before. Furthermore, the ^{1}H NMR spectrum of hyperforin in chloroform-d showed comparatively broad peaks due to the tautomerization and regioisomerism of the hyperforins (Fig. 5). The ^{1}H NMR spectra of hyperforin obtained in acetone-d_6 and methanol-d_4 showed sharper peaks and the lack of the downfield peaks (at 7.00–7.50 ppm) compared to that of chloroform-d_6. Most probably the additional peaks observed in chloroform-d_6 (at 7.00–7.50 ppm) are the protons from enolic OH groups, which may have been de-shielded by other oxygen groups (located in carbons 1 and 9) in the hyperforin molecule (Fig. 5), and are thus observed further downfield. This phenomenon (chemical shift) has been observed earlier with structurally similar molecules.[25,26] In acetone-d_6 or methanol-d_4 the solvent probably interacts with the enolic OH of hyperforin, and thus the upfield proton was not observed. Furthermore, this interaction seems to block the structure of the hyperforin to favor a certain tautomeric form, which explains the sharper peaks observed in acetone-d_6 and methanol-d_4 than in chloroform-d. In the previous NMR data for hyperforin, the ^{1}H-NMR analysis was done in methanol[16] and thus enolic protons were not observed. The ^{1}H NMR analysis by Ruecker *et al.*[24] was made in chloroform, however the compound was not pure hyperforin but hydroperoxycadiforin, which in addition to the hyperforin skeleton has a C_{15}-skeleton of cadinene. In hydroperoxycadiforin the cadinene skeleton is bound to the carbon 8 of hyperforin, and thus the structure of hyperforin is blocked to a keto form (Fig. 5) and the enolic protons could not be observed.

To further study the effect of tautomerization on the ^{1}H NMR spectrum two derivatization reactions were performed to simplify the structure of hyperforin by removing the tautomerization of the hyperforin. Crude SFE extract was treated with (1) MOM–Cl (CH_3OCH_2Cl) and (2) benzoyl chloride (C_6H_4Cl) to convert the enolic OH group to (1) O–MOM and (2) an O-benzoylated group of hyperforin. The ^{1}H NMR spectra of the derivatized hyperforin did not show the downfield peaks (in chloroform-d), and the peaks were clearly sharper than those obtained from the same sample before the derivatization. After deprotecting the sample back to the hyperforin, the additional peaks (around 7 ppm) were observed again and the peak shapes were returned back to the broader shapes. These data confirmed the previous explanation of the tautomeric effect on the appearance of the enolic OH as well as the peak sharpness in the ^{1}H NMR spectra of hyperforin.

Purity and stability of the crude SFE extract

The purity of the crude SFE extract was analyzed by HPLC, ^{1}H NMR (in chloroform-d and methanol-d_4) and TLC, and the results were compared to those obtained from isolated hyperforin and adhyperforin. The purity of hyperforin and adhyperforin in the crude extract obtained by HPLC was 85% (69% hyperforin and 16% adhyperforin). A ^{1}H NMR spectrum was identical to that of hyperforin and adhyperforin. TLC analysis showed strong spots of hyperforin and adhyperforin,



Enol form 1

Enol form 2

Keto form

Fig. 5 Tautomerization of hyperforin; two enolic forms and a keto form.

and only few light spots below hyperforin. These results show that SFE with neat CO_2 under mild conditions gives a comparatively pure mixture of hyperforin and adhyperforin.

The crude sample extract was stable over an extended period of time in methanol (with or without 0.01% ascorbic acid). Hyperforin and adhyperforin have been reported to undergo decomposition almost completely (over 90%) in methanol when exposed to light and air for 2 h after silica gel purification.[14] When the crude SFE extract was dissolved in pure methanol or in methanol with 0.01% ascorbic acid, after 80 h of exposure to direct daylight and air, no decomposition of hyperforin and adhyperforin was observed (by HPLC) in this study. Concentration of St. John's wort extract in an organic solvent was shown to be one of the main sources for peroxide formation, which led to the oxidation and decomposition of hyperforin.[16] During SFE, hyperforin can be trapped in an empty vial and there is no need for evaporation of the solvent after extraction. Furthermore, in the crude SFE extract, some impurities may protect the hyperforin from oxidation, and probably the SFE procedure may inhibit peroxide formation. Because the isolation of pure hyperforin and adhyperforin from SFE extract is possible with minimum sample treatment, the decomposition of the hyperforin can be minimized. This study clearly indicates that extraction of St. John's wort by neat CO_2 under mild conditions gives a fairly enriched mixture of hyperforin and adhyperforin with good stability.

Experimental

Samples and standards

A homogenized dry St. John's wort sample for optimization studies was obtained from the International Nutritional Laboratories (Lolo, Montana, USA). The plant material for a larger scale extraction was collected from Coeur d'Alene, Idaho. The plant was air-dried and homogenized by a mill. Glorogenic acid, rutin, luteolin, quercetin, quercitrin and hypericin standards were purchased from Sigma and hyperforin from ChromaDex. All standards were dissolved in methanol. Luteolin was used as an internal standard for HPLC analysis. Adhyperforin was detected using published data of HPLC chromatograms and retention times relative to hyperforin.[13,14,27]

SFE Procedure

Supercritical fluid extractions were performed with an ISCO (Lincoln, NB) syringe pump (model 260D) connected to a stainless steel extraction vessel placed in a Varian 3400 oven. A stainless steel capillary tubing was connected to the outlet of the extraction vessel and inserted into a glass collection vial that contained a trapping solution outside the oven. The flow rate of the fluid was controlled by a manual valve. Carbon dioxide (99.99% purity) was obtained from Oxarc (Spokane, WA).

One gram of washed sea sand (Fisher Scientific, NJ) was placed in the bottom of the extraction vessel (3.45 ml, Keystone, USA) to fill the void volume of the vessel. On top of the sand was added 300 mg of a dry St. John's wort sample (International Nutritional Laboratories, Montana). Samples were extracted with different temperatures (30–90 °C) and pressures (80–300 atm), varying one parameter at a time. The effect of four different modifiers: methanol, ethanol, 2-propanol and hexane, was studied at 40 °C and 100 atm. Modifier (1.5 ml) was added on top of the weighed plant in the vessel. In most of the SFE experiments, the static extraction time was 15 min followed by 20 min dynamic flushing with a flow rate of about 1.5 ml min^{-1}. Different static times and dynamic times were studied at 40 °C and 100 atm. Ethanol (2 ml) was used as a trapping solvent. After SFE, the extraction system was rinsed with 5 ml of ethanol to remove all the compounds precipitated in the extractor and the connecting lines. The wash solution was added to the trapping solution and the whole crude extract (about 6 ml) was filtered through a PTFE (polytetrafluoroethylene) syringe filter (0.45 μm, Acrodisc 13 CR, Gelman). The filtrate (200 μl) was prepared for the HPLC analysis by adding 100 μl of an internal standard (luteolin, 430 μg ml^{-1}) to the sample.

A larger scale extraction of hyperforin was performed at 40 °C and 100 atm using 10 g of a dry plant (Coeur dAlene, Idaho) in a 50 ml extraction vessel. The static extraction time was 30 min and the flow rate during 20 min dynamic time was about 15 ml min^{-1}. The extracted compounds were trapped in an empty vial. The solubility of the extract was studied by dissolving three 12 mg aliquots of the extract in 1 ml of methanol, ethanol and hexane.

Solvent extraction procedure

The extraction efficiency of three solvents (methanol, ethanol and hexane) was investigated using boiling solvent and with ultrasonication (at ambient temperature) Ultrason-aided extraction was performed by extracting a dry plant (300 mg) twice in 20 ml of the solvent for 30 min. The boiling solvent method was otherwise identical but the extraction time was 15 min. After extraction, the crude sample extract was filtered through a PTFE syringe filter and 400 μl of the filtered extract was prepared for analysis by adding 100 μl of the internal standard (luteolin, 430 ppm) to the sample.

HPLC and spectroscopic analysis

Samples were analyzed by a HPLC (Varian Vista 5500) connected to a UV-200 detector. The injection volume was 40 μl. A Supelcosil LC-18-DB column (25 cm × 4.6 mm, 5 μm, Supelco, US) connected to a Superguard LC-18-DB (2 cm × 4.6 mm, 5 μm, Supelco, US) guard column were used for separation of compounds at a temperature of 30 °C. The solvent gradient system was modified from the previous publication[13] using three solvents: A = water + 85% phosphoric acid (99.7 : 0.3 v/v); B = acetonitrile; and C = methanol. The solvent gradient program was the following: initial, 100% A; at 5 min, 85% A and 15% B; at 25 min, 70% A, 20% B, 10% C; at 35 min, 10% A, 75% B, 15% C; at 50 min, 5% A, 80% B, 15% C, which was retained until 60 min. The flow rate of the mobile phase was 1.0 ml min^{-1} and the peaks were detected at 270 nm. Concentrations of the detected compounds were calculated by comparing the peak area of the individual analyte to that of the internal standard (luteolin) spiked in the sample. The result was corrected with a response factor that was obtained from the analysis of a reference solution (made of standards with known concentrations).

Hyperforin and adhyperforin were isolated from the crude SFE extract (12 mg subsample of large scale extract) by an isocratic HPLC method using acetonitrile–water + 85% phosphoric acid (99.7 : 0.3 v/v) as a mobile phase with a flow rate of 1.0 ml min^{-1}. Hyperforin was collected at a retention time of 10.0–11.5 min and adhyperforin at 12.0–12.5 min. Separated fractions of ten (40 μl) injections were combined and the solvent was evaporated in a N_2 stream.

Thin layer chromatography (TLC) was performed on a siliga gel 60 F254 using ethyl acetate–hexane (1:5 v/v) as a mobile phase. The sample detection was performed by an ultraviolet absorbance and enhanced by spraying with phosphomolybdic acid (20 wt%) in ethanol.

The identification of the samples was performed by ^1H NMR (AMX 300 Bruker, USA) in chloroform-d, acetone-d_6 and methanol-d_4, and by EI-HRMS (JMS-AX505HA JEOL, MA, USA) by a direct probe injection at 60 eV.

Acknowledgement

This material is based upon the work partially supported by the National Science Foundation under Grant no.0097833. The authors would like to thank the International Nutritional Laboratory (Lolo, Montana) and Mr Robert Flagor for providing the plant materials.

References

1 K. Linde, G. Ramirez, C. D. Mulrow, A. Pauls, W. Weidenhammer and D. Melchart, *Br. Med. J.*, 1996, **313**, 253.
2 S. G. Rao, A. U. Laximanarayana, L. U. Saraswathi, G. M. Padma, R. Ganesh and D. R. Kulkarni, *Fitoterapia*, 1991, **6**, 508.
3 A. R. Vickery, *Econ. Bot.*, 1981, 289.
4 C. Hobbs, *Herbal Gram.*, 1989, **18/19**, 24.
5 J. Reynolds, Martindale, *The Extra Pharmacopoeia*, The Pharmaceutical Press, London, 30th edn., 1993.
6 G. Lavie, Y. Mazur, D. Lavie and D. Meruelo, *Med. Res. Rev.*, 1995, **15**, 111.
7 N. D. Weber, B. K. Murray, and J. A. North and S. G. Wood, *Antiviral Chem. Chemother.*, 1994, **5**, 83.
8 D. Meruelo, G. Lavie and D. Lavie, *Proc. Natl. Acad. Sci. USA*, 1988, **85**, 5230.
9 A. Singer, M. Wonnemann and W. E. Muller, *Pharmacol. Exp. Ther.*, 1999, **290**, 1363.
10 S. S. Chatterjee, S. K. Bhattacharya, M. Wonnemann, A. Singer and W. E. Muller, *Life Sci.*, 1998, **63**, 499.
11 G. Laakmann, A. Dienel and M. Kieser, *Phytomedicine*, 1998, **5**, 435.
12 T. B. Ng, F. Liu and Z. T. Wang, *Life Sci.*, 2000, **66**, 709.
13 M. Brolis, B. Gabetta, R. Fuzzatti, R. Pace, F. Panzeri and F. Peterlongo, *J. Chromatogr. A*, 1998, **825**, 9.
14 D. G. Gray, G. E. Rottinghaus, H. E. G. Garrett and S. G. Pallardy, *J. AOAC Int.*, 2000, **83**, 944.
15 F. L. Liu, J. C. Y. W. Ang and D. Springer, *Agric. Food Chem.*, 2000, **48**, 3364.
16 H. C. J. Orth, C. Rentel and P. C. Schmidt, *J. Pharm. Pharmacol.*, 1999, **51**, 193.
17 H. C. J. Orth and P. C. Schmidt, *Pharm. Ind.*, 2000, **62**, 61.
18 P. Maisenbacher and K. A. Kovar, *Planta Med.*, 1992, **58**, 291.
19 Y. Yang, A. Ghairabeh, S. B. Hawthorne and D. J. Miller, *Anal. Chem.*, 1995, **67**, 641.
20 Q. Lang, Ph.D. Dissertation, ch. 4, University of Idaho, Idaho. USA, 1999.
21 L. Verotta, G. Appendino, E. Appendino, J. Jakupovic and E. Bombardelli, *J. Nat. Prod.*, 1999, **62**, 770.
22 L. Verotta, G. Appendino, J. Jakupovic and E. Bombardelli, *J. Nat. Prod.*, 2000, **63**, 412.
23 M. De Shan, L. H. Hu and Z. L. Chen, *J. Nat. Prod.*, 2001, **64**, 127.
24 G. Rœcker, D. Manns., R. Hartmann and U. Bonsels, *Arch. Pharm.*, 1995, **328**, 725.
25 D. Joseph, M.-J. Queiroz and G. Kirsch, *Oppi Briefs*, 1995, **27**, 449.
26 A. Rojas, A. Perez-Encabo, I. Herraiz-Sierra and C. A. Blanco, *Can. J. Chem.*, 2001, **79**, 448.
27 P. Mauri and P. Pietta, *Rapid Commun. Mass Spectrom.*, 2000, **14**, 95.

Facile conversion of oxathioacetals to carbonyl compounds

Subhash P. Chavan,* Shubhada W. Dantale, K. Pasupathy, R. B. Tejwani, Subhash K. Kamat and T. Ravindranathan

Division of Organic Chemistry, Technology National Chemical Laboratory, Pune 411008, India. E-mail: spchavan@dalton.ncl.res.in

Received 21st January 2002
First published as an Advance Article on the web 30th May 2002

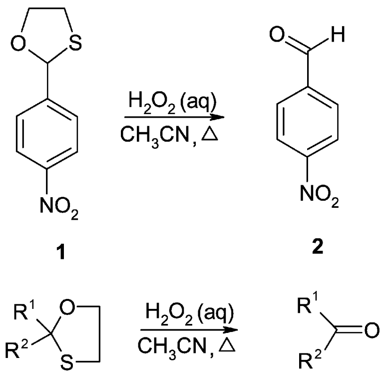
A facile deprotection of oxathiolanes mediated by H_2O_2 is described.

Selective protection and deprotection is the heart and soul of synthetic organic chemistry. Protection of carbonyls as oxathiolanes has been already recognized because of their stability towards various acidic and nucleophilic reagents and ability to form acyl anion equivalents.[1] however it is their deprotection to unmask the carbonyl compounds which attains utmost importance and is of prime concern for lack of general and efficient methods. Some of the conventional methods employed to effect the above conversion require the use of stoichiometric amounts of oxidants,[2,3] refluxing with Raney Nickel,[4] which is often marred with side reactions. Thus the conventional methods are expensive reagents are not easily available. Secondly conventional methods make use of heavy metal based reagents, which adds to the problems of waste disposal.

We have introduced *p*-nitrobenzaldehyde/TMSOTf (cat) as an affective, selective, mild and efficient reagent for deprotection of thioacetals and oxithioacetals.[5] Our interest in selective deprotection has led to development of polymer-supported nitrobenzaldehyde.[6] Our protocol involves 1:1 exchange of oxathiolane under catalytic conditions. Although oxathiolanes are efficiently deprotected to their corresponding carbonyls, one mole of *p*-nitrobenzaldehyde oxathiolane is generated as the by-product in our protocol.

In a quest for an even more attractive and efficient method, we explored a reagent which should be such that it should be commercially available, nonhazardous and nonpolluting. H_2O_2 was the obvious reagent of choice as its usage is accompanied by generation of water as byproduct. This aspect becomes highly desirable in the present era of global awareness of developing environmentally benign technologies. This communication describes the use of H_2O_2 as an efficient oxidant in conversion of oxithioacetals to corresponding carbonyl compounds (Scheme 1) without the aid of any catalyst. Thus when **1** was subjected to treatment with 30% H_2O_2 it was cleanly transformed to *p*-nitrobenzaldehyde in 71% yield. This result may be contrasted with the results of Otera and coworkers[3*d*] where additional oxidant SeO_2 in stoichiometric amounts is required for deprotection of activated oxathiolanes. In order to compare the utility of our method we decided to convert **1** to *p*-nitrobenzaldehyde **2** by the literature reported procedure. Nishada *et al.*[3*e*] have described a very mild reagent *viz.* Ag^+/I_2 combination for deprotection of oxathiolanes. Thus when **1** was treated with $AgNO_3/I_2$, **2** was obtained in 71%. It is obvious that our method compares well with Nishida's conditions not only in terms of yields; moreover it does not involve the use of stoichiometric amount of expensive reagents. Our method may be compared and contrasted with CAN oxidation (61%) or the Raney Nickel procedure (complex mixture), which led to poorer yields of **2**. On comparison of our method with the conventional CAN mediated oxidative deprotection as well as Raney Nickel mediated removal of oxathiol, the superiority of our method over the existing methods become obvious. In order to establish the generality, scope and limitations of our methodology we screened a variety of oxathiolanes (Table 1). It is evident from Table 1 that this protocol works well with a variety of functionalised oxatiolanes. It should be pointed out that thioacetals react less efficiently under these conditions. Efforts are underway to develop a catalyst system to increase the efficiency of this transformation.

Under the similar experimental conditions acetal **3** (Scheme 2) also underwent facile deprotection to acetophenone. This can be attributed to the acidic nature of the commercially available 30% H_2O_2 employed (pH = 2.79). The acetal **3** was getting cleaved under acidic conditions was ascertained by performing the reaction at pH 7.05. Thus when the pH of the 30% H_2O_2 employed was adjusted to pH 7.05 acetal **3** did not undergo deprotection to acetophenone. However, under this reaction condition (pH = 7.05), oxathioacetal **5** was readily converted to



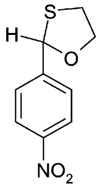
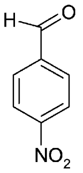
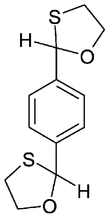
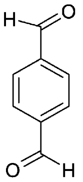
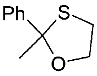
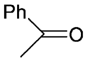
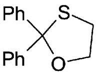
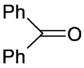
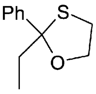
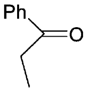
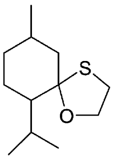
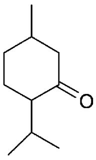
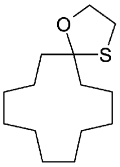
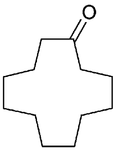
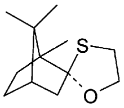
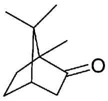
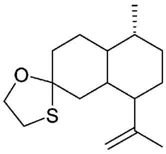
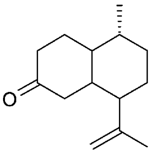
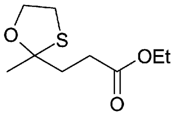
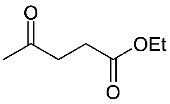
Scheme 1

Green Context

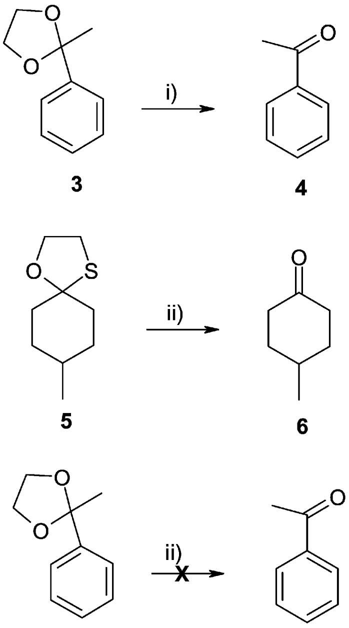
While we should try to reduce the use of protection processes in organic synthesis, protection and deprotection remain important synthetic transformations. Where this is necessary we must strive to simplify the processes, minimise the added weight of protecting group, and minimise waste throughout. Carbonyls are well protected as oxathiolanes because of their stability to various conditions and they do not represent a very large molecular weight addition. However, we must avoid traditional deprotection methods that are based on toxic, expensive or polluting reagents. Here, the effective use of hydrogen peroxide as a cheap and benign deprotecting agent is described. *JHC*

DOI: 10.1039/b200754c

Table 1 Facile conversion of oxathioacetals to carbonyl compounds

Entry	Oxathiolane	Carbonyl	Time/h	Yield (%)
1			2.5	71
2			4	78
3			6	84
4			3	100
5			6	80
6			2	92
7			4	89
8			8	85
9			1.5	81
10			1.5	80

the corresponding carbonyl compound **6** in 90% yield. In conclusion we have demonstrated that oxathiolanes can be readily converted to the corresponding carbonyl compound by simply refluxing it with 30% H_2O_2. Superiority of our methodology is obvious as compared to conventional existing methods of deprotection of oxathiolanes by virtue of the ease of operation, non-polluting nature of reagent and, most importantly, the price of the reagent. Commercial availabity of 30% H_2O_2 and its already well established usage in industry as an oxidant by virtue of its harmless byproduct formation *viz.* water should make this method a highly desirable one ever the conventional oxidative /alkylative methodologies involving stoichiometric quantities of heavy metals.



Scheme 2 *Reagents and conditions*: i, 30% H_2O_2 (1.5 equiv.), CH_3CN, reflux, 2 h, 95%; ii, 30% H_2O_2 (1.5 equiv.), pH = 7.05, reflux, 2 h, 90%.

Typical procedure

To a solution of benzophenone oxathiolane (5.3 g, 0.021 mmol) in distilled acetonitrile (50 ml) was added 30% aqueous H_2O_2 (1.2 ml, 1.5 equiv.) and the mixture was heated at 90–100 °C (bath temp) with stirring. Reaction was monitored by TLC. After completion of the reaction, acetonitrile was removed under reduced pressure and the crude product, benzophenone, was purified by flash chromatography using 5% ethyl acetate–95% light petroleum (bp 60–80 °C) as eluent to give benzophenone in quantitative yield.(3.97 g).

Acknowledgements

S. W. D. and K. P. are thankful to CSIR, India for financial support.

Notes and references

1 (*a*) J. E. Lynch and E. L. Eliel, *J. Am. Chem. Soc.*, 1984, **106**, 2937–2942; (*b*) E. L. Eliel and S. S. Morris Natsche, *J. Am. Chem. Soc.*, 1984, **106**, 2943–2948.

2 H. Perrier, G. Huyer and R. N. Young, *Tetrahedron Lett.*, 1992, **33**, 725–728.

3 (*a*) D. H. R. Barton, P. D. Magnus, G. Smith and D. Zurr, *J. Chem. Soc., Perkin Trans. 1*, 1972, 542–554; (*b*) K. Fuji, K. Ichikawa and E. Fujita, *Tetrahedron Lett.*, 1978, **38**, 3561–3562; (*c*) D. W. Emerson and H. Wynberg, *Tetrahedron Lett.*, 1971, 3445–3448; (*d*) T. Mandai, T. Takeshita, M. Kawada and J. Otera, *Chem. Lett.*, 1984, 1259–1260; (*e*) K. Nishide, K. Yakota, D. Nakamura, T. Sumiya, M. Node, M. Veda and K. Fuji, *Tetrahedron Lett.*, 1993, **34**, 3425–3428.

4 J. Romo, G. Rosenkranz and C. Djerasi, *J. Am. Chem. Soc.*, 1951, **73**, 4961–4964.

5 (*a*) T. Ravindranathan, S. P. Chavan, R. B. Tejwani and J. P. Varghese, *J. Chem. Soc., Chem. Commun.*, 1991, 1750–51; (*b*) T. Ravindranathan, S. P. Chavan, R. B. Tejwani, J. P. Varghese and S. W. Dantale, *J. Chem. Soc., Chem. Commun.*, 1994, 1937–38.

6 T. Ravindranathan, S. P. Chavan and M. M. Awachat, *Tetrahedron Lett.*, 1994, **35**, 8895.

7 1-Methyl-4-propenyl-6-one decahydronaphthalene (Table 1, entry 9): yield: 81%, IR (neat, cm^{-1}): 900, 950, 1050, 1180, 1200, 1250, 1450, 1650, 1710, 2850. ^1H NMR (200 MHz, $CDCl_3$), δ 1.0 (d, 3H), 1.5 (s, 3H), 1.7–2.5 (m, 14H), 4.8 (d, 2H). Mass (*m/z*): 206 (M^+, 15), 123 (30), 107 (35), 95 (18), 91 (25), 82 (20), 77 (50), 67 (47), 55 (100). Ethyl levulinate (Table 1, entry 10): bp 93–94 °C/18 mm Hg, yield: 80%, IR (neat, cm^{-1}): 680, 750, 1220, 1420, 1710, 2890, 3020. ^1H NMR (80 MHz, $CDCl_3$), δ 1.0 (t, 3H), 2.0 (s, 3H), 2.4 (m, 4H), 3.7 (q, 2H).

Synthesis of 1,3,5-triazines in solvent-free conditions catalysed by silica-supported lewis acids

Angel Díaz-Ortiz, Antonio de la Hoz,* Andrés Moreno, Ana Sánchez-Migallón and Gema Valiente

Area de Química Orgánica, Facultad de Química, Universidad de Castilla-la Mancha, E-13071 Ciudad Real, Spain. E-mail: antonio.hoz@uclm.es

Received 26th February 2002
First published as an Advance Article on the web 18th June 2002

The preparation of symmetrically substituted 1,3,5-triazines has been performed by cyclotrimerization of nitriles in solvent-free conditions using silica-supported Lewis acids as catalysts. Although microwave irradiation gives the best overall results in a short time, the best yields were obtained by conventional heating over periods of 24 h. The use of these recyclable and environmentally benign catalysts produces yields similar to those obtained with the more complex and contaminant lanthanide catalysts. This fact, together with the use of solvent-free conditions, makes this procedure an environmentally benign synthetic method.

Introduction

Supramolecular chemistry has been described as 'chemistry beyond the molecule', and the goal in this area is to gain control over the intermolecular non-covalent bond.[1] The principal characteristic of supramolecular chemistry is that building blocks are reversibly linked through intermolecular forces. Due to their characteristic C_3-symmetry, 1,3,5-triazines have been used in multidimensional crystal engineering using halogen···π-interactions,[2] and also in multidimensional crystal engineering involving metal complexes that,[3] in some cases, produce nanometer-sized oligonuclear coordination compounds.[4]

1,3,5-Triazines have also been used as templates in the synthesis of supramolecular porphyrin systems,[5] as complexation agents in analytical chemistry,[6] as multi-step redox systems,[7] as stationary phases in HPLC resolution of racemic compounds,[8] as enantio-differentiating coupling reagents[9] and as high-loading scavenger resins for combinatorial chemistry.[10]

The synthesis of 1,3,5-triazines has been performed by cyclotrimerization of nitriles catalysed by acids, bases[11] or activated magnesium.[12] These reactions require strong reaction conditions, *i.e.* high temperatures, pressures and long reaction times, and give, in most cases, moderate yields. Alternatively, the use of very strong and highly polluting acids[11f] or metals[12] can be considered.

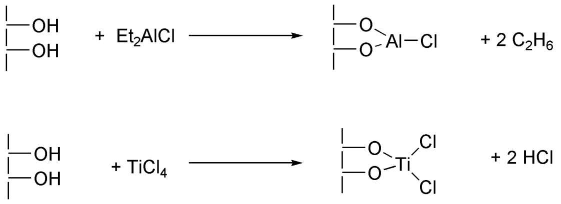
Green or sustainable chemistry is the design, development, and implementation of chemical products and processes aimed at reducing or eliminating the use and generation of substances hazardous to human health and the environment.[13] Among the twelve principles of green chemistry, the use of heterogeneous catalysis is one of the keystones of this new concept.[13]

Supported reagents have become of increased interest in the fields of organic and organometallic synthesis. In this respect, heterogeneous reactions in the presence of organic solvents have been performed with great success.[14] However, an even more green alternative is the use of supported reagents in solvent-free conditions.

Heterogeneous catalysts such as $ZnCl_2$, $TiCl_4$ and Et_2AlCl supported on silica gel have shown great utility as Lewis acid catalysts. The structures of these systems are not known in great detail but it is considered that silica-supported $ZnCl_2$ consists mainly of a dispersion of small particles of $ZnCl_2$ on the surface of silica gel. On the other hand, treatment of silica gel with $TiCl_4$ and Et_2AlCl results in the displacement of two chloride or ethyl groups, respectively, by the silanol groups of the silica gel (Scheme 1).[15]

These catalysts can be stored and recovered after the reaction without loss of catalytic activity. In this regard these catalysts have been used in the cycloaddition of furan with several dienophiles,[16] as well as in the preparation of amino acid derivatives by amidoalkylation of heterocyclic compounds.[17]

Microwave irradiation has shown its utility in many organic reactions. Spectacular accelerations have been observed in numerous cases but, more importantly, the selectivity of many reactions can be modified using microwaves and some reactions that do not occur, or result in very low yields, can be improved using microwaves.[18] Reactions that require harsh conditions, long reaction times, high temperatures and pressures—partic-



Scheme 1

Green Context

The synthesis of symmetrical 1,3,5-triazines is an important transformation and is often carried out by the displacement of chloride from cyanuric chloride, a wasteful method which may be tricky to drive to completion. Here, the use of silica supported Lewis acids and a basic promoter allows the smooth and high yielding synthesis of such molecules in the absence of solvent. Some side reactions are seen ($S_{NAr}2$ and demethylation of methoxyaromatics)—these may also be of interest in different applications. ***DJM***

DOI: 10.1039/b202014a

ularly when sensitive compounds are involved—are the best candidates for improvement using microwaves.

Results and discussion

In this paper we describe the cyclotrimerization of nitriles to afford 1,3,5-triazines in solvent-free conditions using silica-supported $ZnCl_2$, $AlCl_3$ and $TiCl_4$ as catalysts. These systems represent a green alternative to the use of lanthanide ions. For the sake of comparison, we also studied the commonly used lanthanide catalyst yttrium trifluorosulfonate $Y(OTf)_3$. Piperidine and morpholine were used as nucleophiles to induce the cyclotrimerization. We used conventional heating and microwave irradiation as the energy sources and the reactions were performed under pressure in closed vessels.

The best results from these reactions are collected in Table 1.

Reactions under microwave irradiation conditions give the best results in conjunction with short reaction times. However, when the reaction time was increased to 24 h under conventional heating the yields were greatly improved in most cases. Such extended reaction times cannot be employed with microwaves.

The results obtained are slightly better when $Y(OTf)_3$ was used instead of the silica-supported Lewis acids, although the simple manipulation, possible re-utilization and known environmental advantages make the silica systems excellent catalysts for the cyclotrimerization of nitriles. As has been previously described these catalysts can be recovered and stored up to one month, which give rise to high conversions without loss of catalytic activity.[15]

It can be seen from the results that, of the modified silica gels, Si(Zn) gives the best results. This fact has been explained in terms of the Hard–Soft Acid–Base Principle (HSAB): Zn, which is softer than Al and Ti, coordinates more effectively with the soft N atom of the nitrile. The only exceptions to this rule is derivative **8**, where the presence of a second coordinative nitrogen in the pyrazole makes Si(Ti) the best catalyst.

In some examples the nitriles do not produce the expected triazine. For example, the reaction with *p*-methoxybenzonitrile (**5**) produced *p*-hydroxybenzonitrile by nucleophilic attack at the methyl group of the anisole, which is activated by the Lewis acid (Scheme 2).

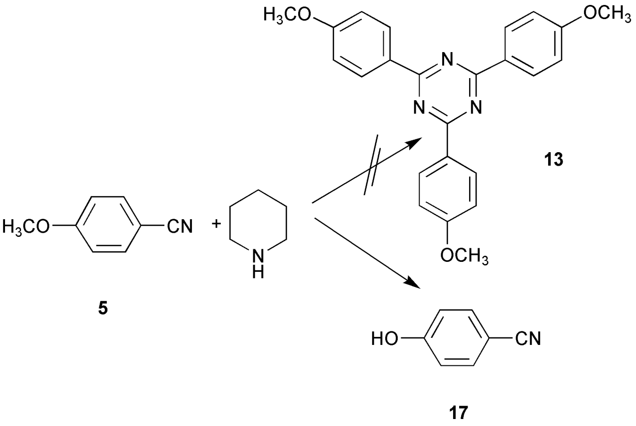
The reaction involving *p*-chlorobenzonitrile (**6**) led to aromatic nucleophilic substitution of the chlorine by both piperidine and morpholine to give **18** and **19**, together with the amidines **20** and **21**, respectively, which are intermediates in the cyclization to the triazine (Schemes 3 and 4).[11e]

The substitution product **19** afforded the corresponding triazine **14** in low yield together with the corresponding amidine **22** (Scheme 5).

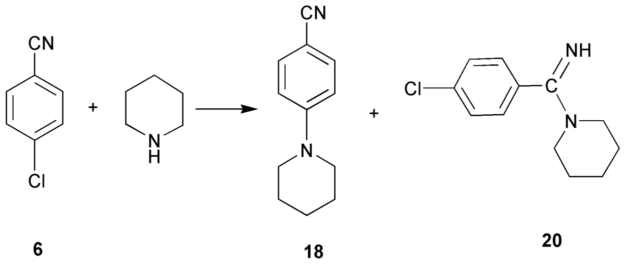
In conclusion, silica gels modified with Lewis acids, especially with $ZnCl_2$, are effective catalysts for the cyclotrimerization of aliphatic and aromatic nitriles to 1,3,5-triazines. The use of reagents supported on silica gel and the absence of solvents means that this process can be classified as an environmentally benign procedure.

Experimental

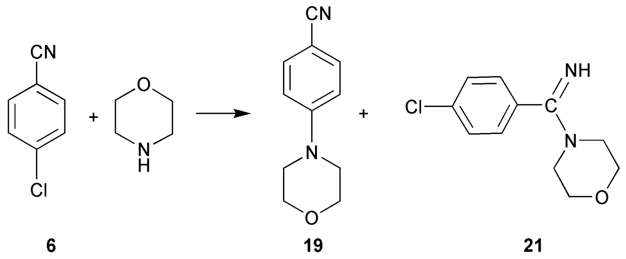
Silica-supported catalysts Si(Zn), Si(Al) and Si(Ti) were prepared from silica gel and $ZnCl_2$, $AlEt_2Cl$ and $TiCl_4$, respectively, according to known procedures.[15] The resulting catalysts were stored under argon. Si(Zn) was activated by heating at 150 °C for 2 h under vacuum while Si(Al) and Si(Ti) were used without prior activation.



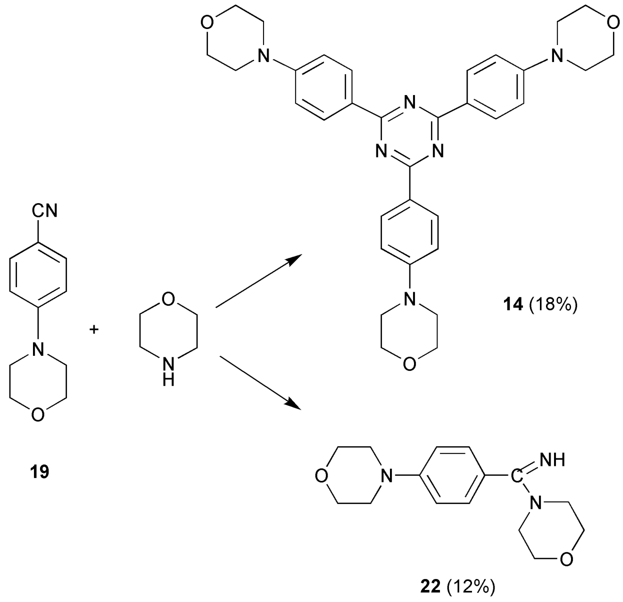
Scheme 2



Scheme 3

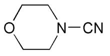
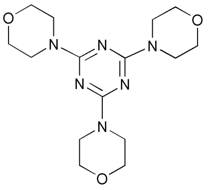
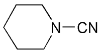
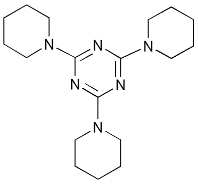
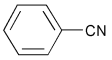
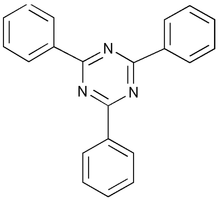
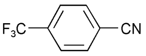
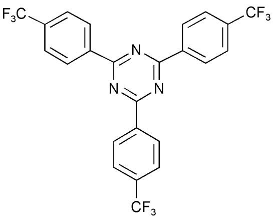
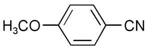
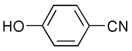
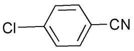
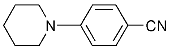
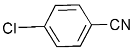
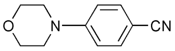
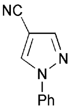
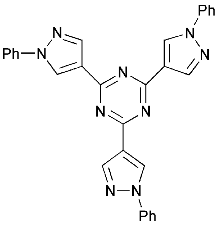
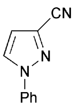
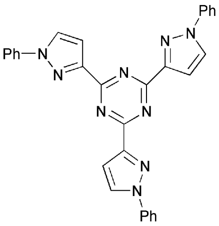


Scheme 4



Scheme 5

Table 1 Cyclotrimerization of nitriles in solvent-free conditions

Starting material	Catalyst	Reaction conditions	Product	Yield (%)
 **1**	$Y(OTf)_3$	200 °C, 24 h	 **9**	84
	$Y(OTf)_3$	160 °C, 210 W, 1 h		37
	Si(Zn)	200 °C, 24 h		60
	Si(Zn)	200 °C, 210 W, 2 min, 120 W, 28 min		50
	Si(Al)	200 °C, 24 h		22
	Si(Al)	200 °C, 210 W, 2 min, 120 W, 28 min		37
	Si(Ti)	20 °C, 24 h		38
	Si(Ti)	200 °C, 210 W, 2 min, 120 W, 28 min		37
 **2**	$Y(OTf)_3$	200 °C, 24 h	 **10**	31
	$Y(OTf)_3$	160 °C, 210 W, 2 min, 150 W, 28 min		40
	Si(Zn)	200 °C, 24 h		75
	Si(Zn)	160 °C, 210 W, 2 min, 150 W, 28 min		35
	Si(Al)	20 °C, 24 h		72
	Si(Al)	115 °C, 210 W, 2 min, 150 W, 28 min		5
	Si(Ti)	200 °C, 24 h		63
	Si(Ti)	120 °C, 210 W, 2 min, 150 W, 28 min		0
 **3**	$Y(OTf)_3$	20 °C, 24 h	 **11**	55
	$Y(OTf)_3$	140 °C, 210 W, 2 min, 45 W, 58 min		0
	Si(Zn)	200 °C, 24 h		13
	Si(Zn)	16 °C, 270 W, 1 h		0
 **4**	$Y(OTf)_3$	200 °C, 12 h	 **12**	42
	Si(Zn)	200 °C, 24 h		35
	Si(Al)	200 °C, 24 h		6
	Si(Ti)	200 °C, 24 h		5
 **5**	$Y(OTf)_3$	200 °C, 24 h	 **17**	54
	$Y(OTf)_3$	160 °C, 210 W, 9 min, 120 W, 51 min		95
	Si(Zn)	200 °C, 24 h		46
 **6**	$Y(OTf)_3$	200 °C, 24 h	 **18**	27[a]
	$Y(OTf)_3$	200 °C, 24 h		72[b]
 **6**	$Y(OTf)_3$	200 °C, 24 h	 **19**	60[c]
 **7**	$Y(OTf)_3$	200 °C, 24 h	 **15**	30
	Si(Zn)	200 °C, 24 h		30
	Si(Al)	200 °C, 24 h		0
	Si(Ti)	200 °C, 24 h		8
 **8**	$Y(OTf)_3$	200 °C, 24 h	 **16**	66
	Si(Zn)	200 °C, 24 h		15
	Si(Al)	200 °C, 24 h		39
	Si(Ti)	200 °C, 24 h		50

[a] **20** (9%). [b] Piperidine, 2 equiv., **20** (5%). [c] Morpholine, 2 equiv., **21** (6%).

2,4,6-Triphenyl-1,3,5-triazine (**11**),[19] cyanopyrazoles **7** and **8** and the corresponding triazines **15** and **16**[11b] have been described previously.

Synthesis of nitriles

***p*-Piperidinobenzonitrile (18)**. Yttrium trifluoromethanesulfonate (0.1 mmol, 0.08 g), *p*-chlorobenzonitrile (10 mmol, 1.37 g) and anhydrous piperidine (20 mmol, 2 ml) were heated under argon in a screw-cap sealed reaction vessel in an aluminium block[20] at 200 °C for 24 h. The crude product was extracted with acetone (2 × 10 ml) and filtered. The filtrate was purified by column chromatography on silica gel using hexane–ethyl acetate 9:1 as the eluent. *p*-piperidinobenzonitrile (**18**) (1.34 g, 72%) eluted first followed by piperidino-*p*-chlorobenzamidine (**20**) (0.2 g, 5%).

p-Piperidinobenzonitrile (18). Mp 55–57 °C (hexane–ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 1.65–1.67 (m, 6H, $H_{3,4,5}$), 3.33 (m, 4H, $H_{2,6}$), 6.80–6.88 and 7.43–7.50 (4H, aryl). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 24.23 (piperidine C_4), 25.23 (piperidine $C_{3,5}$), 48.41 (piperidine $C_{2,6}$), 98.93 (C_1), 114.02 ($C_{3,5}$), 120.32 (CN), 133.45 ($C_{2,6}$), 153.54 (C_4). IR (KBr) ν(cm^{-1}): 2215 ($\nu_{C\equiv N}$), 1605, 1514 ($\nu_{C=C}$). Analysis: Calc. for $C_{12}H_{14}N_2$: C 77.38, H 7.58, N 15.04. Found: C 77.30, H 7.60, N 15.41%. MS (EI): *m/z* 185 (M − 1).

Piperidino-p-chlorobenzamidine (20). Mp 64–65.7 °C (hexane–ethyl acetate). ^{1}H NMR (300 MHz, DMSO, TMS as internal ref.) δ 1.35–1.65 (m, 10H, piperidine), 7.37 and 7.48 (4H, J_{AX} 8 Hz, $J_{AA'}$ 4.4 Hz, $J_{AX'}$ 0.3 Hz, aryl). ^{13}C NMR (300 MHz, DMSO, TMS as internal ref.) δ 24.00 (piperidine C_4), 25.21 (piperidine C_3), 25.91 (piperidine C_5), 42.35 (piperidine C_2), 48.00 (piperidine C_6), 128.47 (aryl $C_{2,6}$), 128.62 (aryl $C_{3,5}$), 133.87 (aryl C_1), 135.26 (aryl C_4), 167.77 ($C_{C=NH}$). IR (KBr) ν(cm^{-1}): 1630 ($\nu_{C=N}$). MS (EI): *m/z* 222.1 (M).

***p*-Morpholinobenzonitrile (19)**. A mixture of yttrium trifluoromethanesulfonate (0.1 mmol, 0.08 g), *p*-chlorobenzonitrile (10 mmol, 1.37 g) and anhydrous morpholine (20 mmol, 1.8 ml) was heated under argon in a screw-cap sealed reaction vessel in an aluminium block[20] at 200 °C for 24 h. The crude product was extracted with acetone (2 × 10 ml) and filtered. The filtrate was purified by column chromatography on silica gel using hexane–ethyl acetate 7:3 as the eluent. *p*-Morpholinobenzonitrile (**19**) (1.12 g, 60%) was eluted first followed by morpholino-*p*-chlorobenzamidine (**21**) (0.12 g, 6%).

Morpholinobenzonitrile (19). Mp 79.6–82.3 °C (hexane–ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 3.27 (t, *J* 5.0 Hz, 4H, $H_{2',6'}$), 3.85 (t, *J* 5.0 Hz, 4H, $H_{3',5'}$), 6.84–6.87 and 7.43–7.50 (4H, aryl). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 47.26 ($C_{2'}$), 66.47 ($C_{3'}$), 100.93 (C_1), 114.04 ($C_{3,5}$), 119.85 (CN), 133.53 ($C_{2,6}$), 153.44 (C_4). IR (KBr) ν(cm^{-1}): 2215 ($\nu_{C=N}$), 1605, 1515 ($\nu_{C=C}$). Analysis: Calc. for $C_{11}H_{12}N_2O$: C 70.19, H 6.43, N 14.88. Found: C 70.11, H 6.58, N 15.09%. MS (EI): *m/z* 188.1 (M).

Morpholino-p-chlorobenzamidine (21). Mp 69–70.7 °C (hexane–ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 3.2–3.9 (m, 9H, morpholine and NH), 7.33–7.43 (4H, aryl). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 66.82 (morpholine $C_{3,5}$), 128.64 (phenyl $C_{2,6}$), 128.85 (phenyl $C_{3,5}$), 133.57 (phenyl C_1), 136.04 (phenyl C_4), 169.34 (C=N). IR (KBr) ν(cm^{-1}): 1625 ($\nu_{C=N}$): MS (EI): *m/z* 224.1 (M).

4-Hydroxybenzonitrile (17). A mixture of yttrium trifluoromethanesulfonate (0.1 mmol, 0.08 g), *p*-methoxybenzonitrile (**5**) (10 mmol, 1.332 g) and anhydrous piperidine (10 mmol, 1ml) was heated under argon in a screw-cap sealed reaction vessel in an aluminium block[20] at 200 °C for 24 h. The crude product was extracted with dichloromethane (30 ml) and filtered. The filtrate was purified by flash chromatography on silica gel using hexane–ethyl acetate, in a gradient 9:1 to 1:1, as the eluent to give 4-hydroxybenzonitrile (**17**) (0.64 g, 54%). ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 6.92–6.97 and 7.53–7.58 (4H, aryl). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 103.03 (C_1), 116.42 ($C_{3,5}$), 119.23 (CN), 134.28 ($C_{2,6}$), 160.18 (C_4). IR (KBr) ν(cm^{-1}): 3290 (ν_{OH}), 2235 ($\nu_{C=N}$).

Synthesis of 2,4,6-trisubstituted 1,3,5-triazines

Method A. Classical heating. A mixture of yttrium trifluoromethanesulfonate (0.1 mmol, 0.08 g), the appropriate nitrile (10 mmol) and anhydrous piperidine (10 mmol, 1 ml) was heated under argon in a screw-cap sealed reaction vessel in an aluminium block[20] at 200 °C for 24 h. Purification was performed as indicated in each case.

Method B. Synthesis using microwave irradiation. A mixture of yttrium trifluoromethanesulfonate (0.1 mmol, 0.08 g), the appropriate nitrile (10 mmol) and anhydrous piperidine (10 mmol, 1 ml) was introduced into a closed Pyrex flask and irradiated in a modified PROLABO Maxidigest microwave reactor[21] at the power/time shown in Table 1.

Method C. Reactions with silica-supported Lewis acids. A mixture of silica-supported Lewis acid [Si(Zn), Si(Al), Si(Ti)] (0.2 mmol, 1 g), the appropriate nitrile (10 mmol) and anhydrous piperidine (10 mmol, 1 ml) was heated under the conditions described in methods A or B as appropriate. The crude product was extracted with the appropriate solvent and silica gel was removed by filtration.

2,4,6-Tris(4-trifluoromethylphenyl)-1,3,5-triazine (12).

Method A. From *p*-trifluoromethylbenzonitrile (**4**) (10 mmol, 1.71 g) for 12 h. The crude product was triturated with diethyl ether (3 × 15 ml) and filtered off to give the product as a white solid (0.71 g, 42%). mp 276.5–278.5 °C (toluene). ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 7.85 (d, *J* 8.8 Hz, 6H, $H_{2,6}$), 8.88 (d, *J* 8.8 Hz, 6H, $H_{3,5}$). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 125.72 ($C_{3,5}$), 129.35 ($C_{2,6}$), 134.4 (q, *J* 32.73 Hz, C_4), 138.75 (C_1), 171.04 ($C_{triazine}$). IR (KBr) ν(cm^{-1}): 1528 ($\nu_{C=C}$, $\nu_{C=N}$) 1321 (ν_{C-F}). Analysis: Calc. for $C_{24}H_{12}F_9N_3$: C 56.15, H 2.36, N 8.18. Found: C 56.64, H 2.52, N 8.32%. MS (EI): *m/z* 513 (M).

2,4,6-Trispiperidino-1,3,5-triazine (10).

Method A. From 1-cyanopiperidine (**2**) (10 mmol, 1.10 g) for 12 h. The crude product was triturated with diethyl ether (3 × 15 ml) and filtered off to give the product as a white solid (0.34 g, 31%). mp 206–209.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 1.48–1.68 (m, 18H, $H_{3',5',4'}$), 3.70 (t, *J* 5.4 Hz, 12H, $H_{2',6'}$). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 25.34 ($C_{4'}$), 26.07 ($C_{3',5'}$), 44.30 ($C_{2',6'}$), 165.67 ($C_{triazine}$). IR (KBr) ν(cm^{-1}): 1532, 1480 ν($_{C=C}$, $\nu_{C=N}$). MS (EI): *m/z* 330.2 (M).

2,4,6-Trismorpholino-1,3,5-triazine (9).

Method A. From morpholinocarbonitrile (**1**) (10 mmol, 1.12 g) and morpholine (10 mmol, 0.9 ml). The crude product was triturated with diethyl ether (3 × 15 ml) and filtered off to give the product as a white solid (0.94 g, 84%). mp 272–275 °C (toluene). ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 3.68 (m, 24H, morpholine). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 43.61 ($C_{2,6}$), 66.87 ($C_{3,5}$), 165.32 ($C_{triazine}$). IR (KBr) ν(cm^{-1}): 1548, 1480, 1453 $\nu_{(C=N}$, $\nu_{C=C)}$. Analysis: Calc. $C_{15}H_{24}N_6O_3$: C 53.56, H 7.19, N 24.98. Found: C 53.80, H 7.22, N 28.37%. MS (EI): *m*/*z* 336.2 (M).

2,4,6-Tris(4-morpholinophenyl)-1,3,5-triazine (14).

Method A. From *p*-morpholinobenzonitrile (19) (5.18 mmol, 0.975 g) and morpholine (9 mmol, 0.8 ml) for 72 h. The crude product was extracted with dichloromethane (2 × 10 ml) and filtered. The filtrate was purified by column chromatography firstly using hexane–ethyl acetate (7:3), then ethyl acetate and finally ethyl acetate–diethylamine (2%). 2,4,6-(4-Morpholinophenyl)-1,3,5-triazine (**14**) (0.172 g, 18%) eluted first, followed by morpholino-*p*-morpholinobenzamidine (**22**) (0.110 g, 12%).

2,4,6-Tris(morpholinophenyl)-1,3,5-triazine (14). Mp 269.7–271.6 °C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 3.33–3.36 and 3.89–3.93 (24 H, morpholine), 7.01–7.04 and 8.64–8.67 (12H, aryl). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 48.04 ($C_{2',6'}$), 66.69 ($C_{3',5'}$), 114.06 ($C_{3,5}$), 130.23 ($C_{2,6}$), 170.44 ($C_{triazine}$). IR (KBr) ν(cm^{-1}): 1608, 1495 $\nu_{(C=C}$, $\nu_{C=N)}$. Analysis: Calc. $C_{33}H_{36}N_6O_3$: C 70.19, H 6.09, N 14.88. Found: C 69.70, H 6.09, N 14.41%. MS (EI): *m*/*z* 564.4 (M).

*Morpholino-*p*-morpholinobenzamidine (22).* Mp 120.6–123.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 3.19 (t, *J* 4.9 Hz, 4H, $H_{2',6'}$ morpholino-phenyl), 3.5–3.75 (m, 8H, morpholine), 3.84 (t, *J* 4.9 Hz, 4H, $H_{3',5'}$ morpholino-phenyl), 6.8–6.9 and 7.3–7.4 (4H, aryl). ^{13}C NMR (300 MHz, $CDCl_3$, TMS as internal ref.) δ 48.28 (morpholine $C_{2,6}$), 66.47–66.85 (morpholine $C_{3,5}$), 114.30 (aryl $C_{3,5}$), 125.47 (aryl C_1), 128.54 (aryl $C_{2,6}$), 152.24 (aryl C_4), 170.49 (C=N). IR (KBr) ν(cm^{-1}): 3220 ν(NH), 1625 $\nu_{(C=N)}$. MS (EI): *m*/*z* 276.3 (M + 1).

Acknowledgments

Financial support from the Spanish DGI (project BQU2001-1095) is gratefully acknowledged.

References

1 (*a*) J. M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, Weinheim, 1995; (*b*) J. W. Steed and J. L. Atwood, *Supramolecular Chemistry*, Wiley, New York, 2000; (*c*) H.-J. Schneider and A. Yatsimirsky, *Principles and Methods in Supramolecular Chemistry*, Wiley, New York, 2000.

2 R. K. R. Jetti, A. Nangia, F. Xue and T. C. W. Mak, *Chem. Commun.*, 2001, 919.

3 (*a*) A. D. Burrows, C. W. Chan, M. M. Chowdhry, J. E. McGrady and D. M. P. Mingos, *Chem. Soc. Rev.*, 1995, 329; (*b*) B. Moulton and M. J. Zaworotko, u*Chem. Rev.*, 2001, **101**, 1629.

4 (*a*) B. F. Abrahams, S. R. Batten, H. Hamit, B. F. Hoskins and R. Robson, *Chem. Commun.*, 1996, 1313; (*b*) B. F. Abrahams, S. R. Batten, H. Hamit, B. F. Hoskins and R. Robson, *Angew. Chem., Int. Ed. Engl.*, 1996, 1690; (*c*) M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi and K. Ogura, *Nature*, 1995, **378**, 469; (*d*) M. Fujita, N. Fujita, K. Ogura and K. Yamaguchi, *Nature*, 1999, **400**, 52; (*e*) M. Albercht, *Angew. Chem., Int. Ed.*, 1999, **38**, 3463; (*f*) S. Sakamoto, M. Yoshizawa, T. Kusukawa, M. Fujita and K. Yamaguchi, *Org. Lett.*, 2001, **3**, 1601.

5 (*a*) D. W. McCallien and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1995, **117**, 6611; (*b*) S. Anderson, H. L. Anderson and J. K. M. Sanders, *J. Chem. Soc., Perkin Trans. 1*, 1995, 2255; (*c*) H. L. Anderson, C. J. Walter, A. Vidal-Ferran, R. A. Hay, P. A. Lowden and J. K. M. Sanders, *J. Chem. Soc., Perkin Trans. 1*, 1995, 2275.

6 W. C. Hoyle and J. Benga, *Talanta*, 1990, **27**, 963.

7 W. K. Gries, E. Günther and S. Hünig, *Liebigs Ann. Chem.*, 1991, 1021.

8 A. Iuliano, E. Attolino and P. Salvadori, *Eur. J. Org. Chem.*, 2001, 3523.

9 Z. J. Kamisnski, B. Kolesinska, J. E. Kaminska and J. Gora, *J. Org. Chem.*, 2001, **66**, 6276.

10 (*a*) A. Marsh, S. J. Carlisle and S. C. Smith, *Tetrahedron Lett.*, 2001, **42**, 3493; (*b*) A. Falchi and M. Taddei, *Org. Lett.*, 2000, **2**, 3419.

11 (*a*) J. H. Forsberg, V. T. Spaziano, S. P. Klump and J. K. M. Sanders, *J. Heterocycl. Chem.*, 1988, **25**, 767; (*b*) H. G. Biedermann and K. Wichmann, *Z. Naturforsch., Teil B*, 1974, **29**, 360; (*c*) D. Martin, M. Bauer and V. A. Pankratov, *Russ. Chem. Rev.*, 1978, **47**, 975; (*d*) E. V. Mørkved, H. Kjøsen and S. M. Neset, *Acta Chem. Scand.*, 1994, **48**, 372; (*e*) A. de la Hoz, A. Díaz-Ortiz, J. Elguero, L. J. Martínez, A. Moreno and A. Sánchez-Migallón, *Tetrahedron*, 2001, **57**, 4397; (*f*) C.-H. Lee and T. Yamamoto, *Tetrahedron Lett.*, 2001, **42**, 3993.

12 R. D. Rieke and M. V. Hansson, *Tetrahedron*, 1997, **53**, 1925.

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

14 (*a*) P. Laszlo, *Preparative Chemistry using Supported Reagents*, Academic Press, 1987; (*b*) Y. Izumi, K. Urabe and M. Onaka, *Zeolite, Clay and Heteropolyacids in Organic Chemistry*, Kodansha–VCH, Tokyo–Weinheim, 1992; (*c*) K. Smith, *Solid Supports and Catalysts in Organic Synthesis*, Ellis Horwood, London, 1992.

15 C. Cativiela, J. M. Fraile, J. I. García, J. A. Mayoral, E. Pires, A. J. Royo, F. Figueras and L. C. de Menórval, *Tetrahedron*, 1993, **49**, 4073.

16 (*a*) J. M. Fraile, J. I. García, D. García, J. A. Mayoral and E. Pires, *J. Org. Chem.*, 1996, **61**, 9479; (*b*) J. M. Fraile, J. I. García, J. Massam, J. A. Mayoral and E. Pires, *J. Mol. Catal. A*, 1997, **43**, 123; (*c*) A. de la Hoz, A. Díaz-Ortiz, J. M. Fraile, M. V. Gómez, J. A. Mayoral, A. Moreno, A. Saiz and E. Vázquez, *Synlett*, 2001, 236; (*d*) J. M. Fraile, J. I. García, M. A. Gómez, A. de la Hoz, J. A. Mayoral, A. Moreno, P. Prieto, L. Salvatella and E. Vázquez, *Eur. J. Org. Chem.*, 2001, **5**, 2891.

17 A. de la Hoz, A. Díaz-Ortiz, M. V. Gómez, J. A. Mayoral, A. Moreno, A. M. Sánchez-Migallón and E. Vázquez, *Tetrahedron*, 2001, 5421.

18 (*a*) D. M. P. Mingos and A. G. Whittaker, *Microwave Dielectric Heating Effects in Chemical Synthesis in Chemistry under Extreme or non-Classical Conditions*, ed. R. van Eldik and C. D. Hubbard, John Wiley and Sons, New York, 1997, p. 479; (*b*) S. Caddick, *Tetrahedron*, 1995, **52**, 10403; (*c*) A. K. Bose, M. J. Manhas, B. K. Banik and E. W. Robb, *Res. Chem. Intermed.*, 1994, **20**, 1; (*d*) C. R. Strauss and R. W. Trainor, *Aust. J. Chem.*, 1995, **48**, 1665; (*e*) S. A. Galema, *Chem. Soc. Rev.*, 1997, **25**, 233; (*f*) A. Loupy and J. L. Luche, Sonochemical and Microwave Activation in Phase Transfer Catalysis, in *Handbook of Phase Transfer Catalysis*, ed. Y. Sasson and R. Neumann, Blackie, London, 1996, p. 369; (*g*) F. Langa, P. de la Cruz, A. de la Hoz, A. Díaz-Ortiz and E. Díez-Barra, *Contemp. Org. Synth.*, 1997, **4**, 373.

19 A. Peralta, A. Llobera and J. M. Saa, *Synthesis*, 1985, 95.

20 M. Begtrup, *J. Chem. Educ.*, 1987, **64**, 974.

21 PROLABO MAXIDIGEST MX350, modified with a mechanical stirrer and an infrared pyrometer. Incident power and temperature was controlled by computer using the software MPX-2 from PACAM Electrónica.

In situ synthesis by salt–surface interaction and the catalytic functionality of the ammonium salt of 12-tungstophosphoric acid†

M. Santhosh Kumar, K. Narasimha Rao, N. Lingaiah, I. Suryanarayana and P. S. Sai Prasad*

*Catalysis & Physical Chemistry Division, Indian Institute of Chemical Technology,
Hyderabad 500 007, India. E-mail: saiprasad@iict.ap.nic.in*

Received 11th January 2002
First published as an Advance Article on the web 18th June 2002

The ammonium salt of 12-tungstophosphoric acid, with the Keggin structure, has been synthesized *in situ* on niobium phosphate (NbP) by salt–surface interaction; the catalyst exhibits high selectivity to benzaldehyde in the vapor phase air oxidation of benzyl alcohol.

Introduction

With the growing concern for environmental pollution, solid heteropolyacids (HPAs) have been extensively used in place of mineral acids to catalyze several organic transformations.[1] Important among the HPAs is 12-tungstophosphoric acid (TPA), which is made up of twelve WO_6 octahedra surrounding the central PO_4 tetrahedron, forming a Keggin structure.[2,3] The HPAs are often used as their ammonium or mixed cationic salts to improve their thermal stability.[4] Of late, the salts have also been used by supporting them on carriers such as SiO_2 to derive the benefit of dispersion, as the bulk compounds possess low surface area.[5] In this respect, the acidic supports are found to offer better stability to the acid/salt, whereas interacting supports like alumina lead to decomposition of the heteropolyacid. The general procedure for the preparation of supported heteropolyacid salts involves preparation of the salt separately and its deposition on the support. However, in most of the studies dealing with the preparation of the supported ammonium salt of TPA (ATPA) the solubility of the salt in the impregnating solution poses a great problem. Hence there is a strong need to identify new methods for the deposition of the salt on supports.

In the present investigation a new method, which overcomes the solubility problem, is reported for the synthesis of supported ATPA catalysts. The method involves a one-step synthesis of the catalyst, which is achieved by interacting the tungsten of the salt (ammonium paratungstate) with the phosphate ion of the niobium phosphate support. A series of catalysts containing a nominal WO_6 content in the range from 5 wt% (abbreviated as NbPW-5) to 15 wt% (NbPW-15), in the finished catalyst samples, have been prepared. X-Ray diffraction (XRD) and Fourier transform infrared (FTIR) spectroscopy have been used to confirm the formation of ATPA in its Keggin structure. The catalysts have been found to offer high selectivity to benzaldehyde, in the aerobic oxidation of benzyl alcohol, an eco-friendly process for the desired product.

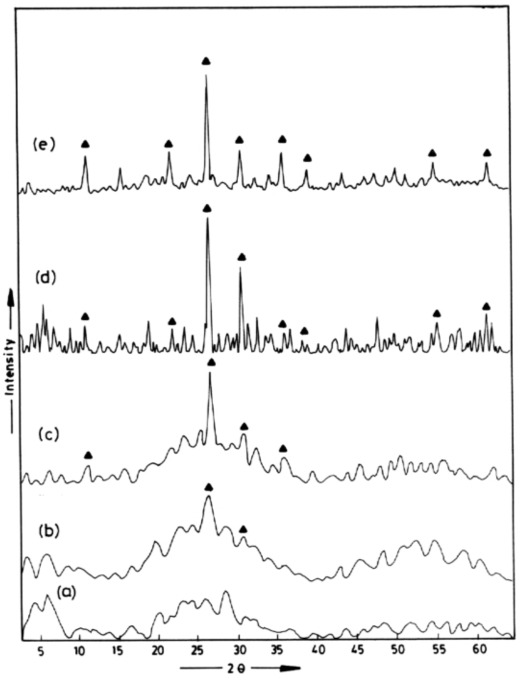


Fig. 1 XRD patterns of the catalysts: (a) pure support, (b) NbPW-5, (c) NbPW-10, (d) NbPW-15 and (e) pure ATPA; (▲) $[(NH_4)_3PO_4\text{-}(WO_3)_{12}\cdot 4H_2O$

Green Context

The immobilisation of catalysts on support materials has been one of the major research and application areas in green chemistry. Effective immobilisation giving stable solid catalysts is, however, a serious difficulty and limits the value of the supported catalysts. Here, a new method of preparing stable supported heteropolyacids is described. These are potentially versatile catalysts for various typically acid-catalysed reactions. To illustrate this, a highly selective oxidation of benzyl alcohol to benzaldehyde is described.

DJM

Results and discussion

Fig. 1 shows the XRD patterns of the NbP support as well as the catalysts. The XRD pattern of the bulk ATPA is also included

---

† IICT Communication No. 01121.

DOI: 10.1039/b200426g

for the sake of comparison. The support is found to be amorphous in nature. Martins *et al.*[6] have also reported the amorphous nature of niobium phosphate up to a calcination temperature of 700 °C. The XRD pattern of the NbPW-5 catalyst displays the signs of formation of ATPA, though not very clearly. Formation of ATPA in a well crystalline form is observed in NbPW-10 and NbPW-15 catalysts. The diffraction data are in agreement with those given by Hayashi and Moffat[7] revealing the formation of $(NH_4)_3PW_{12}O_{40}\cdot 4H_2O$. For NbPW-15 catalyst some small peaks other than those related to the Keggin ion are observed. These peaks may be related to the intermediate compounds formed between the NbP support and ammonium paratungstate. The intensity of the lines also increases with increase in ATPA content. The present observation is significant as it is shown that the synthesis of ATPA, exhibiting Keggin structure, is possible by interacting the tungsten species of the salt with phosphate ion of the support surface.

The FTIR spectra of the NbP support and the catalysts are shown in Fig. 2. The support shows a broad band, due to the phosphate ion, extending between 1006 and 1020 cm^{-1} and a sharp absorption band at 1625 cm^{-1} due to the adsorbed water. The IR spectrum of the NbPW-5 catalyst is also similar to that of the support, except for a slight indication of the formation of ATPA. However, the NbPW-10 and NbPW-15 catalysts show strong bands at 1625, 1412, 1075, 1005, 875, 800 and 630 cm^{-1}. The bands at 1412, 1075, 980, 875 and 800 cm^{-1} correspond to the stretching vibrations of the NH_4^+ ion, $(P–O_d)$, $(W–O_t)$, $(W–O_b–W)$ and $(W–O_c–W)$, respectively. These are in perfect agreement with the FTIR data reported by Belanger and Moffat.[8] An increase in the intensity of the bands with the increase in the ATPA content can be also observed from the spectral data. These results obtained by the IR analysis also confirm the formation of ATPA on the NbP support surface, further indicating the one-step synthesis of the catalysts.

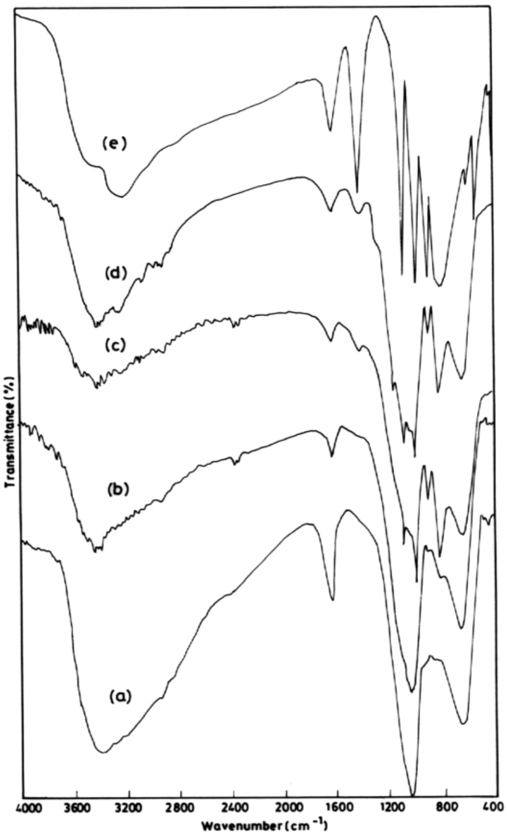


Fig. 2 FTIR spectra of the catalysts: (a) pure support, (b) NbPW-5, (c) NbPW-10, (d) NbPW-15 and (e) pure ATPA

Selective oxidation of benzyl alcohol to benzaldehyde has been the subject of interest of several researchers. Most of the results available in literature,[9,10] reporting high yields of benzaldehyde, relate to the liquid phase reaction conducted in batch mode. However, vapour phase continuous reactions are advantageous in terms of process economics and ease of operation. In the present investigation, the reaction is carried out in the vapour phase and attention has been focused on the change in product distribution after the generation of ATPA on the surface of the support.

The reaction of benzyl alcohol is very interesting because a variety of transformations can occur depending upon the nature of the active sites on the catalyst surface. The main reactions are listed below.

$$2\ C_6H_5CH_2OH \rightarrow 2\ C_6H_5CHO + 2\ H_2 \quad (1)$$

$$2\ C_6H_5CH_2OH \rightarrow C_6H_5CH_2OCH_2C_6H_5 + H_2O \quad (2)$$

$$2\ C_6H_5CH_2OH \rightarrow C_6H_5CHO + C_6H_5CH_3 + H_2O \quad (3)$$

Fig. 3 displays the extent of benzaldehyde conversion on the support and on the catalysts. In the present study we have not observed any products, such as carbon oxides, other than the products from reactions (1), (2) and (3), in significant amounts. The ATPA containing catalysts show higher conversions than the support. This may be due to the distribution of ATPA on the support with increase in the number of active sites. Benzyl alcohol conversion is observed to reach its maximum on the NbPW-10 catalyst. The decrease in conversion beyond 10%

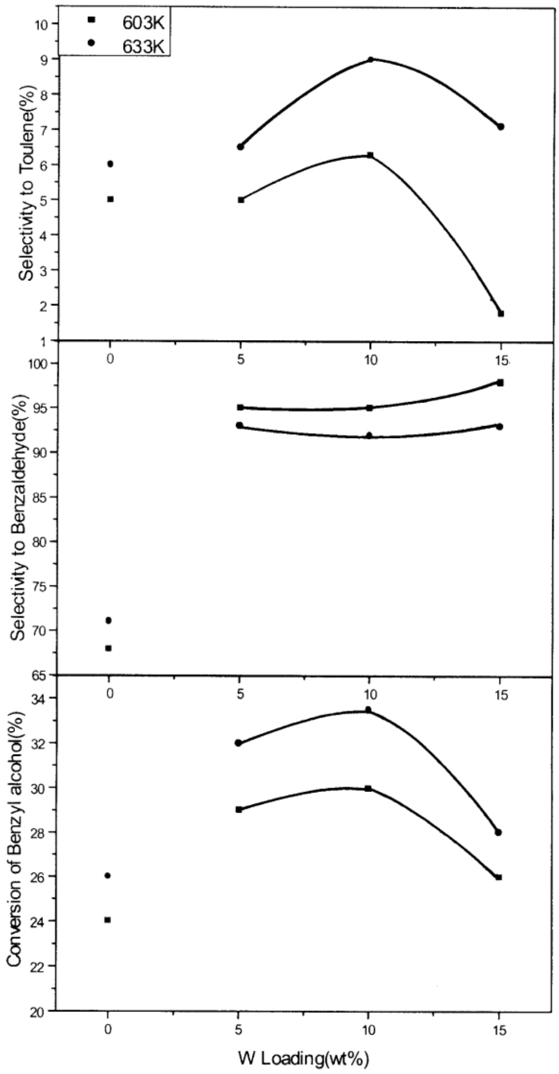


Fig. 3 Effect of WO_6 loading on the product distribution at two reaction temperatures (0% corresponds to the values obtained on the support).

WO_6 loading may be due to the adoption a of bulk nature by ATPA at higher loading.

Fig. 3 also shows the benzaldehyde selectivity obtained on the support as well as the ATPA containing catalysts. The ATPA containing catalysts show high selectivity to benzaldehyde (up to 95%). An important observation is the formation of dibenzyl ether on the support to the extent of 17% and its absence in the products collected during the reaction on the ATPA catalysts. Toluene selectivity is almost the same (7 ± 2%, Fig. 3) on the support as well as the ATPA catalysts implying that the disproportionation reaction (eqn. (3)) is not predominant. The high ratio of benzaldehyde to toluene (*ca.* 19) and the absence of dibenzyl ether in the reaction products are in accordance with the results reported by Athilakshmi and Viswanathan,[11] who carried out air oxidation of benzyl alcohol on bulk heteropolyacid-based catalysts. The disproportionation of benzyl alcohol, resulting in the formation of a 1 : 1 mixture of benzaldehyde and toluene is reported by Jayamani and Pillai.[12] Disproportionation demands the presence of strong acid sites.[12] Instead, the formation of dibenzyl ether (eqn. (2)) on the support surface implies the presence of weakly acidic sites. ATPA is reported[7] to contain weak acid sites with a broader distribution of acid strengths than the parent tungstophosphoric acid. We believe that the high selectivity to benzaldehyde is a manifestation of the predominance of oxidation (dehydrogenation) functionalities (eqn. (1)) over acidic functionalities in the ATPA catalysts, as also reported by Athilakshmi and Viswanathan.[11] Time on stream analysis was carried out for 20 h and revealed that the catalysts were stable.

Thus, it can be concluded that the synthesis of the ammonium salt of the tungstophosphoric acid on the support is possible by salt–surface interaction. The catalyst offers high selectivity to benzaldehyde during the air oxidation of benzyl alcohol. Further studies on the optimization of the yield of benzaldehyde and the thermal stability of the *in situ* synthesized ATPA catalysts is in progress in our laboratory.

Experimental

Niobium phosphate (supplied by CBMM, Brazil) was used as the support. Catalysts with varying ATPA contents were prepared by the excess solution method. Aqueous solutions of ammonium paratungstate (Fluka, Japan) of required concentrations were added to the previously dried support. The excess solution was removed by evaporation on a water bath. The catalyst samples were first dried at 120 °C for 12 h and then carefully calcined in air at 350 °C over a period of 4 h. The XRD patterns of the catalysts were obtained on a Siemens D-5000 diffractometer using Cu-Kα radiation. FTIR Spectra were recorded on a Biorad-175 spectrometer using the KBr disk method.

Air oxidation of benzyl alcohol was studied in the vapor phase at atmospheric pressure in a fixed bed microreactor. About 0.5 g of the catalyst (crushed into particles of size 18/25 BSS mesh to avoid mass transfer limitations) was suspended between two quartz plugs in a glass reactor of 10 mm i.d. The catalyst was initially pretreated in inert atmosphere (dry nitrogen, 30 ml h^{-1}) at 350 °C for 1 h. The reactant, benzyl alcohol, was fed into the reactor by a microprocessor based syringe pump (B. Braun, Germany). Dry air and benzyl alcohol were mixed and heated to the reaction temperature in the preheater part of the reactor. The reaction was carried out isothermally in the temperature range 300–360 °C. After attaining a steady state over a period of 1 h, the liquid products were collected and analyzed by GC, separating them on a SE-30 column using a flame ionization detector. To measure the amount of CO, CO_2 formation during the reaction, a known concentrated alkali trap was used for CO_2 and an ORSAT apparatus for detection of CO.

Acknowledgements

The authors are indebted to Dr K. V. Raghavan, Director, IICT, for his encouragement and permission to publish the results. K. N. R. thanks CSIR, India, for awarding a Senior Research Fellowship.

References

1 N. Mizuno and M. Misono, *Chem. Rev.*, 1998, **98**, 199.
2 J. C. Edwards, C. Y. Thiel, B. Benac and J. F. Knifton, *Catal. Lett.*, 1998, **51**, 77.
3 L. R. Pizzio, C. V. Caceres and M. N. Blanco, *Appl. Catal. A: General*, 1998, **167**, 283.
4 S. Albonetti, F. Cavani, F. Triffiro, M. Gazzano, M. Koutyrev, F. C. Aissi, A. Aboukais and M. Guelton, *J. Catal.*, 1994, **146**, 491.
5 W. C. Cheng and N. P. Luthra, *J. Catal.*, 1988, **109**, 163.
6 R. L. Martins, W. J. Schitine and F. R. Castro, *Catal. Today*, 1989, **5**, 483.
7 H. Hayashi and J. B. Moffat, *J. Catal.*, 1983, **83**, 192.
8 R. Belanger and J. B. Moffat, *Catal. Today*, 1998, **40**, 297.
9 K. Kaneda, T. Yomashita, T. Matsushita and K. Ebitani, *J. Org. Chem.*, 1998, **63**, 1750.
10 K. P. Peterson and R. C. Larock, *J. Org. Chem.*, 1998, **63**, 3185.
11 Athilakshmi and B. Viswanathan, *Catalysis: Modern Trends*, ed. N. M. Gupta and D. K. Chakrabarty, Narosa Publishing House, New Delhi, 1995, p. 311.
12 M. Jayamani and C. N. Pillai, *J. Catal.*, 1983, **82**, 485.

Heck reaction in aqueous medium using Amberlite IRA-400 (basic)†

S. B. Solabannavar, Uday V. Desai and R. B. Mane*

Department of Chemistry, Shivaji University, Kolhapur 416004, India.
E-mail: rbmane@yahoo.com

Received (in Cambridge, UK) 11th April 2002
First published as an Advance Article on the web 4th July 2002

Efficient Heck reaction in aqueous medium using Amberlite IRA-400 (basic) as a base is reported.

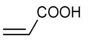
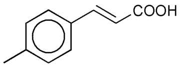
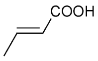
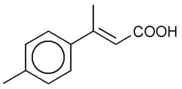
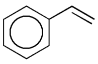
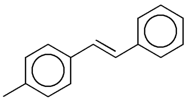
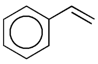
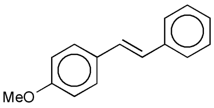
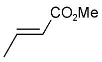
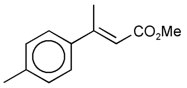
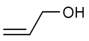
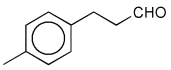
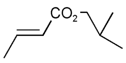
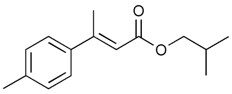
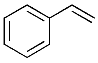
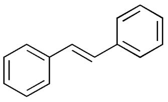
Introduction

The Heck reaction is a very convenient method for the formation of carbon–carbon bonds at unsubstituted vinylic positions.[1] This reaction is greatly facilitated when performed under phase transfer conditions using tetraalkylammonium salts in conjunction with an inorganic base[2] in organic solvents. Earlier green chemistry approaches to the Heck reaction have been the use of water under phase-transfer conditions,[3a–c] ionic liquids[4a,b] and polymer supports such as Amberlite.[5] We report here palladium-catalysed Heck coupling reactions using Amberlite IRA-400 (basic) as a base in water in high yield which are comparable with reported results (Scheme 1). The results are summarized in Table 1.

Green Context

The Heck reaction is an extremely valuable method for carbon–carbon bond formation and it is now widely used in the speciality chemical and pharmaceutical manufacturing industries. Like so many organic reactions it is traditionally run in an organic solvent so that solvent losses are typically the main source of pollution. Here we see how, with the correct choice of catalyst and base, reactions can be successfully run in eco-friendly water as solvent. ***JHC***

Table 1 Heck reaction of *p*-iodotoluene/*p*-iodoanisole/bromobenzene

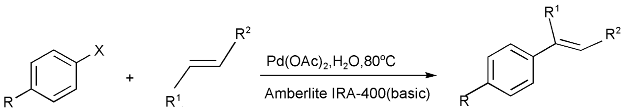
Entry	Olefin	Product	Reaction time/h	Yield[a] (%)	Physical constant[b]/°C	
					Obs.	Lit.
1			7	72.3	196–198	198–199[9a]
2			7	68.5	128–130	128–130[9d]
3			4	76.3	118–120	120[9a]
4			4	71.0	134–136	135–136[9c]
5			7	70.0	275 (l)	275 (l)[9d]
6			7	69.5	220–224 (l)	220–230 (l)[9a]
7			10	73.4	260 (l)	260 (l)[9a]
8			6	63.0	122	122–124[9b]

[a] Yields refer to pure isolated products. [b] (l) = liquid and bp quoted; otherwise mp.

---

† Dedicated to the memory of Late Dr Nitiraj R. Mane.

DOI: 10.1039/b203592h



R = H,-Me,-OMe, X = Br, I
R^1 = -H,-Me
R^2 = -COOH,-C_6H_5,-CO_2Me,- CH_2OH,-$CO_2CH_2CH(Me)_2$, etc.

Scheme 1

Results and discussion

A base is generally added to the Heck reaction[6] to regenerate Pd(0) from 'HPdX' by neutralization of HX. In the Heck reaction cycle, after the migratory insertion comes the step in which Pd(0) is released by 'HPdX' elimination to give alkene. The termination occurs by nucleophilic attack at Pd, which either by nucleophilic substitution or by reductive elimination of co-ordinated nucleophile leads to the release of Pd(0). If PdH is not scavenged rapidly by base, readdition to the double bond may occur with isomerisation. The Amberlite resin acts as a base and is converted into a quaternary ammonium salt which might also be assisting the Heck reaction. There are reports in the literature,[7,8] that quaternary ammonium salts can effect the reduction of Pd(II) to Pd(0) and thus stabilize the palladium catalyst, leading to acceleration of the Heck reaction. Thus, the use of Amberlite IRA-400 (basic) serves dual purpose in assisting Heck reaction in aqueous medium as a base and as a phase-transfer catalyst after salt formation.

The reaction is clean, simple and the resin can be regenerated and recycled. The work-up procedure is simple compared to those applied for other bases.

Experimental

A mixture of palladium acetate (45 mg, 0.2 mmol), aryl halide (20 mmol), olefinic compound (25 mmol) and Amberlite IRA-400 (basic) 3 g in water (6 ml) was stirred at 80 °C for 4–10 h. The mixture was cooled and filtered to remove the resin which was washed with diethyl ether. The ether layer was separated and the aqueous layer extracted with ether. The combined ether extract was washed with water and dried over anhydrous sodium sulfate. Removal of ether furnished the products which were purified by crystallization or by distillation.

Acknowledgement

S. B. S. thanks U.G.C. New Delhi for the award of a Teacher Fellowship.

References

1 (*a*) R. F. Heck, *J. Am. Chem. Soc.*, 1968, **90**, 5518; (*b*) R. F. Heck, *Org. React.*, 1982, **27**, 345; (*c*) R. F. Heck, *Palladium Reagents in Organic Synthesis*, Academic Press, London, 1985; (*d*) J. Tsuji, *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*, John Wiley & Sons, Chichester, 1995; (*e*) A. de Meijere and F. F. Meyer, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2379; (*f*) W. Cabri and I. Candiani, *Acc. Chem. Res.*, 1995, **28**, 2; (*g*) S. Brase and A. de Meijere, in *Metal Catalyzed Cross-Coupling Reactions*, ed. F. Diederich and P. J. Stang, Wiley, New York, 1998, ch. 3; (*h*) N. J. Whitecombe, K. K. Hii and S. E. Gibson, *Tetrahedron*, 2001, **57**, 7449–7476.

2 (*a*) T. Jeffery, *J. Chem. Soc., Chem. Commun.*, 1984, 1287; (*b*) T. Jeffery, *Tetrahedron Lett.*, 1985, **26**, 2667; (*c*) T. Jeffery, *Tetrahedron Lett.*, 1990, **31**, 6641.

3 (*a*) T. Jeffery, *Tetrahedron Lett.*, 1994, **35**, 3051; (*b*) N. A. Bumagin, V. V. Bykov, L. I. Sukhomlinora, T. P. Tolstaya and I. P. Beletskaya, *J. Organomet. Chem.*, 1995, **486**, 259; (*c*) J. X. Wang, Z. L. Y. Hu, B. Wei and L. Bai, *J. Chem. Res. (S)*, 2000, 484–485.

4 (*a*) A. J. Carmichael, M. J. Earle, J. D. Holbrey, P. B. McCormac and K. R. Seddon, *Org. Lett.*, 1999, **1**, 997–1000; (*b*) R. Sheldon, *Chem. Commun.*, 2001, 2399–2407.

5 G. Bouhadir and B. Meunier, *Patent WO 01/43874 A1*, publication date 20010621, CAN 13561142.

6 R. Benhaddou, S. Czernecki and G. Ville, *J. Chem. Soc., Chem. Commun.*, 1988, 247.

7 I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009–3066.

8 R. R. Deshmukh, R. Rajagopal and K. V. Srinivasan, *Chem. Commun.*, 2001, 1544.

9 (*a*) *Dictionary of Organic Compounds*, ed. J. Buckingham and F. Macdonald, Chapman and Hall, London, 5th edn., 1982; (*b*) *Aldrich Catalog Handbook of Fine Chemicals*, 1998–1999, p. 1525; (*c*) *Dictionary of Organic Compounds*, ed. J. R. A. Pollock and R. Steyens, Eyre and Spottiswoode (Publishers) Ltd., London, 4th edn., 1965; (*d*) S. B. Solabannavar, V. B. Helvi, U. V. Desai and R. B. Mane, *Synth. Commun.*, 2002, in press.

Combined microwave and ultrasound assisted Williamson ether synthesis in the absence of phase-transfer catalysts

Yanqing Peng[ab] **and Gonghua Song***[ab]

[a] *Institute of Pesticides & Pharmaceuticals, East China University of Science & Technology, Shanghai 200237, China. E-mail: ghsong@ecust.edu.cn*
[b] *Shanghai Key Laboratory of Chemical Biology, Shanghai 200237, China*

Received 11th February 2002
First published as an Advance Article on the web 4th July 2002

The combined microwave and ultrasound assisted Williamson reaction proves an efficient and ecologically valuable route for preparing ethers in the absence of organic auxiliary substances such as phase-transfer catalysts.

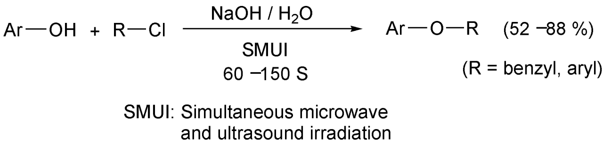
Introduction

The Williamson reaction is a very useful transformation in organic synthesis since the products are of value in both industrial and academic applications.[1] The Williamson synthesis usually involves the employment of an alkali-metal salt of the hydroxy compounds and halides. These reactions are generally performed using organic solvents[2] or with phase-transfer catalysts[3] and followed by refluxing for several hours.

The application of ultrasonic irradiation in a wide variety of chemical transformations has gained significant potential in the last two decades.[4] A number of PTC-catalyzed reactions have also been shown to benefit from the mass transport enhancement by sonication.[5] The employment of microwave techniques for chemical synthesis has also attracted considerable interest in recent years.[6] The reason is that this technology can enhance the selectivity and reactivity, increase the chemical yields and shorten the reaction time. Recently, many studies have reported a dramatic rate increase in phase-transfer catalysis under microwave irradiation.[7]

It was reported many years ago that Williamson ether synthesis is promoted by ultrasound irradiation in the presence of phase-transfer catalysts.[8] Microwave irradiation has also been found to be a valuable tool to accelerate this reaction. Some of these microwave-assisted reactions have been carried out either in homogeneous alcoholic solutions[9] or by using solid alkali-metal phenolates.[10] In contrast, many microwave-assisted Williamson reactions have been performed in the presence of phase-transfer catalysts, *e.g.* quaternary ammonium salts[11] or polyethylene glycol.[12]

Although the chemical effects of simultaneous microwave and ultrasound irradiation (abbreviated SMUI) in some organic reactions has been mentioned several years ago,[13] as yet, however, the application of this promising technique in organic synthesis has not received much attention. Recently, we have found that the combination of simultaneous microwave and ultrasound irradiation is highly advantageous in the aqueous–organic biphase hydrazinolysis of esters due to the substantial enhancement of heat and mass transfer.[14] Integration of these two technologies would offer a general synthetic method, which would clearly augment existing techniques. Continuing our recent studies in the field of SMUI-assisted organic synthesis and broadening the application of this valuable protocol, we describe here Williamson ether synthesis promoted by SMUI in the absence of any auxiliary substances such as phase-transfer catalysts. It provides an efficient, economical and eco-friendly method for preparing useful ethers (Scheme 1).



$$\mathrm{Ar{-}OH} + \mathrm{R{-}Cl} \xrightarrow[\text{SMUI}\ 60-150\ \text{S}]{\mathrm{NaOH}/\mathrm{H_2O}} \mathrm{Ar{-}O{-}R}\quad (52-88\ \%)\quad (\mathrm{R} = \text{benzyl, aryl})$$

Scheme 1

To demonstrate the general applicability of this methodology, a serial of benzyl phenyl ethers and diphenyl ethers have been synthesized under SMUI.

Results and discussion

As outlined in Table 1, diphenyl and benzyl phenyl ethers were obtained in satisfactory yields. In comparison, 4-nitrophenol was less reactive under the employed experimental conditions and required 150 s to afford a 52% yield of 4-nitrophenyl benzyl ether (entry 5) whereas the yield reached 83% in 60 s with phenol (entry 1).

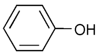
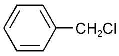
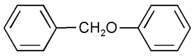
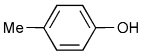
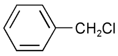
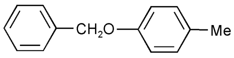
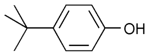
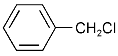
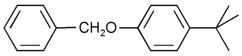
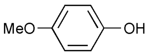
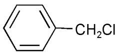
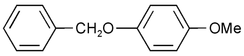
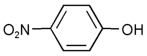
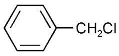
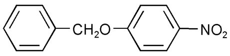
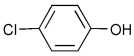
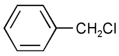
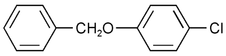
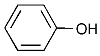
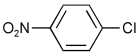
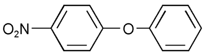
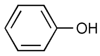
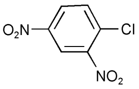
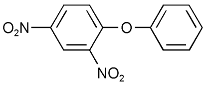
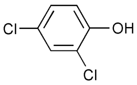
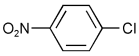
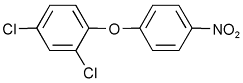
Control experiments have also been performed in order to indicate the superiority of combined microwave and ultrasound assisted reaction. The reaction between benzyl chloride and phenol in an organic–aqueous biphasic system without surfactants was chosen as a model under different reaction conditions (Table 2). As shown in the table, when reactants were magnetically stirred for 16 h under conventional reflux (benzyl chloride–phenol–NaOH = 12:10:20 mmol, monitored by TLC), only a 41% yield of benzyl phenyl ether was obtained. With sonication, a higher yield (67%) was achieved in 2 h. This reaction was also carried out under microwave irradiation

Green Context

The Williamson synthesis has been one of the most important routes to ethers for 150 years. As a synthetic procedure little has changed in that period with the familiar inorganic base–organic substrate compatibility problem requiring an organic solvent and a phase-transfer catalysis. Here we see a break from that tradition with a combination of microwave and ultrasound irradiation effectively removing the need for any auxiliaries. The chemicals required are reduced to substrates plus base and water—simplifying the process in keeping with the principles of green chemistry.
JHC

DOI: 10.1039/b201543a

Table 1 Combined microwave and ultrasound assisted Williamson ether synthesis

Entry	Phenol	Halide	Ether	Time/s	Yield[a] (%)
1				60	83
2				60	81
3				60	84
4				60	80
5				150	52
6				80	88
7				80	81
8				90	70
9				100	79

[a] All yields refer to isolated products which were characterized by mp and spectral (IR and ^{1}H NMR) data.

without stirring to gave a moderate yield (46%) of the desired product. Only 60 s was needed to obtain an 83% yield of ether under simultaneous microwave and ultrasound irradiation. These results indicated unambiguously the superiority of reaction under combined microwave and ultrasound irradiation in terms of reaction time and yield.

Irradiation of liquids by power ultrasound leads to cavitation phenomena: microbubbles present in the solution undergo growth, vibration and finally implosion. In liquid–liquid heterogeneous chemical systems, ultrasound irradiation can lead to beneficial processes at liquid–liquid or solid–liquid interfaces, such as microemulsification. It has been shown that the use of a two-phase system in conjunction with ultrasound irradiation is the method of choice to obviate the needs of phase-transfer catalysts, however, the accomplishment of these reactions also needs a relatively long duration.[15] Under SMUI, heterogeneous organic reactions could be accelerated dramatically in contrast to those by ultrasound irradiation alone.

Throughout the 1990s, there has been a move away from the ‘command and control’ approach to environmental protection to a more scientifically and economically beneficial approach known as green chemistry.[16] Two clauses of the 12 principles of green chemistry[17] are, (1) the use of auxiliary substances (*e.g.* solvents, separation agents, *etc.*) should be made unnecessary wherever possible or if used be innocuous; (2) energy requirements should be recognized for their environmental and economic impacts and should be minimized. Winterton[18] suggested that laboratory and research chemists should anticipate heat and mass transfer limitations to help them access the relative ‘greenness’ of a process.

SMUI provides highly efficient dielectric heating along with intensive mass transport in heterogeneous systems, resulting in dramatic reaction rate enhancement, reduction in energy consumption for chemical transformation, and heat emission to the environment (thermal pollution). Moreover, the obviation of organic solvents in SMUI-promoted organic reactions is another advantage for ecological protection.

Table 2 Heterogeneous Williamson synthesis of benzyl phenyl ether under different conditions

Run	Method	Time	Yield[a] (%)
1	Conventional reflux	16 h	41
2	Ultrasound (50 W) + reflux	2 h	67
3	Microwave (200 W)	50 min	46
4	SMUI (mw 200 W + us 50 W)	60 s	83

[a] Isolated yields.

Many surfactants are chemically inert and persist in the environment for a long period,[19] thus the influence of these compounds to the environment can not be ignored. For example, cationic surfactants, particularly quaternary ammonium salts, often have a rather strong cytotoxicity.[20] On the other hand, it is difficult to recover phase-transfer catalysts from a homogeneous solution. Therefore, the preclusion of phase-transfer catalysts by using the SMUI technique in heterogeneous organic synthesis is also profitable from the environmental point of view.

In summary, this method is simple, fast and environmentally friendly. The development of this combination technique might open an extremely promising new area in the field of organic synthesis.

Experimental

The combined microwave and ultrasound assisted Williamson reactions were carried out in the apparatus described previously.[14] The reagents and solvents are commercially available. All of the products are known compounds and identified by melting point data (uncorrected), IR (recorded on Nicolet Nexus 470 spectrophotometer in KBr) and ^{1}H NMR (recorded on a 500 MHz Bruker AM 500 spectrometer with TMS as internal standard) spectra.

General procedure

An organic–aqueous biphase mixture of 4-chlorophenol (1.28 g, 10 mmol), benzyl chloride (1.51 g, 12 mmol) and NaOH (0.80 g, 20 mmol) in 10 mL of water was introduced into a 25-mL two-necked Pyrex flask. The tip of a detachable horn was immersed just under the liquid surface in order to obtain optimal sonication. The ultrasound and microwave source were switched on successively (power level: ultrasound 50 W, microwave 200 W) and the mixture was irradiated by combined microwave and ultrasound irradiation for 80 s. On completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and the crude product was separated. Recrystallization from aqueous ethanol afforded 1.92 g (88% yield based on the phenol) of the pure ether.

Characterization data

Benzyl phenyl ether (1). Mp 40–41 °C (lit.[21] 40 °C); IR (KBr, cm^{-1}): 3040, 1540, 1500, 1460, 1030; δ_H ($CDCl_3$): 5.10 (s, 2H, CH_2), 7.00–7.31 (m, 5H, Ar-H), 7.35–7.43 (m, 5H, Ar-H).

Benzyl 4-methylphenyl ether (2). Mp 42–43 °C (lit.[22] 41 °C); IR (KBr, cm^{-1}): 3010, 1580, 1520, 1240, 1020; δ_H ($CDCl_3$): 2.18 (s, 3H, CH_3), 4.82 (s, 2H, CH_2), 6.85–7.10 (m, 4H, Ar-H), 7.30–7.44 (m, 5H, Ar-H).

Benzyl 4-*tert*-butylphenyl ether (3). Mp 64–65 °C (lit.[23] 63–64 °C); IR (KBr, cm^{-1}): 3015, 1605, 1510, 1370, 1250, 1025; δ_H ($CDCl_3$): 1.31 (s, 9H, *t*-Bu), 5.05 (s, 2H, CH_2), 6.88–7.45 (m, 9H, Ar-H).

Benzyl 4-methoxyphenyl ether (4). Mp 71 °C (lit.[24] 69–70 °C); IR (KBr, cm^{-1}): 3035, 1500, 1445, 1540, 1250, 1090, 1060; δ_H ($CDCl_3$): 3.56 (s, 3H, CH_3), 5.88 (s, 2H, CH_2), 6.70–7.05 (m, 4H, Ar-H), 7.33–7.56 (m, 5H, Ar-H).

Benzyl 4-nitrophenyl ether (5). Mp 108 °C (lit.[25] 106–107 °C); IR (KBr, cm^{-1}): 3050, 1600, 1580, 1500, 1350, 1250, 1010; δ_H ($CDCl_3$): 5.12 (s, 2H, CH_2), 7.00 (d, 2H, Ar-H), 7.34 (s, 5H, Ar-H), 8.14 (d, 2H, Ar-H).

Benzyl 4-chlorophenyl ether (6). Mp 69–70 °C (lit.[23] 70–72 °C); IR (KBr, cm^{-1}): 3060, 1510, 1450, 1250, 1025; δ_H ($CDCl_3$): 5.08 (s, 2H, CH_2), 6.77 (d, 2H, Ar-H), 7.16 (d, 2H, Ar-H), 7.32–7.46 (m, 5H, Ar-H).

4-Nitrodiphenyl ether (7). Mp 61–62 °C (lit.[21] 61–61.5 °C); IR (KBr, cm^{-1}): 2930, 1590, 1530, 1490, 1340, 1250, 1010; δ_H ($CDCl_3$): 6.65–7.60 (m, 7H, Ar-H), 7.83-8.30 (m, 2H, Ar-H).

2,4-Dinitrophenyl phenyl ether (8). Mp 69–70 °C (lit.[26] 69–70 °C); IR (KBr, cm^{-1}): 3090, 1590, 1540, 1525, 1480, 1350, 1280; δ_H ($CDCl_3$): 7.10–7.61 (m, 6H, Ar-H), 8.43 (m, 1H, Ar-H), 8.91 (m, 1H, Ar-H).

2,4-Dichlorophenyl 4-nitrophenyl ether (9). Mp 72 °C (lit.[27] 71–72 °C); IR (KBr, cm^{-1}): 3050, 1610, 1585, 1520, 1430, 1360, 1260; δ_H ($CDCl_3$): 7.24 (m, 1H, Ar-H), 7.24–7.58 (m, 4H, Ar-H), 8.17(m, 2H, Ar-H).

Acknowledgements

This work was partially supported by National Nature Science Foundation of China.

References

1 A. W. Williamson, *J. Chem. Soc.*, 1852, **4**, 229; O. C. Dermer, *Chem. Rev.*, 1934, **14**, 409; A. Hassner and C. Stumer, *Organic Syntheses Based on Name Reactions and Unnamed Reactions*, Pergamon, Kidlington, 1994, p. 419.

2 S. R. Sandler and W. Karo, *Organic Funtional Group Preparations, I*, Academic Press, New York, 1983, p. 132.

3 F. Montanari and P. Tundo, *J. Org. Chem.*, 1981, **46**, 2125; J. G. Heffernan and D. C. Sherrington, *Tetrahedron Lett.*, 1983, **24**, 1661; R. Neumann and Y. Sasson, *J. Mol. Catal.*, 1985, **31**, 81; C. J. Thoman, T. D. Habeeb, M. Huhn, M. Korpusik and D. F. Slish, *J. Org. Chem.*, 1989, **54**, 4476; J. Alvarez-Builla, J. J. Vaquero, J. L. Garcia Navio, J. F. Cabello, C. Sunkel, M. Fau de Casa-Juana, F. Dorrego and L. Santos, *Tetrahedron*, 1990, **46**, 967; S. N. Tan, R. A. Dryfe and H. H. Girault, *Helv. Chim. Acta*, 1994, **77**, 231.

4 N. Serpone and P. Colarusso, *Res. Chem. Intermed.*, 1994, **20**, 635–679; T. J. Mason, *Chem. Soc. Rev.*, 1997, **26**, 443; P. Cintas and J-L. Luche, *Green Chem.*, 1999, **1**, 115.

5 I. Z. Shirgaonkar and A. B. Pandit, *Ultrason. Sonochem.*, 1996, **3**, S135; J-X. Wang and K. Zhao, *Synth. Commun.*, 1996, **26**, 1617; B. S. Bhatkhande and S. D. Samant, *Ultrason. Sonochem.*, 1998, **5**, 7; R. Guilet, J. Berlan, O. Louisnard and J. Schwartzentruber, *Ultrason. Sonochem.*, 1998, **5**, 21; X. Li, J. Santos and X. R. Bu, *Tetrahedron Lett.*, 2000, **41**, 4057.

6 A. Loupy, A. Petit, J. Hamelin, F. Texier-Boullet, P. Jacquault and D. Mathé, *Synthesis*, 1998, 1213; R. S. Varma, *Green Chem.*, 1999, **1**, 43; C. R. Strauss, *Aust. J. Chem.*, 1999, **52**, 83; R. S. Varma, *Pure Appl. Chem.*, 2001, **73**, 193; P. Lidstrom, J. Tierney, B. Wathey and J. Westman, *Tetrahedron*, 2001, **57**, 9225.

7 Z. Finta, Z. Hell and L. Toke, *J. Chem. Res. (S)*, 2000, 242; J-X. Wang, Z. Liu, Y. Hu, B. Wei and L. Bai, *J. Chem. Res. (S)*, 2000, 484; J-X. Wang, L. Bai and Z. Liu, *Synth. Commun.*, 2000, **30**, 971; J. Li, J. Pang, G. Cao and Z. Xi, *Synth. Commun.*, 2000, **30**, 1337; S. Chatti, M. Bortolussi and A. Loupy, *Tetrahedron Lett.*, 2000, **41**, 3367; S. Chatti, M. Bortolussi and A. Loupy, *Tetrahedron*, 2000, **56**, 5877; D. Bogdal and M. Warzala, *Tetrahedron*, 2000, **56**, 8769; S. Chatti, M. Bortolussi and A. Loupy, *Tetrahedron*, 2001, **57**, 4365; H. Rodriguez, R. Perez, M. Suarez, A. Lam, N. Cabrales and A. Loupy, *Heterocycles*, 2001, **55**, 291; For a recent review, see: S. Deshayes, M. Liagre, A. Loupy, J-L. Luche and A. Petit, *Tetrahedron*, 1999, **55**, 10851 and references therein.

8 R. S. Davidson, A. Safdar, J. D. Spencer and B. Robinson, *Ultrasonics*, 1987, **25**, 35.

9 R. N. Gedye, F. E. Smith, K. Westway, H. Ali, L. Baldisera and L. Laberge, *Tetrahedron Lett.*, 1986, **27**, 279; R. N. Gedye, F. E. Smith and K. Westway, *Can. J. Chem.*, 1988, **66**, 17; G. Majetich and R. Hicks, *Res. Chem. Intermed.*, 1994, **20**, 61.

10 J-X. Wang, M. Zhang, Z. Xing and Y. Hu, *Synth. Commun.*, 1996, **26**, 301; G. Bratulescu, Y. Le Bigot and M. Delmas, *Synth. Commun.*, 1997, **27**, 1037.

11 Y. Yuan, D. Gao and Y. Jiang, *Synth. Commun.*, 1992, **22**, 2117; Y. Jiang, J. Pang and Y. Yuan, *Chin. Chem. Lett.*, 1994, **5**, 29; D. Bogdal, J. Pielichowski and A. Boron, *Synth. Commun.*, 1998, **28**, 3029; Y. Yuan, Y. Jiang, J. Pang, X. Zhang and C. Yang, *Gazz. Chim. Ital.*, 1993, **123**, 519; D. Bogdal, J. Pielichowski and K. Jaskot, *Org. Prep. Proc. Int.*, 1998, **30**, 427.

12 J-X. Wang, M. Zhang and Y. Hu, *Synth. Commun.*, 1998, **28**, 2407.

13 F. Chemat, M. Poux, J-L. Di Martino and J. Berlan, *J. Microwave Power Electromag. Energy*, 1996, **31**, 19; F. Chemat, M. Poux and S. A. Galema, *J. Chem. Soc., Perkin Trans. 2*, 1997, 2371.

14 Y. Peng and G. Song, *Green Chem.*, 2001, **3**, 302.

15 S. Moon, L. Duchin and J. V. Cooney, *Tetrahedron Lett.*, 1979, **19**, 3917; S. L. Regen and A. Singh, *J. Org. Chem.*, 1982, **47**, 1587; R. S. Varma, K. P. Naicker and D. Kumar, *J. Mol. Catal. A: Chem.*, 1999, **149**, 153.

16 P. T. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, 2000.

17 P. T. Anastas, L. B. Bartlett, M. M. Kirchhoff and T. C. Williamson, *Catal. Today*, 2000, **55**, 11.

18 N. Winterton, *Green Chem.*, 2001, **3**, G73.

19 R. D. Swisher, *Surfactant Biodegradation*, 2nd edn., Marcel Dekker, New York, 1987.

20 E. Jungermann, *Cationic Surfactants*, Marcel Dekker, New York, 1970.

21 J. Buckingham and S. M. Donaghy, *Dictionary of Organic Compounds*, Chapman and Hall, New York, NY, 5th edn., 1982.

22 N. M. Cullinane, R. A. Woolhouse and G. B. Carter, *J. Chem. Soc.*, 1962, 2995.

23 K. Dilts and M. Durand, *J. Chem. Educ.*, 1990, **67**, 74.

24 M. Paventi and A. S. Hay, *J. Org. Chem.*, 1991, **56**, 5875.

25 E. J. Rowe, K. L. Kaufman and C. Piantadosi, *J. Org. Chem.*, 1958, **23**, 1622.

26 D. Ayediran, T. O. Bamkole, J. Hirst and I. Onyido, *J. Chem. Soc., Perkin Trans. 2*, 1977, 1580.

27 K. Naumann, A. Creuzburg and S. Heidenreich, *Chem.Abstr.*, 1971, **74**, 42137h.

The allylic oxidation of unsaturated steroids by *tert*-butyl hydroperoxide using surface functionalised silica supported metal catalysts

Jorge A. R. Salvador and James H. Clark*

Clean Technology Centre, Chemistry Department, University of York, York, UK YO10 5DD.
E-mail: jhc1@york.ac.uk

Received 11th February 2002
First published as an Advance Article on the web 28th June 2002

Metal complexes based on Co(II), Cu(II), Mn(II) and V(II) immobilised on mesoporous silica, efficiently catalyse the selective allylic oxidation of unsaturated steroids and valencene, and can be easily recovered and reused.

Introduction

Allylic oxidation is a fundamental organic reaction of significant interest to organic chemists with applications in areas ranging from agricultural products to pharmaceuticals.[1,2] The allylic oxidation of steroids is a particularly important subject and has attracted interest over many years. The Δ^5-steroids can be oxidised to 5-en-7-ones, which are known as inhibitors of sterol biosynthesis and have some use in cancer chemotherapy.[3]

The allylic oxidation of unsaturated steroids such as Δ^5-steroids, has traditionally been performed with chromium reagents such as CrO_3–pyridine complex,[4] CrO_3 and 3,5-dimethylpyrazole,[5] pyridinium chlorochromate, (PCC),[6,7] pyridinium dichromate (PDC),[7] sodium chromate,[8] sodium dichromate in acetic acid,[9] pyridinium fluorochromate,[10] and 3,5-dimethylpirazolium fluorochromate(VI).[11] However, the great excess of ecologically and physiologically undesirable chromium reagent and the large volume of solvent required in these procedures, in combination with the difficult work-up and the production of environmentally hazardous chromium residues, causes such procedures to be inconvenient on a commercial scale.

Of greater preparative interest has been the use of hydroperoxides combined with different types of catalyst.[12–19] Despite the good yields reported with CrO_3,[12] hexacarbonylchromium $Cr(CO)_6$,[13,14] pyridinium dichromate,[15] and $RuCl_3$[16] to prepare allylic oxidation products from Δ^5-steroids, the toxicity of the chromium compounds and the high cost of the ruthenium catalyst hinders commercialisation of the procedures.

More environmentally acceptable methods based on the use of copper salts and copper metal have been reported[19] but a difficult separation step is needed to remove the catalyst which cannot easily be recovered and reused.

Hence there is need for a simple, efficient, safe and cost effective procedure for selectivity effecting the allylic oxidation of steroids and especially where the separation stages of the reaction are simple and enable catalyst recycling.

The heterogenisation of inorganic reagents and catalysts useful in organic reactions is a very important area[20] and led us to recently report the use of $Co(OAc)_2{\cdot}4H_2O$ as catalyst in heterogeneous forms for this type of allylic oxidation reaction.[21]Here we report the use of other steroids and non-steroids compounds as substrates and cobalt, copper, manganese and vanadium catalysts in heterogeneous forms (prepared as reported previously,[22,23] Fig. 1) for this type of reaction.

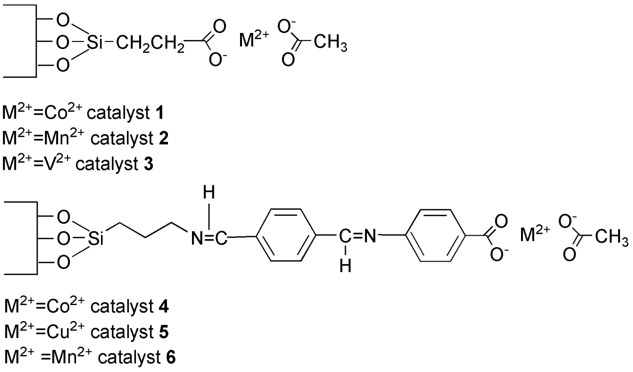


Fig. 1

Results and discussion

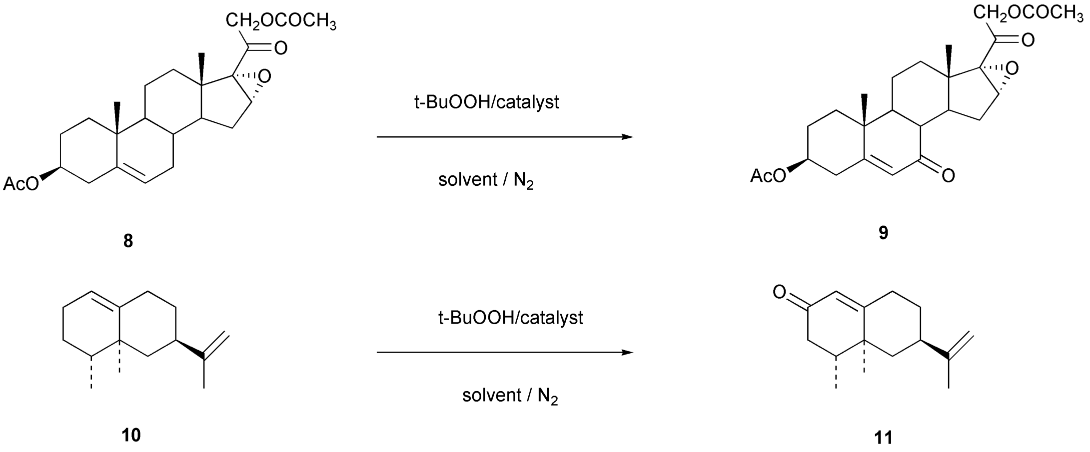
Recently we reported the use of $Co(OAc)_2{\cdot}4H_2O$ as catalyst in heterogeneous forms (catalyst **1**, $Co(OAc)_2/SiO_2$, catalyst **2** and **5**) for this type of allylic oxidation reaction.[21] In order to ascertain the efficacy of the oxidative system (*t*-BuOOH/catalyst **2**) a more polar substrate, the steroid **8** was used as substrate leading to the formation of the allylic oxidation product **9** in a very high yield and very high selectivity, (Scheme 1, Table 1).

Similar oxidation can be performed on valencene **10**. Using the catalyst **2**, the sesquiterpenoid nootkatone **11**, a major contributor to the aroma of grapefruit present in commercial flavourings was the major product (75%), although the catalyst **5** gave the nootkatone in 70% yield, (Table 1).

Green Context

The oxidation of naturally occurring alkenes such as steroids and terpenoid compounds can lead to a range of very useful products. Usaing traditional oxidants is wasteful and alternatives are required. Here, the use of various transition metal salts attached to silica as catalysts in such oxidations is described, with *tert*-butyl hydroperoxide as primary oxidant. Products are formed in good to excellent yields. This paper demonstrates that the promising results with these catalysts using model compounds can be transferred to bulkier substrates. *DJM*

DOI: 10.1039/b201500p



Scheme 1

Table 1 Allylic oxidation with cobalt catalyst

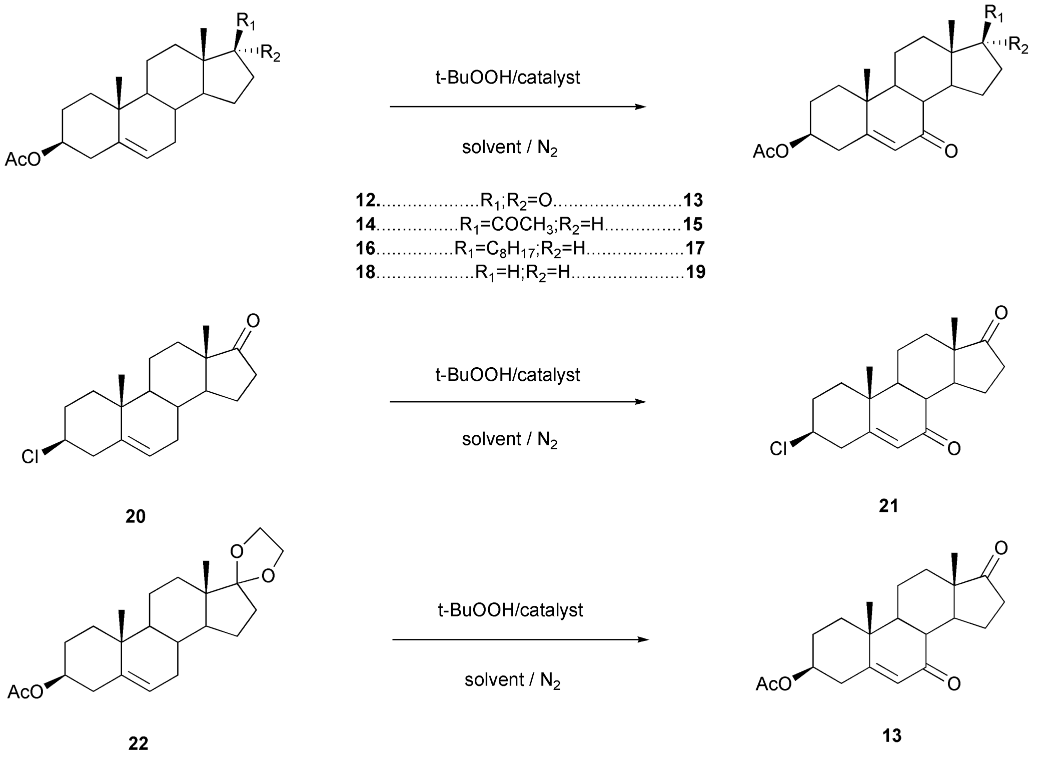
Substrate/mmol	*t*-BuOOH[a]/ml	Catalyst/cobalt mmol	Solvent	Time/h	Temp./°C	Product	Isolated yield (%)
8/0.16	0.2	**1**/0.002	CH_3CN	20	50	**9**	84[b]
10/2.45	2.4	**1**/0.018	CH_3CN	24	55	**11**	75[c]
10/2.45	2.4	**4**/0.025	CH_3CN	24	55	**11**	70[c]

[a] 5.0–6.0 M solution in decane (Aldrich). [b] Traces of starting material and a by product are visible in TLC plates but not detectable in ^1H NMR spectrum (300 MHz) of the crude product. [c] Recovered by flash chromatography (ethyl acetate–light petroleum (bp 40–60 °C).

Despite the good yields with the copper catalyst in homogeneous conditions reported in a previous communication[19] the catalyst cannot be easily recovered and reused which encouraged us to use heterogeneous forms of a copper catalyst **5** for this type of allylic oxidation reaction.Using Δ^5-steroids **8**, **12–22** and valencene **10** as substrates (Schemes 1 and 2) allylic oxidation products **9**, **13–21** and **11** were obtained in very high isolated yields, 72–86% (Table 2).The reactions were generally performed in acetonitrile except for the substrate **16** which required benzene as solvent.

These reactions are very selective compared to those carried out using $Fe(acac)_3$ as catalyst reported by Kimura and Muto.[17] $Mo(CO)_6$ has also been described as a catalyst for this reaction but this led to epoxidation of the cholesteryl acetate under similar oxidative conditions.[18] On the contrary, using manganese catalysts **2** and **6** and vanadium catalyst **3**, the allylic oxidation occurs in very good yields (Table 3).

While the product yields of the allylic oxidations are very similar under homogeneous[19] and heterogeneous conditions the easier recovery of the catalyst in heterogeneous conditions,



Scheme 2

Table 2 Allylic oxidation with copper catalyst

Substrate/mmol	*t*-BuOOH[a]/ml	Catalyst/copper mmol	Solvent	Time/h	Temp./°C	Product	Isolated yield (%)
8/0.16	0.2	**5**/0.0004	CH_3CN	18	50	**9**	85
10/2.45	2.4	**5**/0.008	CH_3CN	24	50	**11**	75[c]
12/2	2.4	**5**/0.006	CH_3CN	18	55	**13**	86
12/2	2.4	**5**/recycled	CH_3CN	24	55	**13**	84
14/2	2.4	**5**/0.006	CH_3CN	20	55	**15**	81[b]
14/2	2.4	**5**/recycled	CH_3CN	20	55	**15**	79[b]
16/1	1.2	**5**/0.06	Benzene	48	70	**17**	72[c]
18/2	2.4	**5**/0.006	CH_3CN	24	55	**19**	74[c]
20/1	1.2	**5**/0.01	CH_3CN	24	55	**21**	78[c]
22/1	1.2	**5**/0.003	CH_3CN	24	55	**13**	80
23/0.53	0.6	**5**/0.002	CH_3CN	10	55	**24**	72[c]
25/1	1.2	**5**/0.01	CH_3CN	24	55	**26**	75[c]

[a] 5.0–6.0 M solution in decane (Aldrich). [b] Traces of starting material and a by product are visible in TLC plates but not detectable in ^{1}H NMR spectrum (300 MHz) of the crude product. [c] Recovered by flash chromatography (ethyl acetate–light petroleum (bp 40–60 °C).

Table 3 Allylic oxidation with manganese and vanadium catalysts

Substrate/mmol	*t*-BuOOH[a]/ml	Catalyst/metal mmol	Solvent	Time/h	Temp./°C	Product	Isolated yield (%)
12/2	2.4	**2**/0.06	CH_3CN	24	55	**13**	82[b]
12/2	2.4	**3**/0.06	CH_3CN	24	55	**13**	73[c]
12/2	2.4	**6**/0.082	CH_3CN	24	55	**13**	81[b]
12/2	2.4	**6**/recycle	CH_3CN	24	55	**13**	77[b]

[a] 5.0–6.0 M solution in decane (Aldrich). [b] Traces of starting material and a by product are visible in TLC plates but not detectable in ^{1}H NMR spectrum (300 MHz) of the crude product. [c] Recovered by flash chromatography (ethyl acetate–light petroleum (bp 40–60 °C).

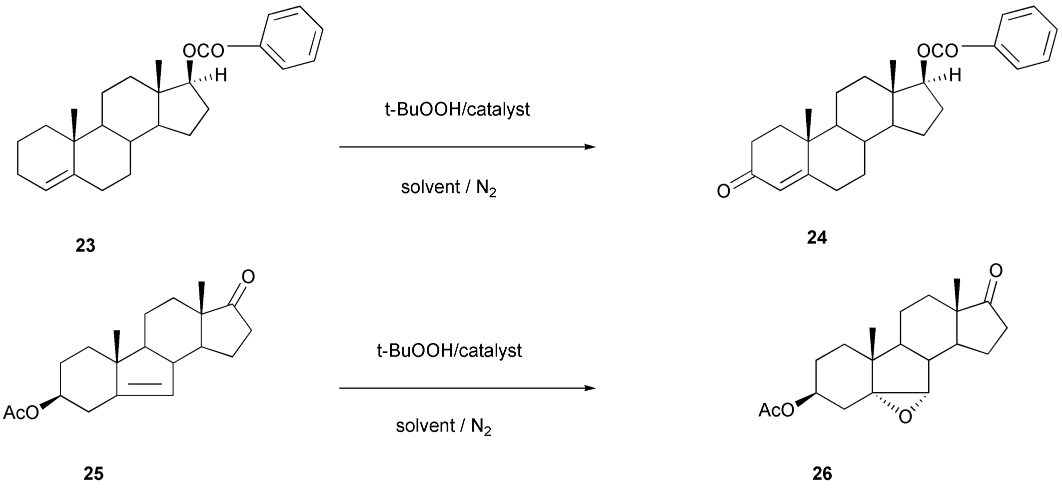
make these more environmentally friendly processes. Furthermore, using the heterogeneous catalysts **5** and **6**, it was possible to reuse the catalyst with only a small reduction in the products yields, under similar experimental conditions (79% for recycled catalyst **5**, Table 2, and 77% for recycled catalyst **6**, Table 3).

No significant reaction occurs in the absence of catalyst or in the presence of the catalyst support only. The dioxolane group present in the steroid **22** was removed in the presence of the copper catalyst **5** corroborating the previous findings.[24] The catalytic process is also effective for other unsaturated steroids. The substrate **23** gives testosterone benzoate **24** in a yield of 72% (Scheme 3).

The use of 3β-acetoxy-7-nor-androst-5-en-17-one **25** as substrate prepared according to the method of Knof[25] led us to obtain the 5α,6α-epoxide **26** as the major product. The absence of C-7 and the fact that the axial hydrogen at C-4 lies on the more hindered β-face of the molecule reduces the tendency of β-nor-5-enes to undergo allylic oxidative reactions involving bulky reagents that may initially coordinate to the double bond. Thus the axial attack on the π-system of 3β-acetoxy-7-nor-androst-5-en-17-one **25** will be favoured from the less-hindered α-face leading to the formation of the 5α,6α-epoxide **26**.

Conclusions

In conclusion, we have discovered an efficient and relatively environmentally friendly method for allylic oxidation of unsaturated steroids and valencene in very good yields and high selectivity.The reaction requires *t*-BuOOH as oxidant and a supported and easily recoverable and reusable catalyst such as Co(II), Cu(II), Mn(II), and V(II).



Scheme 3

Experimental

The steroids used as substrates were commercially available from Sigma and Aldrich. Reaction solvents were distilled before use according to standard procedures. Kieselgel 60 HF_{254}/Kieselgel 60G was used for TLC analysis. Melting points were determined with a Reichert microscope apparatus and were uncorrected. IR spectra were performed in a JASCO FT/IR-420 spectrophotomer.^{1}H and ^{13}C NMR were recorded on a Bruker AMX 300 in $CDCl_3$ solution with Me_4Si as internal standard.

Allylic oxidation catalized by cobalt catalyst (general procedure)

In a typical reaction, to a solution of valencene **10** (0.54 ml/2.45 mmol) in acetonitrile (15 ml) under nitrogen, catalyst **4** (0.06 g/0.025 mmol) and *tert*-butyl hydroperoxide (*ca.* 2.4 ml/12 mmol) were added. After 24 h under magnetic stirring at 55 °C, the catalyst was removed by filtration and the solution was poured into sodium sulfite solution (10% aq.) and extracted with diethyl ether. The extract was washed with an aq. saturated solution of $NaHCO_3$, water, dried and evaporated to dryness. The residue after flash chromatography (light petroleum (bp 40–60 °C)–ethyl acetate) gave nootkatone **11** (0.40 g, yield 75%). Mp 30–32 °C, lit.,[26] 33–35 °C; IR: 1617, 1662, 2967, 3024, 3078 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.93 (d, J = 6.8 Hz, 3H, 15-H_3), 1.07 (s, 3H, 14-H_3), 1.69 (s, 3H, 13-H_3), 4.69 (m, 2H, 12-H_2), 5.72 (s, 1H, 1-H_1); ^{13}C NMR ($CDCl_3$,75 MHz): δ 109.12 (C^{12}), 124.44 (C^1), 148.87 (C^{11}), 170.82 (C^{10}), 199.79 (C^2).

Allylic oxidation catalized by copper catalyst (general procedure)

In a typical reaction, to a solution of 20-oxopregn-5-en-3β-yl acetate **14** (0.72 g/2 mmol) in acetonitrile (12 ml) under nitrogen, catalyst **5** (0.015 g/0.006 mmol) and *tert*-butyl hydroperoxide (*ca.* 2.4 ml/12 mmol) were added. After 20 h under magnetic stirring at 55 °C, the catalyst was removed by filtration and the solution was poured into sodium sulfite solution (10% aq.) and extracted with diethyl ether. The extract was washed with an aq. saturated solution of $NaHCO_3$, water, dried and evaporated to dryness to give 7,20-dioxopregn-5-en-3-β-yl acetate **15** (0.60 g, yield 81%), mp 151–152 °C (MeOH), lit.,[27]153–153.5 °C; IR: 1243, 1630, 1670, 1704, 1726, 2945, 3012 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.65 (s, 3H, 18-H_3), 1.21 (s, 3H, 19-H_3), 2.05 (s, 3H, CH_3CO), 2.13 (s, 3H, 21-H_3), 4.72 (m, 1H, 3α-H), 5.72 (m, 1H, 6-H); ^{13}C NMR ($CDCl_3$,75 MHz): δ 72.00 (C^3) 126.41 (C^6), 164.13 (C^5), 170.23 (CH_3CO), 201.11 (C^7), 209.64 (C^{20}).

9. Mp 175–177 °C (ethyl acetate–*n*-hexane); IR: 1230, 1671, 1721, 1731, 1752, 2945 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.12 (s, 3H, 18-H_3), 1.22 (s, 3H, 19-H_3), 2.05 (s, 3H, CH_3CO), 2.15 (s, 3H, CH_3COO at C^{21}), 3.82 (s, 1H, 16β-H), 4.65 (q_{AB}, δ_A = 4.71, δ_B = 4.61, J_{AB} = 17.4 Hz, 2H, 21-H_2), 4.72 (m, 1H, 3α-H), 5.72 (m, 1H, 6-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 61.98 (C^{16}), 65.84 (C^{21}), 69.53 (C^{17}), 71.90 (C^3), 126.25 (C^6), 164.93 (C^5), 170.24, 170.30 (2 × CH_3CO), 199.37 (C^{20}), 200.57 (C^7).

13. Mp 181–183 °C (MeOH); lit.,[28] 184 °C; IR: 1231, 1627, 1671, 1723, 1739, 2951, 3008 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.9 (s, 3H, 18-H_3), 1.24 (s, 3H, 19-H_3), 2.05 (s, 3H, CH_3CO), 4.73 (m, 1H, 3α-H), 5.76 (m, 1H, 6-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 71.90 (C^3), 126.43 (C^6), 164.79 (C^5), 170.19 (CH_3CO), 200.66 (C^7), 220.14 (C^{17}).

17. Mp 156–158 °C (MeOH); lit.,[4] 157–158 °C; IR: 1237, 1629, 1669, 1730, 2938, 3028 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.68 (s, 3H, 18-H_3), 1.21 (s, 3H, 19-H_3), 0.86 (d, J = 6.6 Hz, 6H, 26-H_3, 27-H_3), 0.92 (d, J = 6.6 Hz, 3H, 21-H_3), 2.05 (s, 3H, CH_3CO), 4.69 (m, 1H, 3α-H), 5.70 (m, 1H, 6-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 72.17 (C^3), 126.64 (C^6), 163.82 (C^5), 170.22 (CH_3CO), 201.87 (C^7).

19. Mp 177–179 °C (EtOH–H_2O); lit.,[29] 178–180 °C; IR: 1234, 1667, 1725, 2940 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.72 (s, 3H, 18-H_3), 1.21 (s, 3H, 19-H_3), 2.06 (s, 3H, CH_3CO), 4.72 (m, 1H, 3d-H), 5.72 (m, 1H, 6-H); ^{13}C NMR ($CDCl_3$,75 MHz): δ 72.84 (C^3), 127.28 (C^6), 164.84 (C^5), 171.00 (CH_3CO), 202.58 (C^7).

21. Mp 189–191 °C (MeOH); lit.,[30] 189–191 °C; IR 1457, 1652, 1730, 2943, 3030 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.90 (s, 3H, 18-H_3), 1.25 (s, 3H, 19-H_3), 3.84 (m, 1H, 3α-H), 5.74 (m, 1H, 6-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 57.92 (C^3), 125.90 (C^6), 164.82 (C^5), 200.81 (C^7), 220.22 (C^{17}).

24. Mp 193–194 °C (acetone–light petroleum (bp 60–80 °C)), lit.,[31] 191–193 °C; IR: 1269, 1451, 1578, 1596, 1614, 1668, 1703, 2974, 3028, 3060 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.94 (s, 3H, 18-H_3), 1.16 (s, 3H, 19-H_3), 4.81 (t, J = 8.2 Hz, 1H, 17α-H), 5.69 (s, 1H, 4-H), 7.40 (t, J = 7.3 Hz, 2H, 3′-H and 5′-H), 7.52 (t, J = 7.2 Hz, 1H, 4′-H), 8.00 (d, J = 7.0 Hz, 2H, 2′-H and 6′-H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 82.85 (C^{17}), 123.86 (C^4), 128.24 ($C^{3'}$ and $C^{5'}$), 129.40 ($C^{2'}$ and $C^{6'}$), 130.49 ($C^{1'}$), 132.74 ($C^{4'}$), 166.34 (C^5), 170.84 (C_6H_5COO), 199.35 (C^3).

26:. Mp 167–169 °C (ethyl acetate–hexane), lit.,[32] 170–172 °C; IR: 1245, 1723, 1738, 2970 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.81 (s, 3H, 18-H_3), 0.88 (s, 3H, 19-H_3), 1.98 (s, 3H, CH_3CO), 3.33 (s, 1H, 6β-H), 4.91 (m, 1H, 3α-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 58.94 (C^6), 68.45 (C^5), 71.93 (C^3), 170.07 (CH_3CO), 219.68 (C^{17}).

Allylic oxidation catalyzed by manganese and vanadium catalysts (general procedure)

In a typical reaction, to a solution of 17-oxoandrost-5-en-3β-yl acetate **12** (0.66 g/2 mmol) in acetonitrile (12 ml) under nitrogen, catalyst **2** (0.2 g/0.06 mmol) and *tert*-butyl hydroperoxide (*ca.* 2.4 ml/12 mmol) were added. After 24 h under magnetic stirring at 55 °C, the catalyst was removed by filtration and the solution was poured into sodium sulfite solution (10% aq.) and extracted with diethyl ether. The extract was washed with an aq. saturated solution of $NaHCO_3$, water, dried and evaporated to dryness to give 7,17-dioxoandrost-5-en-3β-yl acetate **13** (0.57 g, yield 82%).

Acknowledgments

We wish to thank the RAEng-EPSRC for a Clean Technology Fellowship (to J. H. C.) and the Universidade de Coimbra for financial support (to J. A. R. S.).

References

1 J. Muzart, *Bull. Soc. Chim. Fr.*, 1986, **65**, 2.
2 P. C. Bulman Page and T. J. Mccarthy, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford–New York–Seoul–Tokyo, 1991, vol. 7, p. 83.
3 Y. Sato, Y. Sonoda, M. Morisaki and N. Ikekawa, *Chem. Pharm. Bull.*, 1984, **32**, 3305; K. P. Cheng, H. Nagana, L. Bang and G. Ourisson, *J. Chem. Res. (S)*, 1997, 217; H. Nagana, J. P. Poyser, K. P.

Cheng, L. Bang and G. Ourisson, *J. Chem. Res. (S)*, 1997, 218; V. Kumar, A. Alain, G. Ourisson and B. Luu, *Synth. Commun.*, 1987, **17**, 1279.

4 G. W. Dauben, M. Lorber and D. S. Fullerton, *J. Org. Chem.*, 1969, **34**, 3587; D. S. Fullerton and C. M. Chen, *Synth. Commun.*, 1976, **6**, 217.

5 W. G. Salmond, M. A. Barta and J. L. Havens, *J. Org. Chem.*, 1978, **43**, 2057.

6 E. J. Parish, S. Chitrakorn and T.-Y. Wei, *Synth. Commun.*, 1986, **16**, 1371.

7 E. J. Parish and T.-Y. Wei, *Synth. Commun.*, 1987, **17**, 1227.

8 C. W. Marshall, R. E. Ray, I. Laos and B. Reigel, *J. Am. Chem. Soc.*, 1957, **79**, 6308.

9 A. Amann, G. Ourisson and B. Luu, *Synthesis*, 1987, 1002.

10 E. J. Parish, H. Sun and S. A. Kizito, *J.Chem. Res. (S)*, 1996, 544.

11 U. Bora, M. K. Chaudhuri, D. Dey, D. Kalita, W. Kharmawphlang and G. C. Mandal, *Tetrahedron*, 2001, **57**, 2445.

12 J. Muzart, *Tetrahedron Lett.*, 1987, **28**, 4665.

13 A. J. Pearson, Y. S. Chen, Y. S. Hsu and T. Ray, *Tetrahedron Lett.*, 1984, **25**, 1235.

14 A . J. Pearson, Y. S. Chen, G. R. Hang, S. Y. Hsu and T. Ray, *J.Chem .Soc., Perkin Trans. 1*, 1985, 267.

15 N. Chidambaran and S. Chandrasekaran, *J. Org. Chem.*, 1987, **52**, 5048.

16 R. A. Miller, W. Li and G. R. Humprey, *Tetrahedron Lett.*, 1996, **37**, 3429.

17 M. Kimura and T. Muto, *Chem. Pharm. Bull.*, 1979, **27**, 109.

18 M. Kimura and T. Muto, *Chem. Pharm. Bull.*, 1980, **28**, 1836.

19 J. A. R. Salvador, M. L . Sáe Melo and A. S. Campos Neves, *Tetrahedron Lett.*, 1997, **38**, 119.

20 J. H. Clark, *Catalysis of Organic Reactions using Supported Inorganic Reagents*, VCH, New York, 1994; *Chemistry of Waste Minimisation*, ed. J. H. Clark, Chapman and Hall, London, 1995.

21 J. A. R. Salvador and J. H. Clark, *Chem. Commun.*, 2001, 33.

22 A. J. Butterworth, J. H. Clark, P. H. Walton and S. J. Barlow, *Chem. Commun.*, 1996, 1859.

23 J. Chisen, I. C. Chisen, J. S. Rafelt, D. J. Macquarrie and J. H. Clark, *Chem. Commun.*, 1997, 2203.

24 J. Wang, C. Zhang, Z. Qu, Y. Hou, B. Chen and P. Wu, *J. Chem. Res. (S)*, 1999, 294.

25 L. Knof, *Justus Liebigs Ann. Chem.*, 1962, **657**, 171; R. M. Scribner in *Organic Reactions in Steroid Chemistry*, ed. J. Fried and J. A. Edwards, van Nostrand Reinhold, New York, 1972, vol. 2, p. 434.

26 S. F. Arantes, A. Farooq and J. R. Hanson, *J. Chem. Res. (M)*, 1999, 801.

27 C. W. Marshall, R. E. Ray, I. Laos and B. Riegel, *J. Am. Chem. Soc.*, 1957, **79**, 6308.

28 J. R. Billeter and K. Miescher, *Helv. Chim. Acta*, 1948, **31**, 629.

29 V. E. M. Chambers, W. A. Denny, J. M. Evans, E. R. H. Jones, A. Kasal, G. D. Meakins and J. Pragnell, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1500.

30 H. A. Lardy and P. Marwah, *World Pat.*, WO 9947485, 1999.

31 M. Havel, J. Velek, J. Pospisek and M. Soucek, *Collect. Czech. Chem. Commun.*, 1979, **44**, 2443.

32 J. Joska, J. Fajkos and F. Sorm, *Collect. Czech. Commun.*, 1963, **28**, 82.

An improved preparation of ionic liquids by ultrasound

Jean-Marc Lévêque,*[a] Jean-Louis Luche,[a] Christian Pétrier,[a] Rudy Roux[a] and Werner Bonrath[b]

[a] *Laboratoire de Chimie Moléculaire et Environnement, ESIGEC, Université de Savoie, 73376 Le Bourget du Lac cedex, France. E-mail: jean-marc.leveque@univ-savoie.fr*
[b] *Roche Vitamins Ltd, Research and Development, VFCR, Building –214/071, Grenzacherstr. 124, CH 4070- Basel, Switzerland. E-mail: werner.bonrath@roche.com*

Received 10th April 2002
First published as an Advance Article on the web 4th July 2002

The use of ionic liquids (ILs) as a novel class of environmentally friendly solvents is now of topical interest among the chemical community, worried about the environmental impact of chemicals. Many reactions of organic chemistry have thus been re-examined since the 1990s. Nevertheless, even if a given preparation of ILs does not represent any particular difficulty, the reaction times appear to be long and the use of large amounts of classical solvents for the synthesis and the purification steps is crucial. This article presents preliminary work performed for the ultrasound assisted preparation of several 1-butyl-3-methylimidazolium salts (BF_4, PF_6, CF_3SO_3 and BPh_4). In all cases a clear yield increase results and a dramatic reduction of the reaction time accompanied by an improved quality of the products occurs. After a short and simple work-up, the ILs are ready to use without a further purification step. Moreover, an original and simple analytical way to follow the reaction in real time is also presented.

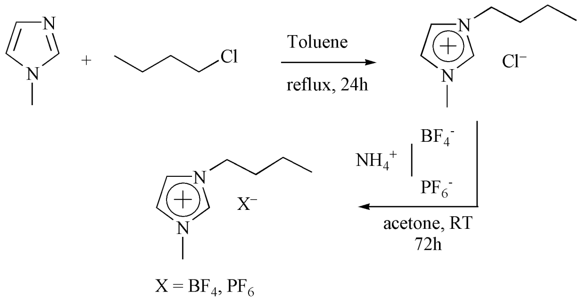
Introduction

The use of classical solvents in organic synthesis, such as diethyl ether, acetone, THF and others, generates a large amount of waste, usually environmentally toxic. The difficulty in treating these materials, not only to separate them, but also their destruction, dramatically increases the total cost of production for a compound. The introduction of cleaner technologies has thus become a major topic for both industry and academia. Water could be obviously an alternative to commercial solvents in some industrial processes but it is far from offering a general solution to the problem. A better approach is provided by the emergence of ionic liquids (ILs) which are receiving renewed attention as green solvents. Ionic liquids are, in fact, not new as the first known, ethylammonium nitrate, was discovered in 1914.[1] Since then, a large variety of liquids with mp < 100 °C have been prepared with highly interesting properties such as highly ionic character, virtual absence of vapor pressure, lack of flammability, and above all ease of reuse. However, it is only recently that the literature provides examples of their applications in organic chemistry such as Diels–Alder cycloadditions,[2] Heck coupling,[3] hydrogenation[4] or Friedel–Craft reactions,[5] in most cases with remarkable improvements.[6] The more commonly studied and used ILs contain the imidazolium and pyridinium cations associated with common weakly coordinating anions (BF_4, PF_6, CF_3SO_3, *etc.*) and are liquids at or near room temperature.

Results and discussion

We focused our interest on 1-butyl-3-methylimidazolium salts (BMIX) usually prepared in two steps (Scheme 1): Menschutkin quaternisation[7] of 1-methylimidazole by butyl halide (bromide or chloride) followed by the anion exchange, a Finkelstein reaction,[8] with ammonium salts such as tetrafluroroborate, hexafluorophosphate or trifluoromethanesulfonate. In addition to their common large electrochemical window, thermal stability, *etc.* ILs with low coordinating anions display several advantages as compared to the parent chloride or bromide compounds, such as a lower melting point, a reasonable price, and more importantly, an improved stability towards moisture.

These liquids are very polar and immiscible with various organic solvents although they can dissolve a wide range of organic and inorganic materials. Importantly, $BMIPF_6$ is totally hydrophobic whereas $BMIBF_4$ is hydrophilic at a temperature above 5 °C. Thus, only by changing the counter anion, does the hydrophilic character change to hydrophobic. A point that can represent a drawback for research is the commercial availability of ILs. A few ILs can be purchased in small amounts for laboratory experiments but their price is barely affordable for



Scheme 1

Green Context

The use of ionic liquids is currently very popular and much work is appearing regarding their utility as solvents in a range of reactions. This paper provides improvements to their synthesis, in particular the metathesis step, which should lead to a cleaner route to the production of these solvents. The improvement appears to rely on the acceleration of reaction rates in biphasic systems, giving faster ion exchange under mild conditions. ***DJM***

DOI: 10.1039/b203530h

exploratory experimental campaigns, making a rapid and inexpensive route to laboratory scale synthesis desirable. Moreover, literature descriptions are frequently inaccurate, and the reaction times are exceedingly long, using large amounts of usual solvents. These reasons prompted us to envisage synthetic improvements by sonochemical methods.

Since both chemical steps are driven by an ionic pathway, the former in a homogeneous medium and the latter in a heterogeneous medium, no chemical effect of ultrasonic irradiation, at first sight, would be expected. The mechanical effects, however, could be expected to influence the biphasic Finkelstein reaction since ultrasound has a recognized potential to increase the rates of heterogeneous reactions.[9] The lower the incident frequency, the more efficient and harsher will be the cavitation bubble collapse. The emitted shock waves reduce the size of particles suspended in the medium, thus increasing the specific reactive surface of the solids, leading, on the one hand, to a homogeneous particle distribution throughout the medium, and on the other, a rate enhancement.[10]

We chose to use the heterogeneous procedure for the anion metathesis instead of the homogeneous one because the latter makes use of aqueous HBF_4 and HPF_6, aggressive and unstable acids, both liberating HF upon decomposition, and both acids must be kept at low temperature to avoid rapid decomposition. Moreover, the BF_4 derivative is water soluble and its work-up requires the use of dichloromethane, considered as highly toxic in the chemical industry, to recover the material.[11]

In addition, another problem was to know when the exchange reaction could be considered as terminated. Since ILs are good electrolytes, with applications in industrial electrochemical processes, we designed a conductimetric cell permitting a real time measurement of the change of the total medium conductivity, expecting a plateau to be reached at the end of the anion exchange. This cheap 'home-made' analytical system was tested on both silent and ultrasonic modes for the preparation of the BF_4 and PF_6 salts.

On silent mode, *e.g.* magnetic stirring at 500 rpm, it is interesting that for $BMIBF_4$ and $BMIPF_6$, a plateau is reached after less than 30 h reaction at room temperature, which is substantially shorter than generally cited in the literature.[12,13] Confirmation that the reaction was completed was obtained by isolating the expected product in 80–90% yield after work-up. The color was brown to black and a purification step was required before use. The two plots in Fig. 1 show the general shape obtained under magnetic stirring for both ILs. The initial conductivity is measured with the magnetic stirrer off. When stirring is switched on, a rapid increase of the conductivity is observed, corresponding to the dispersion of the solids into the medium. A first plateau is reached, corresponding probably to the reduction of particle size under the effect of the stirring.[14] Then, the reactions proceed smoothly and a constant increase of the conductivity is observed to reach a second plateau, indicative of the completion of the anion exchange.

Both plots show a similar shape even if the jump of conductivity is different for $BMIBF_4$ and $BMIPF_6$. These results are not only reproducible but also the general shape remains similar whatever the initial concentration of reactants.

The two plots in Fig. 2 show the general shape obtained for both salts under ultrasonic irradiation at 30 kHz.

As in stirred experiments, the initial conductivity has been taken with the power source (*i.e.* ultrasonic generator) off. Then, power is turned on and a rapid increase of the conductivity is observed to reach a first plateau. This plateau is much shorter than with magnetic stirring. Indeed, through the effect of shock waves generated by the bubble collapse, suspended solids undergo a rapid size comminution leading to a fine suspension in less than 5 min, as compared to 5–8 h necessary on magnetic stirring. Then, similarly to the stirred reaction, the sonicated reaction proceeds to reach the second plateau indicating the end of the reaction. After *ca.* 1 h, the reaction can be considered as terminated, which should be compared to the 30 h necessary on silent mode, all parameters being otherwise equal. The color of the resulting products is pale yellow in contrast to the brown material obtained on magnetic stirring. Even if the color does not represent an infallible criterion of purity, it is understandable that a pale yellow medium is more suitable in further uses. After simple filtration, removal of the organic solvent and centrifugation (to remove any traces of the suspended fine particles of the resulting salts), the purity of each IL thus prepared was investigated by IR and ^1H NMR, giving spectra consistent with literature and confirming that ILs prepared in this way can be directly used after this very simple work-up.

Contrary to the system used in silent mode, it is not possible to immerse the conductimetric cell inside the reactor because of ultrasound waves. The propagation of sound throughout the medium not only leads to an incoherent value of the conductivity but the collapsing bubbles attack and erode the platinum surface of the electrodes. Fig. 3 details the set-ups used for magnetic stirring and under ultrasonic irradiation.

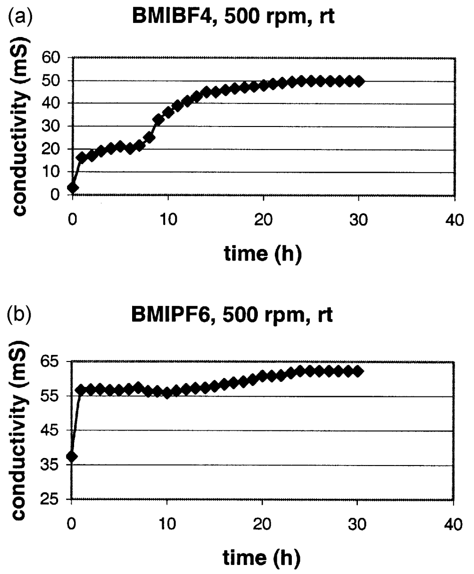


Fig. 1 Conductimetry curves for the preparation of (a) $BMIBF_4$ and (b) $BMIPF_6$ under stirring.

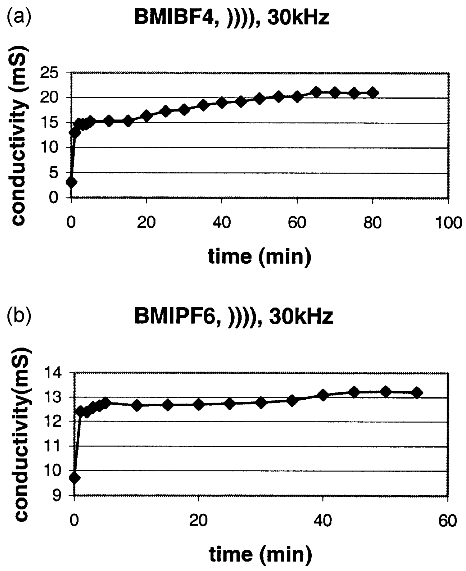


Fig. 2 Conductimetry curves for the sonochemical preparation of (a) $BMIBF_4$ and (b) $BMIPF_6$.

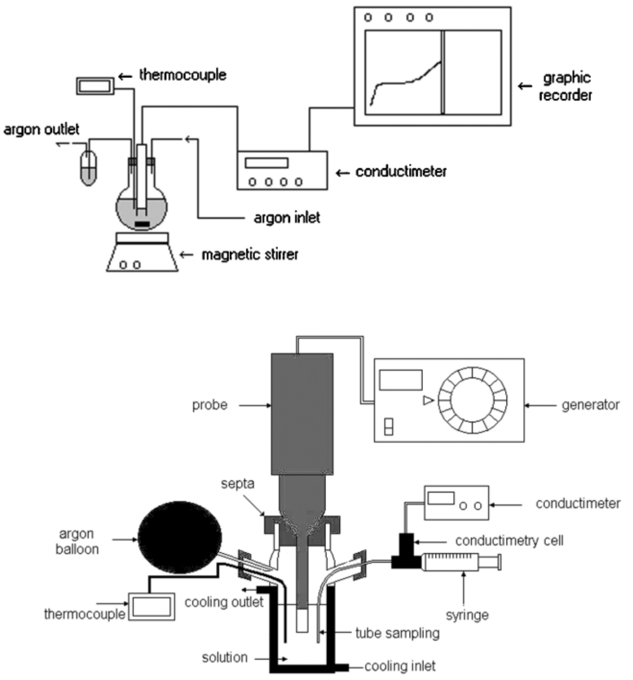


Fig. 3 Set-up for (a) stirred experiments and (b) ultrasonic experiments.

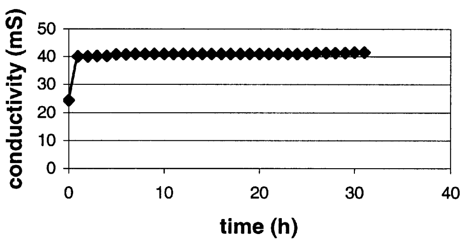
The 'home-made' conductimetric cell is a very simple system consisting of two metallic pieces set at a separation of 1 cm and inserted in a PVC tube, and linked to a conductimeter, to detect only variations of the total conductivity in the reaction vessel.

As a primary conclusion of this work, ultrasonic irradiation enhances dramatically the anion exchange for the preparation of both ILs from ammonium salts and BMICl. Moreover, the 'home-made' conductimetric system allows the formation of ILs based on both anions cited above, to be followed on a real time basis.

We envisaged an extension to other ammonium salts to complete this preliminary work. Our first choice was ammonium trifluoromethanesulfonate (triflate), $BMICF_3SO_3$, a well known and commonly used IL.[15] The two plots in Fig. 4 show the conductimetric curves obtained under magnetic stirring and ultrasonic irradiation.

As for the two previous examples, we observe for both ultrasonic irradiation and magnetic stirring an increase of the total conductivity of the system to reach a plateau, considered to be the particle size reduction step. The subsequent reaction should proceed but no change in the conductivity during the reaction is observed. Nevertheless, the reaction was stopped after 1 h sonication or 30 h stirring. The yield reached 90% for both methods and the purity, checked by ^1H NMR spectroscopy is consistent with literature data. Thus ultrasonic irradiation also dramatically enhances the reaction rate for the CF_3SO_3 derivative, probably through the same particle size reduction effect. Unfortunately, it seems that the overall conductivity of the starting materials is similar to that of the resulting products in this instance. The color obtained under ultrasound is satisfactory and CF_3SO_3 derivative does not need any further treatment, apart from filtration, solvent removal and centrifugation.

(a) **BMICF3SO3, 500 rpm, rt**



(b) **BMICF3SO3,)))), 30 kHz**

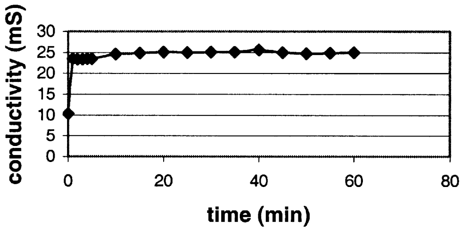


Fig. 4 Conductimetry curves for the preparation of $BMICF_3SO_3$ under (a) magnetic stirring and (b) under ultrasonic irradiation.

We believe that this method could be applied to a broader scope, to access as yet unknown ILs. Therefore, we made the choice to investigate an ammonium salt with a bulky counter anion, ammonium tetraphenylborate, ILs with BPh_4 anion being mentioned in literature only once, to the best of our knowledge. We followed the typical procedure described above. Moreover, according to the previous results, if the conductimetric method is valid for stirring then it should also be valid for ultrasonic irradiation. Thus, we recorded the conductimetry variation of the sonicated experiment, as shown in Fig. 5.

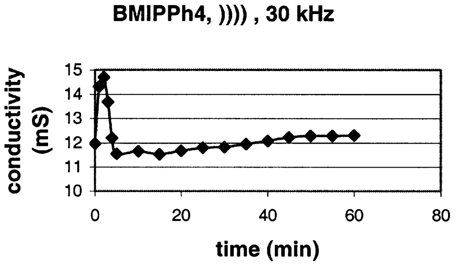


Fig. 5 Conductimetry curve for the preparation of $BMIPPh_4$ under ultrasonic irradiation.

The reaction was stopped after 1 h and the expected product was obtained, after typical work-up, in up to 90% yield as a white solid melting at 130 °C [^1H NMR ($CDCl_3$, 400 MHz): δ 7.52 (2H, d), 6.97 (2H, t), 6.77 (1H, t), 5.85 (1H, dd), 5.66 (1H, dd), 4.60 (1H, s), 3.12 (2H, t), 2.70 (1H, s), 1.32 (2H, qnt), 1.12 (2H, m), 0.89 (3H, t); ^{13}C NMR ($CDCl_3$, 400 MHz): δ 165.0, 136.2, 135.2, 126.5, 122.5, 122.5, 120.9, 53.0, 49.5, 36.0, 32.2, 19.9, 13.9]. The melting point of this compound is higher than 100 °C, admittedly an upper limit for a salt to be classified as an ionic liquid. Nevertheless, we can emphasize that the conductimetric method is validated with this example. Finally, the general shape of the curve in Fig. 5 shows a rapid increase of the conductivity at the beginning of the experiment, contrary to the first plateau for the PF_6 and BF_4 derivatives. This can be explained by the difference of the particle size of the considered starting ammonium salts. Both NH_4PF_6 and NH_4BF_4 (Fig. 6(a) and (b)) present a larger particle size than NH_4BPh_4 (Fig. 6(c)), which is a very fine powder.

Thus, when the generator is switched on, ultrasound instantaneously disperses the latter without reducing the particle size for the other two salts, leading to a dispersion. Thus the reaction proceeds to reach the second and final plateau.

Experimental

General

BMICl used in this study, was prepared from 1-methylimidazole and 1-chlorobutane in toluene as described in ref. 4.

On magnetic stirring, a very low (*ca.* 2 mL min^{-1}) dynamic argon pressure was used to keep an inert atmosphere without

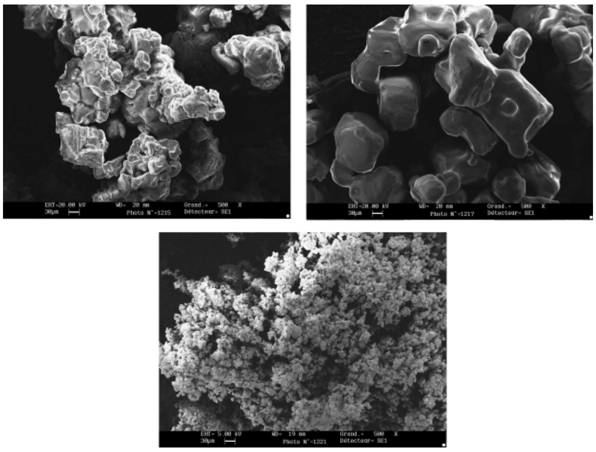


Fig. 6 SEM images for (a) NH_4PF_6, (b) NH_4BF_4 and (c) NH_4BPh_4.

flushing out the solvent. Under sonication, a static argon pressure was used. All solvents were distilled from and kept over the appropriate drying agents under argon. Ammonium salts were dried *in vacuo* and kept under argon. All conductivity values given for both ultrasonic and silent modes were corrected for a standardized temperature of 25 °C.[16] ^1H and ^{13}C NMR spectra were recorded on a AC 400 BRUKER spectrometer. IR spectra were recorded on a Perkin-Elmer spectrum RX-1 spectrophotometer. Both series of spectra conform to published data.[11]

The melting point of the BPh_4 derivative was measured on a Koffler hot stage while SEM images were taken on a LEICA Stereoscan 440.

General procedure for stirred experiments

The conductivity was measured with a Tacussel CDM 210 conductimeter. The platinum electrode was positioned 1 cm under the surface of the liquid, at a distance of 1 cm from the magnetic stirrer and connected to the graphic recorder.

To a solution of BMICl (5.23 g, 30 mmol) in dry acetone (30 mL), NH_4X ($X = BF_4$, PF_6 or CF_3SO_3 30 mmol) was added, the argon pressure applied and the experiment carried out for 30 h at room temperature. Then, the solution was filtered through Celite, the solvent evaporated under vacuum, and the brown to black IL recovered in 80–90% yield.

General procedure for sonicated experiments

To a solution of BMICl (5.23 g, 30 mmol) in dry acetone (30 mL), NH_4X ($X = BF_4$, PF_6, CF_3SO_3 or BPh_4, 30 mmol) was added to the ultrasonic reactor shown schematically in Fig. 3. Then the ultrasonic reactor was connected to a cryostat and fitted with an argon balloon, a thermocouple, and the conductimetric cell (see Fig. 3(b)) connected to a glass syringe to pump the solution in to the cell and measure the conductivity throughout the experiment. The conductivity was measured with a Tacussel CDRV 62 conductimeter. The slurry was irradiated (Ultrasons Annemasse generator) at 30 kHz for 1 h at 20–24 °C (cooling bath at 5 °C). Then, the solution was filtered, the solvent evaporated under vacuum, and the pale yellow to orange IL recovered, after centrifugation, in 80–90% yield.

Acknowledgment

We gratefully thank Roche Vitamins, Basel, Switzerland, for their generous support and C. Fachinger and J. Suptil for their valuable technical assistance.

References

1 P. Walden, *Bull. Acad. Imp. Sci. (St-Petersburg)*, 1914, 405–422.

2 (*a*) M. J. Earle, P. B. McCormac and K. R. Seddon, *Green Chem.*, 1999, **1**, 23–25; (*b*) T. Fischer, A. Sethi, T. Welton and J. Woolf, *Tetrahedron Lett.*, 1999, **40**, 793–796; (*c*) C. W. Lee, *Tetrahedron Lett.*, 1999, **40**, 2461–2464.

3 (*a*) W. A. Herrmann and V. P. W. Böhm, *J. Organomet. Chem.*, 1999, **572**, 141–145; (*b*) J. Howarth and A. Dallas, *Molecules*, 2000, **5**, 851–855.

4 P. A. Z. Suarez, J. E. L. Dullius, S. Einloft and R. F. de Souza, *Polyhedron*, 1996, **15**, 1217–1219.

5 M. J. Earle P. B. McCormack and K. R. Seddon, *Chem. Commun.*, 1998, 2245–2246.

6 (*a*) J. D. Holbrey and K. R. Seddon, *Clean Products Processes*, 1999, 223–236; (*b*) T. Welton, *Chem. Rev.*, 1999, **99**, 2071–2083.

7 (*a*) N. Z. Menschutkin, *Phys. Chem.*, 1890, **6**, 41–57; (*b*) J. A. Zoltewicz and L. W. Deady, *Adv. Heterocycl. Chem.*, 1978, **22**, 71–121.

8 R. Bohlmann, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 6, pp. 203–223.

9 (*a*) K. S. Suslick, D. J. Casadonte and S. J. Doktycz, *J. Chem. Mater.*, 1989, **1**, 6–8; (*b*) T. Ando and T. Kimura, *Adv. Sonochem.*, 1991, **2**, 211–251; (*c*) A. Loupy and J. L. Luche, in *Synthetic Organic Sonochemistry*, ed. J. L. Luche, Plenum Press, New York, 1998, pp. 107–166.

10 W. Lauterborn and C. D. Ohl, *Ultrason. Sonochem.*, 1997, **4**, 65–75.

11 P. Seongsoon and R. J. Kazlauskas, *J. Org. Chem.*, 2001, **66**, 8395–8401.

12 P. A. Z. Suarez, S. Einloft, J. E. L. Dullius, R. F. de Souza and J. Dupont, *J. Chem. Phys.*, 1998, **95**, 1626–1639.

13 C. M. Gordon, J. D. Holbrey, A. R. Kennedy and K. R. Seddon, *J. Mater. Chem.*, 1998, **8**, 2627–2636.

14 At the beginning of the reaction, both solids are deposited at the bottom of the flask and the liquid phase is clear. When the first plateau is reached, some small particles begin to be suspended in the medium. When the reaction ends after 5–8 h, a suspension of fine particles appears instantaneously and the overall conductivity begins to increase. This phenomenon establishes that both solids undergo size reduction before reaction proceeds.

15 P. Bonĥote, A.-N. Dias, N. Papageorgiou, K. Kalyanasundaram and M. Grätze, *Inorg. Chem.*, 1996, 1168–1178.

16 *L'analyse de l'eau*, ed. J. Rodier, Dunod, Paris, 8th edn., 1996, pp. 60–61.

Microwave assisted acylation of methoxyarenes catalyzed by EPZG® catalyst

Eva Veverková, Mária Meciarová, Battsengel Gotov and Štefan Toma

Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University, SK-842 15 Bratislava, Slovakia. E-mail: toma@fns.uniba.sk

Received 30th April 2002
First published as an Advance Article on the web 4th July 2002

Solventless acylation and benzoylation of 1-methoxynaphthalene, 2-methoxynaphthalene and anisole with different acyl chlorides and anhydrides catalyzed with EPZG® under microwave irradiation were studied. The high yields of the monoacylation products were achieved in a very short time and diacetylation products were also isolated.

Introduction

Friedel–Crafts acylations (including benzoylations and sulfonylations) are very important reactions carried out industrially. Intermediates for pharmaceutical, perfumes, flavours, fragrances, dyes, plastics, antioxidants, stabilizers, fungicides, pesticides *etc.* are prepared using these reactions. It is, however, well known that Lewis acid-catalyzed reactions suffer from some serious disadvantages. Their use leads to large volumes of hazardous waste. The classical Friedel–Crafts process uses an acid chloride in combination with a greater than stoichiometric amount of aluminium chloride (the use of anhydrides would require more than 2 equivalents of $AlCl_3$) to organic substrate and the product is released by using a water quench with the resulting emission of 3 equivalents of HCl. Neutralization of HCl leads to the production of 3 equivalents of salt waste that is contaminated with aluminium hydroxide. It is now possible to reduce or eliminate the use and generation of hazardous substances using new types of catalysts. The solid catalysts that are easily recoverable, reusable, safe-to-handle, with reasonable activities, with good selectivities, are of great interest in this context.

Acid clays with exchangeable cations were found to be very good Friedel–Crafts acylation catalysts.[1–3] Clay supported Lewis acids are especially good Friedel–Crafts catalysts[4,5] and are therefore commercialized. A review focused on the use of heterogeneous catalysts in the production of fine and speciality chemicals was published recently.[6] The major emphasis in this review is put on oxidation reactions including the production of hydroquinone, caprolactam, and alkene oxides, and clay-supported catalysts such as clayzic, which are commercially available for acid-catalysed reactions, in particular Friedel–Crafts reactions.

Baudry-Barbier *et al.* described the preparation, characterization and performance of rare-earth-supported catalysts in the Friedel–Crafts acylations of benzene, thiophene, naphthalene, anisole and 2-methoxynaphthalene and in a variety of syntheses of aromatic ketones.[7] Choudary *et al.* investigated Friedel–Crafts acylation of aromatic ethers with acid anhydrides in the presence of mesoporous material, cation-exchanged K10 montmorillonites.[8] Selective acylation was a significant achievement with the formation of 1-acyl-2-methoxynaphthalene, 4-acyl anisole and 4-acyl veratrole from the corresponding aromatic ethers. Acylation of 2-methoxynaphthalene with acetic anhydride on a series of dealuminated HBEA-zeolites in nitrobenzene was described recently.[9] Friedel–Crafts acylation of 2-methoxynaphthalene catalyzed by metal triflates was studied by Kobayashi and Komoto.[10] Under the conditions described 2-methoxynaphthalene reacted with acetic anhydride in nitromethane–lithium perchlorate to afford 2-acetyl-6-methoxynaphthalene. Acylation of aromatic ethers has also been studied under microwave irradiation in the presence of various catalysts, metallic chlorides, oxides or triflates.[11] It was shown that microwaves have a specific interaction with the arylketone produced and especially with its catalyst-complexed form. However, a microwave non-thermal effect has not been observed, either for the yield or for the isomeric ratios of various products. The main goal of this work was a thorough study of the Friedel–Crafts acylations of different methoxyarenes using environmentally friendly EPZG® catalysts.

Results and discussion

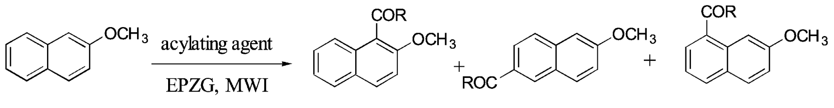
We examined the Friedel–Crafts reaction of aromatic ethers with acylchlorides and anhydrides using EPZG® as catalyst and microwave irradiation to enhance the reaction rate.

Performing the acylation of 2-methoxynaphthalene (**1**) (Scheme 1) with acetyl, propionyl, butyryl and phenylacetyl chlorides produces 6-acyl-2-methoxynaphthalenes (**3a–d**) with a small amount of 1-acylated (**2**) and 8-acylated (**4a–d**) regioisomers (Table 1, entries 1, 3, 5, 7). We assume that 1-acylated products are formed in the early stages of the reaction. During the acylation reaction with acyl chlorides as acylating agents hydrogen chloride is evolved and probably the catalytic isomerization of **2** to **3** takes place. An important change of regioselectivity was observed when the corresponding anhydrides were used as the acylating agents. 1-Acylated products (**2a,c**) were obtained as the major products when 2-methoxynaphthalene reacted with acetic, propionic and butyric anhydrides (Table 1, entries 2, 4, 6). The acylation reactions using anhydrides as acylating agents represented a

Green Context

Electrophilic acylations are much more challenging than the corresponding alkylations, and few satisfactory green protocols exist. This paper decribes the use of a commercial solid acid catalyst coupled to microwaves which brings about the acylation of anisoles in moderate to good yields in very short times. While the ultimate coupling of an acid and an arene has not been achieved here, the use of anhydrides is a promising step. ***DJM***

DOI: 10.1039/b204194b



1 **2a-e** **3a-e** **4a-e**

a R=CH_3
b R=CH_3CH_2
c R=$CH_3CH_2CH_2$
d R=$PhCH_2$
e R=Ph

Scheme 1

Table 1 Results of the Friedel–Crafts reactions on 2-methoxynaphthalene **1;** reaction time 5 min; power setting 120 W.

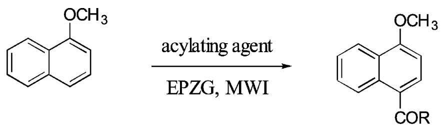
Entry	Compound	Acylating agent	T_{final}/ °C	Total yield (%)	Product distribution 2	3	4
1	**a**	CH_3COCl^b	92	37	11	60	29
2	**a**	$(CH_3CO)_2O^b$	94	42	79	17	4
3	**b**	$CH_3CH_2COCl^a$	112	44	0	90	10
4	**b**	$(CH_3CH_2CO)_2O^a$	115	52	80	15	5
5	**c**	$CH_3CH_2CH_2COCl^a$	143	51	0	92	8
6	**c**	$(CH_3CH_2CH_2CO)_2O^a$	170	55	74	26	0
7	**d**	$PhCH_2COCl^a$	140	46	0	91	9
8	**e**	$PhCOCl^a$	128	68	0	76	24
9	**e**	$PhCOCl^b$	134	72	0	75	25
10	**e**	$(PhCO)_2O^a$	117	52	0	82	18

[a] Mole ratio 2-methoxynaphthalene : acylating agent was 1 : 1. [b] Mole ratio 2-methoxynaphthalene : acylating agent was 1 : 2.

chlorine-free route and isomeration is impossible. On the other hand, it is interesting that the use of benzoyl chloride and benzoic anhydride (Table 1, entries 8, 10) gave similar results and in both cases the predominant adduct was 6-benzoyl-2-methoxynaphthalene (**3e**). This could be explained by greater stability of $PhCO^+$ cation and therefore more easy isomerisation of **2e**.

For comparison, Kobayashi and Komoto[10] described similar results of Friedel–Crafts acylation of 2-methoxynaphthalene with acetic anhydride catalyzed by metal triflates. The reactions proceeded in the presence of a catalytic amount of a metal triflate such as $Sb(OTf)_3$ or $Ga(OTf)_3$ in $MeNO_3$–$LiClO_4$ at 50 °C for 40 h gave 0–83% of 1-acylated regioisomer and 1–92% of 6-acylated regioisomer.

The acylation reactions on 1-methoxynaphthalene (Scheme 2) took place selectively in the position four. Low boiling point of acetyl chloride (51–52 °C) and propionyl chloride (80 °C) probably caused relatively low yields of 1-acetyl-4-methoxynaphthalene (**6a**) (38%) and 4-methoxy-1-propionylnaphthalene (**6b**) (42%) (Table 2, entries 1, 4). To improve the yields we performed these reactions with two equivalents of acetyl chloride and propionyl chloride. The yield of 1-acetyl-4-methoxynaphthalene (**6a**) increased to 63% and the yield of 4-methoxy-1-propionylnaphthalene (**6b**) increased to 67% (Table 2, entries 2, 5). Using anhydrides of acetic acid and propionic acid instead of their chlorides, yield of 1-acetyl-4-methoxynaphthalene (**6a**) was 75% and the yield of 4-methoxy-1-propionylnaphthalene (**6b**) was 84% (Table 2, entries 3, 6).



5 **6a** R=CH_3
6b R=CH_3CH_2

Scheme 2

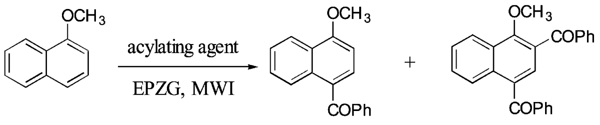
Table 2 Results of the Friedel–Crafts acylation reactions on 1-methoxynaphthalene **5**

Entry	Acylating agent	Mole ratio **5** : acylating agent	Time/ min	T_{final}/°C	Product	Yield (%)
1	CH_3COCl	1 : 1	2	175	**6a**	38
2	CH_3COCl	1 : 2	3	176	**6a**	63
3	$(CH_3CO)_2O$	1 : 1	4	185	**6a**	75
4	CH_3CH_2COCl	1 : 1	3	178	**6b**	42
5	CH_3CH_2COCl	1 : 2	3	178	**6b**	67
6	$(CH_3CH_2CO)_2O$	1 : 1	4	187	**6b**	84

Power setting 180 W.

The selectivity of the benzoylation reactions on 1-methoxynaphthalene (Scheme 3) was similar. Using 1 equivalent of benzoyl chloride as a benzoylating agent gave 73% of 1-benzoyl-4-methoxynaphthalene (**7**) as the only product. Interesting results were achieved when 2 equivalents of benzoyl chloride were used. Besides 70% of 1-benzoyl-4-methoxynaphthalene (**7**) 21% of 1,3-dibenzoyl-4-methoxynaphthalene (**8**) was isolated from the reaction mixture (Table 3, entries 1, 2). No dibenzoyl product was observed when 2 equivalents of benzoyl chloride were used in the case of 2-methoxynaphthalene (Table 1, entry 9). The reactions with benzoic anhydride gave 42% of 1-benzoyl-4-methoxynaphthalene (**7**). Prolonging the reaction time from 4 to 8 min did not affect the reaction course (Table 3, entries 3, 4).

To check if the acylation with high boiling acyl chlorides would enhance the yield of acylation an experiment with phenylacetyl chloride (**9**) was performed (Scheme 4). 1-Phenyl-



5 **7** **8**

Scheme 3

Table 3 Results of the Friedel–Crafts benzoylation reactions on 1-methoxynaphthalene **5**

Entry	Acylating agent	Mole ratio **5** : acylating agent	Time/ min	T_{final}/°C	Yield of **7** (%)	Yield of **8** (%)
1	PhCOCl	1 : 1	2	243	76	0
2	PhCOCl	1 : 2	2	256	70	21
3	$(PhCO)_2O$	1 : 1	4	224	42	0
4	$(PhCO)_2O$	1 : 1	8	225	45	0

Power setting 180 W.

acetyl-4-methoxynaphthalene (**10**) was isolated as the main product (45%) and an unexpected byproduct 1-(4-methoxy-1-yl)-1-(5-methoxy-1-yl)-2-phenylethene (**11**) was isolated in 15% yield. Product **11** could be formed by the Friedel–Crafts alkylation of 1-methoxynaphthalene with an enol form of **10**. Changing the mole ratio 1-methoxynaphthalene:phenylacetylchloride from 1 : 1 to 1 : 2 had no influence on the results (Table 4).

Table 4 Results of the Friedel–Crafts acylation reactions on 1-methoxynaphthalene **5** with phenylacetyl chloride **9**

Entry	Mole ratio **5** : **9**	Time/min	T_{final}/°C	Yield of **10** (%)	Yield of **11** (%)
1	1 : 1	4	238	45	15
2	1 : 2	4	240	48	12

Power setting 180 W.

Benzoylation of anisole with EPZG® catalyst under microwave irradiation was studied recently.[12] Using an equimolar amount of benzoyl chloride, 83% of benzoyl anisole was achieved and the isomer ratio *o* : *p* was 18 : 82. The observed diacylation of 1-methoxynaphthalene prompted us to check if a diacylation of anisole would not be possible. The reaction with two equivalents of benzoyl chloride and the results are given in the Scheme 5. 2,4-Dibenzoylanisole (**16**) was isolated as the main product (20%). Combined yields of 4-benzoylanisole (**14**) and 2-benzoylanisole (**15**) were 17% and the isomer ratio **14** : **15** was 14 : 3, similar to that obtained using 1 equivalent of benzoyl chloride. Benzoic acid (4-benzoylphenyl) ester (**17**) (8%), benzoic acid (2,4-dibenzoylphenyl) ester (**18**) (16%) and 2,4-dibenzoylphenol (**19**) (2%) were isolated as byproducts. Product **17** is a result of demethylation and subsequent acylation of **14** and product **18** is a result of the similar reaction sequence on **16**.

Benzoylation of less reactive aromatics catalyzed by EPZG® catalysts under microwave irradiation has been described recently.[12] Benzoylation of benzene with benzoyl chloride gave 19% of benzophenone after 20 min of microwave irradiation. Benzoylation of toluene afforded 36% yield of the products. The obtained iosmer ratio *o* : *m* : *p* was 17 : 6 : 77. No benzoylation of benzene or toluene was observed under the same conditions when benzoic anhydride was used as the benzoylating agent. No benzoylation nor acylation of any aromatics catalyzed by EPZG® catalyst under microwave irradiation was observed when acids were used as the acylating agents.

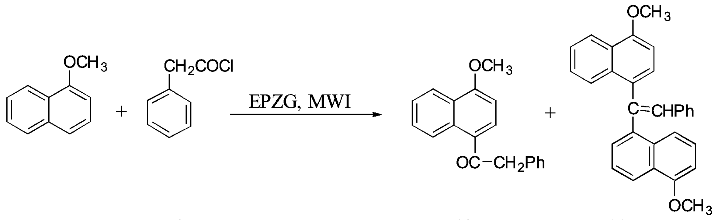
The EPZG® catalyst can be easily recovered (filtered from the process) and used in the next reaction without any significant effect on the reaction course.[12]

Conclusion

Application of EPZG® catalyst under microwave irradiation in the Friedel–Crafts acylation reactions allows (i) a shortening of the reaction time, (ii) simplification of work-up of the reaction mixtures after the reactions, (iii) performing of the reactions without solvent.

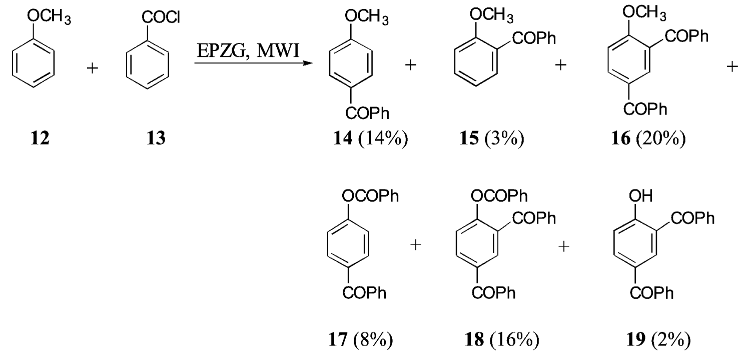
Experimental

Starting materials were either commercially available or prepared according to literature procedure. The substrates were purified (distilled or chromatographed) before application in the reactions. The Envirocat EPZG® is synthesized and supplied by Contract Chemicals, UK. It is a free flowing yellow–green powder having a bulk density of 0.76 g cm^{-3} and surface area of *ca.* 250 m^2 g^{-1}. The ^{1}H NMR spectra were recorded at 300 MHz on a Varian Gemini spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. The ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$. The IR spectra were recorded on a Perkin Elmer 1600 FT-IR instrument as 2% solutions in chloroform. Melting points were determined on a Kofler hot stage and are uncorrected. The GC spectra were recorded on a GC TRACE 2000 Series instrument, MS spectra were recorded on a VOYAGER spectrometer. All microwave experiments were carried out in the SYNTHEWAVE 402, Prolabo reactor, power setting 120 and 180 W, respectively.



5 **9** **10** **11**

Scheme 4 *Conditions*: time = 4 min, T_{final} = 106 °C, power setting = 180 W.



12 **13** **14** (14%) **15** (3%) **16** (20%)

17 (8%) **18** (16%) **19** (2%)

Scheme 5

The general procedure for microwave Friedel–Crafts reactions on 1- and 2-methoxynaphthalenes and anisole

Methoxyarene (0.02 mol), acyl chloride or anhydride of carboxylic acid (0.02 mol) were ground together in a mortar with EPZG® catalyst (500 mg). The reaction mixture was then microwave-irradiated without solvent for 4 min. The final temperature of the reactions mixture are given in Tables 1–4. After cooling to room temperature, the reaction mixture was dissolved in dichloromethane (50 mL) and the solid catalyst was filtered off. The organic solution was washed with saturated aqueous $NaHCO_3$ (30 mL), dried with anhydrous Na_2SO_4, filtered and evaporated on a rotary vacuum evaporator to give a crude product. The crude products were chromatographed on silica using isohexane–ethyl acetate (7 : 1) as the eluent.

1-Acetyl-2-methoxynaphthalene (2a). White solid, mp 55–56 °C (lit.[10] 54.5–56.5 °C). ^{1}H and ^{13}C NMR data consistent with lit.[10]

2-Acetyl-6-methoxynaphthalene (3a). White solid, mp 104–106 °C (lit.[10] 104.5–106 °C).^{1}H and ^{13}C NMR data consistent with lit..[10]

1-Acetyl-7-methoxynaphthalene (4a). White solid, mp 65–66 °C (lit.[13] 66.5–67.5 °C); δ_H (300 MHz, $CDCl_3$) 2.71 (3H, s, $COCH_3$), 3.92 (3H, s, OCH_3),7.17 (1H, dd, J = 2.6 Hz, 8.9 Hz, Ar-H), 7.31 (1H, dd, J = 7.5 Hz, 8.1 Hz, Ar-H), 7.72 (1H, d, J = 8.9 Hz, Ar-H), 7.89 (1H, d, J = 8.1 Hz, Ar-H), 8.01 (1H, d, J = 7.5 Hz, Ar-H), 8.37 (1H, d, J = 2.6 Hz, Ar-H); δ_C (75 MHz, $CDCl_3$) 29.7, 55.3, 104.5, 121.9, 123.6, 128.2, 129.6, 130.4, 131.9, 132.9, 133.3, 169.8, 199.9.

2-Methoxy-1-propionylnaphthalene (2b). Colourless oil (lit.[14] mp 37 °C). ^{1}H NMR data consistent with lit.;[15] δ_C (75 MHz, $CDCl_3$) 9.6, 33.9, 55.9, 118.9, 119.1, 124.7, 127.3, 128.0, 133.9, 136.3, 137.9, 161.1, 200.8.

6-Methoxy-2-propionylnaphthalene (3b). White solid, mp 114.5–115.5 °C (lit.[15] 114–115 °C). ^{1}H NMR data consistent with lit.;[15] δ_C (75 MHz, $CDCl_3$) 7.9, 31.0, 55.6, 109.4, 123.2, 125.1, 128.0, 129.9, 130.4, 136.1, 136.4, 159.0, 199.1.

7-Methoxy-1-propionylnaphthalene (4b). Colourless oil. ν_{max} ($CHCl_3$) 1688, 1438, 1608, 1520, 1475, 1440, 1392, 1270, 1180, 1139, 1110 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.27 (3H, t, J = 7.2 Hz, CH_2CH_3), 3.08 (2H, t, J = 7.2 Hz, CH_2CH_3), 3.95 (3H, s, OCH_3), 7.17 (1H, dd, J = 2.6, 8.9 Hz, Ar-H), 7.31 (1H, dd, J = 7.5, 8.2 Hz, Ar-H), 7.73 (1H, d, J = 8.9 Hz, Ar-H), 7.88 (1H, d, J = 8.2 Hz, Ar-H), 7.91 (1H, d, J = 7.5 Hz, Ar-H), 8.25 (1H, d, J = 2.6 Hz, Ar-H); δ_C (75 MHz, $CDCl_3$) 8.9, 34.9, 55.5, 104.4, 119.5, 122.2, 129.1, 129.8, 130.2, 132.1, 132.9, 139.5, 159.8, 205.0; GC-MS: *m*/*z*. (rel. intensity), 214 (100, M$^+$), 185 (72), 142 (8), 71 (9).

2-Butanoyl-2-methoxynaphthalene (2c). White solid, mp 43–45 °C (lit.[15] 46–47 °C). ^{1}H NMR data consistent with lit.;[15] δ_C (75 MHz, $CDCl_3$) 13.9, 17.9, 43.2, 56.2, 119.2, 125.0, 127.3, 127.7, 135.8, 135.4, 139.6, 161.0, 200.9.

2-Butanoyl-6-methoxynaphthalene (3c). White solid, mp 87 °C (lit.[15] 88–89 °C). ^{1}H NMR data consistent with lit.;[15] δ_C (75 MHz, $CDCl_3$) 14.2, 18.3, 40.7, 55.6, 106.0, 119.9, 124.9, 127.3, 128.1, 129.7, 131.3, 132.8, 137.4, 159.9, 200.4.

1-Butanoyl-7-methoxynaphthalene (4c). Colourless oil. ν_{max} ($CHCl_3$) 1690, 1640, 1610, 1520, 1480, 1445, 1400, 1278 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.03–1.07 (3H, t, J = 7.2 Hz, $CH_2CH_2CH_3$), 1.78–1.86 (2H, m, $CH_2CH_2CH_3$), 3.01–3.07 (2H, t, J = 7.2 Hz, $CH_2CH_2CH_3$), 3.93 (3H, s, OCH_3), 7.19 (1H, dd, J = 2.5 Hz, 8.8 Hz, Ar-H), 7.32 (1H, dd, J = 7.9 Hz, 8.0 Hz, Ar-H), 7.73 (1H, d, J = 8.8 Hz, Ar-H), 7.89 (1H, d, J = 8.0 Hz, Ar-H), 8.00 (1H, d, 7.9 Hz, Ar-H), 8.20 (1H, d, J = 2.5 Hz, Ar-H); δ_C (75 MHz, $CDCl_3$) 12.9, 17.2, 42.7, 54.4, 103.2, 118.2, 121.0, 128.2, 128.8, 130.8, 131.1, 132.8, 139.5, 158.5, 203.7. GC-MS: *m*/*z*. (rel. intensity), 228 (88, M$^+$), 185 (100), 157 (7), 142 (12), 71 (8).

2-Phenylacetyl-6-methoxynaphthalene (3d). White solid, mp 114–115 °C (lit.[16] 113–115 °C). ^{1}H NMR data consistent with lit.;[16] δ_C (75 MHz, $CDCl_3$) 45.4, 55.5, 105.8. 119.7, 125.1, 126.8, 127.2, 127.9, 128.7, 129.5, 130.3, 131.2, 134.9, 137.3, 159.9, 197.3.

1-Phenylacetyl-7-methoxynaphthalene (4d). Colourless oil; ^{1}H NMR data consistent with lit.;[16] δ_C (75 MHz, $CDCl_3$) 45.7, 55.3, 108.8, 124.1, 124.5, 127.2, 128.0, 129.3, 133.1, 133.4, 134.5, 136.1, 137.6, 161.0, 197.6.

2-Benzoyl-6-methoxynaphthalene (3e). White solid, mp 84–86 °C (lit.[16] 82–84 °C). ^{1}H NMR data consistent with lit.;[16] δ_C (75 MHz, $CDCl_3$) 55.5, 105.8, 119.7, 126.6, 127.0, 128.3, 130.0, 131.0, 132.0, 132.1, 132.7, 137.0, 138.2, 159.7, 196.6.

1-Benzoyl-7-methoxynaphthalene (4e). White solid, mp 84.5–86 °C (lit.[16] 86.5–87 °C). ^{1}H NMR data consistent with lit.;[16] δ_C (75 MHz, $CDCl_3$) 55.3, 103.9, 119.5, 121.9, 128.4, 129.4, 129.5, 129.9, 130.4, 131.5, 132.5, 133.0, 134.3, 138.8, 158.9, 198.3.

1-Acetyl-4-methoxynaphthalene (6a). White solid, mp 72–73 °C (lit.[17] 68–70 °C). ^{1}H and ^{13}C NMR data consistent with lit.[18]

4-Methoxy-1-propionylnaphthalene (6b). White solid, mp 58–59 °C (lit.[19] 57 °C). ^{1}H NMR data consistent with lit.;[20] δ_C (75 MHz, $CDCl_3$) 9.6, 34.0, 55.7, 102.9, 121.0, 125.1, 128.2, 128.9, 129.1, 129.4, 134.5, 136.2, 159.3, 198.9.

1-Benzoyl-4-methoxynaphthalene (7). White solid, mp 84–86 °C (lit.[21] 83–84 °C). ^{1}H and ^{13}C NMR data consistent with lit.[22]

1,3-Dibenzoyl-4-methoxynaphthalene (8). White solid, mp 132–133 °C; ν_{max} ($CHCl_3$) 2705, 1670, 1605, 1572, 1513, 1456, 1378, 1260, 1182, 1105, 875, 723 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.90 (3H, s, OCH_3), 7.43–7.49 (4H, m, Ar-H), 7.56–7.66 (5H, m, Ar-H), 7.86–7.90 (4H, m, Ar-H), 8.04–8.24 (1H, m, Ar-H), 8.34–8.38 (1H, m, Ar-H); δ_C (75 MHz, $CDCl_3$) 63.5, 123.5, 124.7, 126.1, 127.2, 128.3, 128.5, 128.6, 129.0, 129.2, 130.1, 130.4, 131.4, 133.3, 133.6, 133.7, 137.2, 138.2, 157.7, 195.9, 196.8; GC-MS: *m*/*z*. (rel. intensity), 366 (33, M$^+$), 349 (11), 289 (21), 275 (26), 189 (19), 105 (100), 77 (55).

4-Methoxy-1-phenylacetylnaphthalene (10). White solid, mp 76–77 °C (lit.[23] 78–79 °C); δ_H (300 MHz, $CDCl_3$) 4.05 (3H, s, OCH_3), 4.36 (2H, s, $COCH_2$), 6.79 (1H, d, J = 8.3 Hz, Ar-H), 7.23–7.32 (5H, m, Ar-H), 7.50–7.53 (1H, m, Ar-H), 7.55–7.60 (1H, m, Ar-H), 8.09 (1H, d, J = 8.3 Hz, Ar-H), 8.30 (1H, d, J = 8.3 Hz, Ar-H), 8.90 (1H, d, J = 8.3 Hz, Ar-H); δ_C (75 MHz, $CDCl_3$) 29.7, 48.1, 55.8, 102.0, 122.1, 125.9, 126.1, 126.7, 127.1, 128.6, 128.7, 129.4, 131.4, 132.3, 135.5, 159.2, 199.6; GC-MS: *m*/*z*. (rel. intensity), 276 (8, M$^+$), 185 (100), 157 (22), 142 (12), 127 (14), 114 (30).

1-(4-Methoxy-1-yl)-1-(5-methoxy-1-yl)-2-phenylethene (11). White solid, mp 218–220 °C; $\delta_{\rm max}$ ($CHCl_3$) 2724, 2640, 1593, 1515, 1463, 1425, 1321, 1242, 11164, 1105, 1090, 1018, 822 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.96 (3H, s, OCH_3), 4.01 (3H, s, OCH_3), 6.67 (1H, d, J = 8.1 Hz, Ar-H), 6.76 (1H, d, J = 8.1 Hz, Ar-H), 6.94–7.04 (6H m, Ar-H, C=CH), 7.23 (1H, d, J = 8.1 Hz, Ar-H), 7.25–7.29 (1H, m, Ar-H), 7.31 (1H, d, J = 8.1 Hz, Ar-H), 7.36–7.40 (1H, m, Ar-H), 7.47–7.50 (2H, m, Ar-H), 7.93 (1H, d, J = 8.1 Hz, Ar-H), 8.28 (1H, d, J = 8.1 Hz, Ar-H), 8.31–8.34 (1H, m, Ar-H), 8.54–8.57 (1H, m, Ar-H); δ_C (75 MHz, $CDCl_3$) 55.4, 55.5, 103.3, 103.8, 122.1, 122.4, 125.0, 125.1, 125.7, 125.8, 126.0, 126.1, 126.5, 126.6, 126.7, 127.3, 127.9, 128.1, 129.0, 131.7, 132.4, 133.7, 134.9, 136.8, 137.6, 138.7, 154.7, 155.1; GC-MS: *m*/*z*. (rel. intensity), 416 (100, M$^+$), 385 (18), 339 (16), 326 (11), 307 (12), 258 (80), 243 (26), 215 (26), 168 (15), 156 (21), 126 (12), 91 (7), 77(3).

4-Benzoylanisole (14). White solid, mp 64–66 °C (lit.[24] 62–64 °C). ^{1}H and ^{13}C NMR data consistent with lit.[24] GC-MS: *m*/*z*. (rel. intensity), 212 (95, M$^+$), 135 (100), 77 (20).

2-Benzoylanisole (15). White solid, mp 34–66 °C (lit.[25] 36–37 °C). ^{1}H and ^{13}C NMR data consistent with lit.[26] GC-MS: *m*/*z*. (rel. intensity), 212 (46, M$^+$), 197 (21), 135 (100), 105 (27), 77 (53).

2,4-Dibenzoylanisole (16). White solid, mp 124 °C (lit.[27] 122–123 °C); δ_H (300 MHz, $CDCl_3$) 3.89 (3H, s, OCH_3), 6.97 (1H, d, J = 8.7 Hz, Ar-H), 7.45–7.57 (6H, m, Ar-H), 7.79 (1H, d, J = 8.7 Hz, Ar-H), 7.83 (4H, d, J = 8.7 Hz, Ar-H), 8.20 (1H, s, Ar-H); GC-MS: *m*/*z*. (rel. intensity), 316 (78, M$^+$), 301 (27), 239 (100), 105 (76), 77 (48).

Benzoic acid (4-benzoyl phenyl) ester (17). White solid, mp 113 °C (lit.[28] 113–114 °C). ^{1}H NMR data consistent with lit.;[29] GC-MS: *m*/*z*. (rel. intensity), 302 (100, M$^+$), 225 (49), 197 (22), 105 (32), 77 (32).

Benzoic acid (2,4-dibenzoyl phenyl) ester (18). White solid, mp 145–147 °C (lit.30 144–145 °C); δ_H (300 MHz, $CDCl_3$) 7.35–7.74 (4H, m, Ar-H), 7.47–7.56 (5H, m, Ar-H), 7.62 (1H, t, J = 7.4 Hz, Ar-H), 7.79–7.86 (4H, m, Ar-H), 8.05–8.09 (2H, m, Ar-H); GC-MS: *m*/*z*. (rel. intensity), 406 (22, M$^+$), 361 (5), 301 (18), 223 (8), 195 (5), 105 (100), 77 (48).

2,4-Dibenzoylphenol (19). White solid, mp 100–102 °C (lit.[31] 101 °C). ^{1}H NMR data consistent with lit.;[32] GC-MS: *m*/*z*. (rel. intensity), 302 (5, M$^+$), 198 (7), 141 (2), 105 (100), 77 (24).

Acknowledgement

Our thanks are due to Contract Chemicals, UK for generous gift of Envirocat EPZG®. The authors thank Dr. E. Soľcániová and her staff of Institute of Chemistry of Comenius University for ^{1}H and ^{13}C NMR analyses, Dr. R. Kubinec and his staff of Institute of Chemistry of Comenius University for GC-MS analyses. This work was supported by the VEGA-Grant Agency, Grant No 1/7348/20.

References

1 A. Cornelis, A. Gerstmans, P. Laszlo and Z. I. Mathy, *Catal. Lett.*, 1990, **6**, 103.
2 P. Laszlo and A. Mathy, *Helv. Chim. Acta*, 1987, **70**, 577.
3 A. Vaccari, *Catal. Today*, 1998, **41**, 53.
4 J. H. Clark and D. J. Macquarrie, *Chem. Soc. Rev.*, 1996, 303.
5 P. Laszlo, *J. Phys. Org. Chem.*, 1998, **11**, 356.
6 J. H. Clark and D. J. Macquarrie, *Org. Process Res. Dev.*, 1997, **1**, 149.
7 D. Baudry-Barbier, A. Dormond and F. Duriau-Montagne, *J. Mol. Catal. A: Chem.*, 1999, **149**, 215.
8 B. M. Choudary, M. Sateesh, M. L. Kantam and K. V. R. Prasad, *Appl. Catal. A: General*, 1998, **171**, 155.
9 A. Berreghis, P. Ayrault, E. Fromentin and M. Guisnet, *Catal. Lett.*, 2000, **68**, 121.
10 S. Kobayashi and I. Komoto, *Tetrahedron*, 2000, **56**, 6463.
11 Ch. Laporte, J. Marquié, A. Laporterie, J. R. Desmurs and J. Dubac, *C. R. Acad. Sci., Ser. IIc*, 1999, 455.
12 E. Veverková, B. Gotov, R. Mitterpach and Š. Toma, *Collect. Czech. Chem. Commun.*, 2000, **65**, 644.
13 P. McCloskey, *J. Chem. Soc.*, 1965, 3811.
14 I. N. Zemzina, I. P. Tsurkervanik and N. Yu. Novgorodova, *Zh. Org. Khim.*, 1970, **6**, 132.
15 C. Giordano and M. Villa, *Synth. Commun.*, 1990, **20**, 383.
16 S. Pivsa-Art, K. Okuro, M. Miura, S. Murata and M. Nomura, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1703.
17 M. H. Karger and Y. Mazur, *J. Org. Chem.*, 1971, **36**, 540.
18 S. Perumal, G. Vasuki and D. A. Wilson, *Magn. Reson. Chem.*, 1990, **28**, 257.
19 K. Kindler and T. Li, *Chem. Ber.*, 1941, **74**, 321.
20 W. B. Smith, D. L. Deavenport and A. M. Ihring, *J. Am. Chem. Soc.*, 1972, **94**, 1959.
21 M. E. Gross and H. P. Lankelma, *J. Am. Chem. Soc.*, 1951, **73**, 3439.
22 T. Teitei, D. Wells and W. H. F. Sasse, *Aust. J. Chem.*, 1975, **28**, 571.
23 A. Takuwa, H. Iwamoto, O. Soga and K. Maruyama, *J. Chem. Soc., Perkin Trans 1*, 1986, 1627.
24 D. F. Taber and M. R. Sethuraman, *J. Org. Chem.*, 2000, **65**, 254.
25 G. Hill and F. L. Harris, *J. Org. Chem.*, 1977, **42**, 3306.
26 P. J. Wagner, M. A. Meador and B. S. Park, *J. Am. Chem. Soc.*, 1990, **112**, 5199.
27 I. P. Tsukervanik, N. G. Sidorova and I. A. Stempnevskaia, *Zh. Org. Khim.*, 1970, **6**, 535.
28 M. J. S. Dewar and L. S. Hart, *Tetrahedron*, 1970, **26**, 973.
29 B. Kaboudin, *Tetrahedron*, 1999, **55**, 12865.
30 M. R. Bhatt and N. M. Shaw, *J. Indian. Chem. Soc.*, 1956, **33**, 318.
31 R. Martin and G. Cotton, *Bull. Chem. Soc. Chim. Fr.*, 1973, 1442.
32 P. Hrdlovic, N. Schubertová and R. Palovcík, *Collect. Czech. Chem. Commun.*, 1971, **36**, 1942.

Genuinely catalytic Fries rearrangement using sulfated zirconia

James H. Clark,*[a] Mohammad G. Dekamin[a] and Firouz Matloubi Moghaddam[b]

[a] *Clean Technology Centre, Department of Chemistry, The University of York, Heslington, York, UK YO10 5DD. E-mail: jhc1@york.ac.uk*

[b] *Department of Chemistry, Sharif University of Technology, P. O Box, 11365-9516 Tehran, Iran*

Received 23rd April 2002
First published as an Advance Article on the web 1st July 2002

The reactivity of different carboxylate esters for the Fries rearrangements has been investigated in a solvent-free reaction using sulfated zirconia as a solid acid catalyst.

Introduction

Friedel–Crafts reactions are widely used in industry,[1] but they suffer from the use of highly corrosive, hazardous and polluting Lewis or Bronsted acids, such as AlX_3 (X = Cl, Br or I), BF_3, $TiCl_4$, $FeCl_3$, $ZnCl_2$, $ZrCl_4$, $SnCl_4$, HF, H_2SO_4 and commonly in more than equivalent amounts. As water quenching is necessary at the end of reaction, the process leads to large volume of hazardous waste.[1,2]

Among Friedel–Crafts reactions, the Fries rearrangement is very useful in the manufacture of important pharmaceuticals including acetaminophen and salbutamol,[2] UV adsorbents[3] and pesticides.[4] Some alternative solid acid catalysts including zeolites,[5,6] transition metals triflates,[7] ionic melts[8] and solid sulfonated resins[6,9] have been reported for Friedel–Crafts reactions. These catalysts generally suffer from low activity (especially in acylations and Fries reactions with other than highly activated substrates) low selectivity, and poisoning of the catalyst and its subsequent deactivation. Thus, there remains a need to find new environmentally benign solid acid catalysts for use in this area.

Sulfated Zirconia (SZ) has found several applications for catalysing important reactions in industry such as Friedel–Crafts alkylation, hydrocarbon isomerisation and nitration.[10–12] Here, we wish to report for the first time, the use of SZ as a reusable catalyst for the Fries rearrangement of aromatic carboxylate esters under solvent-free condition.

Results and discussion

We have shown before that the benzoylation of benzene with benzoyl chloride in the presence of different types of commercial SZ can be completed after 48 h at 85 °C. The turnover numbers (the number of moles of desired product formed per mole of catalyst at the end of the reaction period) were greater than 20. Faster reactions can be achieved by using more reactive substrates, such as anisole which gives complete reaction after 1 h at 140 °C.[10] These findings encouraged us to study the reactivity of benzoate esters for the Fries rearrangement, a reaction similar to the above reactions in terms of substrate reactivity and regioselectivity. It is also interesting that the use of $ZrCl_4$ for the selective rearrangement of phenyl acetate derivatives reported in recent years requires four equivalents of the Lewis acid.[13]

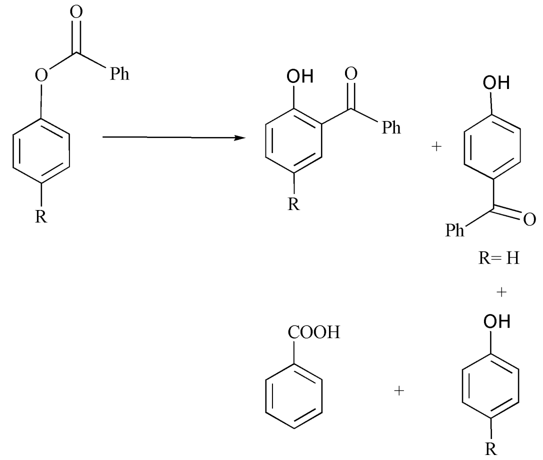
We have found that the thermal Fries rearrangement of benzoate esters can be catalysed by optimally activated SZ[14] under solvent-free condition. Thus, phenyl benzoate (substrate to catalyst mole ratio = 1.9) reacts to give 22% of the Fries products after 4 h at 150 °C (Table 1, entry 1). The catalyst is *o*-selective, however the percentage of the hydrolysis product is somewhat high (Scheme 1). Stronger coordination of Friedel–Crafts products with the catalyst compared to substrate is a well-known phenomenon.[15] In the case of the Fries rearrangement this can be enhanced by the presence of the hydroxyl moiety in the product and that has led some research groups to use such compounds for the preparation of bidentate Lewis acid catalysts.[16] Heating the reaction mixture for longer times and also using dried substrate gives higher level of conversions and relatively little hydrolysis (Table 1, entries 2, 4). The catalyst is reusable and can be reactivated to restore the original activity (for example, see Table 1, entry 3). Using higher temperatures and shorter reaction times leads to higher (60%) conversion but selectivity decreases. Other results are given in Table 1.

Using the more reactive derivative, 4-methylphenyl benzoate gives slightly better conversion and selectivity (Table 1, entry 8). In this case, another commercial type of the catalyst exhibits less selective catalytic activity (Table 1, entry 12).[14] Further experiments show that the catalyst is only active in the early stages of the reaction (Table 1, entries 8–14). This can be explained by the reaction of the products with the surface of the catalyst to release water into the reaction mixture.[16] This will lead both to competitive hydrolysis reaction as observed and to the deactivation of the catalyst by product adsorption which can be reactivated by thermally desorbing the organics. It is interesting that the extent of the hydrolysis reaction is the same at different reaction times indicating that this is controlled simply by the amount of water present (Table 1, entries 1–5 and 8–14).

Green Context

The Friedel–Crafts Fries rearrangment is important in the manufacture of pharmaceuticals. Advances have been made in avoiding traditional, highly polluting Lewis or Bronsted acids through the development of solid acid catalysts, but to date these suffer from low acidity, selectivity and deactivation. In contrast solid sulfated zirconia is a reusable stable catalyst for the Fries rearrangement, established for solvent free conditions. This has implications in minimizing waste with improved efficiencies. ***DJH***

DOI: 10.1039/b203943p

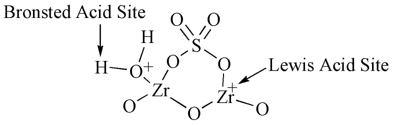


Scheme 1

Surface area analysis of the catalyst before and after the reaction shows that BET surface area is decreased by up to 1/3. For example the BET surface area for the catalyst used in the entry 10 is 108 $m^2 g^{-1}$ compared to 163 $m^2 g^{-1}$ for the fresh catalyst. The data obtained from thermal analysis shows at temperatures higher than 400 °C that the used catalyst loses about 3–4% of its initial weight while for the fresh catalyst the weight loss is $< 1\%$. These findings are consistent with the proposed reaction of the product with the catalyst and the observed ability to reactivate the used catalyst thermally.

Using higher substrate to catalyst mole ratios proves genuine catalysis with catalyst turnover numbers considerably greater than 1 although the reaction selectivity decreases slightly (Table 2). The effect of microwave dielectric heating was also investigated following our earlier works using this technique for the promotion of organic reactions.[17–19] Higher conversions and selectivities are obtained and the *o*/*p* ratio is increased up to 50 (Table 1, entries 7 and 15).

In conclusion, the catalytic activity of SZ (see Scheme 2) as a reusable solid acid catalyst for Fries reactions has been proven in a solvent-free process. The activity of the catalyst is superior to other solid acids, such as zeolites, and with better reaction selectivity.[5] Importantly the catalyst can be reactivated after poisoning with product restoring its original activity. The separation of the catalyst from the reaction mixture can be performed simply by suspension in acetone and subsequent filtration. Further investigation of this methodology and the use of SZ for the direct C-acylation of phenols is under investigation and will be presented in due course.



Scheme 2 One of the proposed models for SZ.[20] Phenolic products of the reaction can substitute the water molecules.

Table 2 Effect of different substrate to catalyst mole ratios at 200 °C after 24 h in the Fries rearrangement of 4-methylphenyl benzoate

Entry	Substrate/ catalyst mole ratio	Conversion (%)	Fries rearr. (%)	Selectivity (%)	Catalyst turnover number
1	0.95	73	60	82	0.69
2	1.9	56	45	81	1.06
3	3.8	44	34	77	1.67
4	7.6	41	30	73	3.12
5	17.54	35	26	74	6.14
6	20.0	35	24	69	7.0

Experimental

The chemicals were purchased from Aldrich except for the SZ which was supplied by MEL chemicals. When using dried substrates, they were initially ground and then dried for 8 h at 10 °C lower than their mp under reduced pressure. A GC method was used for determination of reactions yields, with dodecane as external standard. The reaction products were compared to authentic samples and further identification was achieved by GC–MS. All the experiments were performed under atmospheric pressure and protected from air moisture by a calcium chloride guard. Surface area analysis was completed using an ASAP 2010 Porosimeter. Thermal analysis of the catalyst was performed using a Thermal Scientific STA 625. A household Proline microwave with maximum power of 700 W was used in this study.

General procedure for the Fries rearrangement (Table 1, entry 10)

4-Methylphenyl benzoate (11.5 mmol, 2.43 g) was placed in a one-neck 25 ml flask and 600 °C-calcined SZ added (6.05

Table 1 Fries rearrangements catalysed by sulfated zirconia (substrate to catalyst mole ratio = 1.9)

Entry	R	*T*/°C (*t*/h)	Conversion (%)	Fries rearr. (%) (*o*/*p*)	Selectivity (%)	Catalyst turnover number
1	H	150 (4)	33	22 (2.03)	67	0.63
2	H	150 (48)	46	33 (3.19)	72	0.87
3[a]	H	150 (48)	47	32 (2.5)	68	0.89
4[b]	H	150 (48)	49	38 (3.11)	77	0.93
5[c]	H	Reflux (48)	29	22 (1.2)	76	0.55
6	H	200 (16)	60	40 (1.63)	67	1.14
7[d]	H	M.W (high) (10 min)	68	67 (50)	99	1.29
8	Me	150 (48)	50	39	78	0.95
9	Me	150 (24)	40	32	80	0.76
10	Me	200 (24)	56	45	81	1.06
11	Me	200 (48)	60	49	82	1.14
12[e]	Me	200 (24)	56	42	75	1.06
13	Me	200 (4.5)	42	31	74	0.80
14	Me	200 (12)	44	33	75	0.84
15[f]	Me	M.W (med.-high) (10 min)	60	52	87	1.14

[a] Catalyst used in experiment 2 was reactivated for 3 h at 550 °C. [b] Dried substrate was used. [c] Dry toluene was used as solvent. [d] The reaction mixture was irradiated continuously at 700 W. [e] SZ denoted as XZO682/2 was used. [f] The reaction mixture was irradiated 3 times with 4 min intervals.

mmol, 4 mmol Zr/g catalyst, 1.5 g). The mixture was protected from moisture and equipped with a condenser and calcium chloride guard. The mixture was put in an oil-bath at 200 °C and stirred for 24 h. Then, the mixture was cooled to ambient temperature and suspended in acetone (60 ml × 4). The filtrate was analyzed by GC using dodecane (5.75 mmol, 0.977 g) as external standard.

Acknowledgment

We thank MEL Chemicals for providing the sulfated zirconia. M. G. D. acknowledges the Ministry of Science, Research and Technology of Iran for his scholarship. We are also grateful to members of the York Green Chemistry Group for helpful discussions.

References

1 G. A. Olah, *Friedel–Crafts chemistry*, Wiley-Interscience, New York, 1983; J. H. Clark, *Catalysis of Organic Reactions by Supported Inorganic Reagents*, VCH, New York, 1994, ch. 3, p. 41.
2 P. Metivier, *Fine Chemicals through Heterogeneous Catalysis*, ed. R. A. Sheldon and H. Van Bekkum, Wiley–VCH, Weinheim, 2001, ch. 4, p. 161; M. Guisnet and G. Perot, *Fine Chemicals through Heterogeneous Catalysis*, Wiley–VCH, Weinheim, 2001, ch. 5, p. 211.
3 W. B. Motherwell and S. Vazquez, *Tetrahedron Lett.*, 2000, **41**, 9667 and references therein.
4 F. Terunori and I. Masaharn, *Jpn. Kokai Tokkyo Koho JP*, 60,252,444, 1985; *Chem. Abstr.*, 1986, 104, 168144q.
5 A. Vogt, H. W. Kouwenhovn and R. Prins, *Appl. Catal. A: General*, 1995, **123**, 37 and references therein.
6 A. Heidekum, M. A. Harmer and W. F. Hoelderich, *J. Catal.*, 1998, **176**, 260.
7 S. Kobayashi, M. Moriwaki and I. Hachiya, *Tetrahedron Lett.*, 1996, **37**, 2053.
8 J. R. Harjani, S. J. Nara and M. M. Salunkhe, *Tetrahedron Lett.*, 2001, **42**, 1979.
9 G. A. Olah, M. Arvanaghi and V. V. Krishnamurthy, *J. Org. Chem.*, 1983, **48**, 3359.
10 J. H. Clark, G. L. Monks, D. J. Nightingale, P. M. Price and J. F. White, *J. Catal.*, 2000, **193**, 348.
11 P. M. Price, J. H. Clark, K. Martin, D. J. Macquarrie and T. W. Bastock, *Org. Process Res. Dev.*, 1998, **2**, 221.
12 G. D. Yadav and J. J. Nair, *Microporous Mesoporous Mater.*, 1999, **33**, 1.
13 D. C. Harrowven and R. F. Dainty, *Tetrahedron Lett.*, 1996, **37**, 7659.
14 Two types of SZ provided by MEL Chemicals, denoted as XZO999/1 and XZO682/1, were used in this study. The first one provided better catalytic activity for the Fries rearrangements in our hands.
15 U. Freese, F. Heinrich and F. Roessner, *Catal. Today*, 1999, **49**, 237.
16 For a notable report using zirconium and 2-hydroxydiarylketones in this context, see: H. Hanawa, S. Kii, N. Asao and K. Marouka, *Tetrahedron Lett.*, 2000, **41**, 5543 and references therein.
17 F. Matloubi Moghaddam and M. G. Dekamin, *Tetrahedron Lett.*, 2000, **41**, 3479.
18 F. Matloubi Moghaddam and M. G. Dekamin, *Tetrahedron Lett.*, 2001, **42**, 8119.
19 F. Matloubi Moghaddam, M. Ghaffarzadeh and S. H. Abdi-Oskui, *J. Chem. Res. (S)*, 1999, 575.
20 K. Arata and M. Hino, *Appl. Catal.*, 1990, **59**, 197.

Tetrahydropyranylation of alcohols catalyzed by polyaniline salts

S. Palaniappan,* M. Sai Ram and C. A. Amarnath

Organic Coatings and Polymers Division, Indian Institute of Chemical Technology,
Hyderabad 500 007, India

Received 17th June 2002
First published as an Advance Article on the web 12th July 2002

Polyaniline salts have been used as catalysts for the tetrahydropyranylation of alcohols in a process being reported for the first time. The catalytic use of polyaniline salts is practical because of their easy preparation, recovery and reusability.

Introduction

The replacement of current chemical processing with more environmentally benign alternatives is an increasingly attractive subject.[1] The tetrahydropyranyl (THP) group is often the protective group of choice for peptides,[2] nucleotides,[3] carbohydrates[4] and steriods.[5] The THP group is a versatile protecting group for alcohols and phenols in organic synthesis owing to its stability under strongly alkaline conditions, to Grignard and alkyllithium reagents, to reduction with inorganic hydrides, and to alkylating and acylating agents, and the THP group has been widely used for hydroxy protection.[6] In addition to the well known protic and Lewis acids,[7] other reagents and catalysts such as pyridinium *p*-toluenesulfonate,[8] the hydrochloride salt of poly(4-vinylpyridine),[9] iodotrimethylsilane,[10] triphenylphosphene hydrobromide,[11] montmorillonite,[12] bis(trimethylsilyl)sulfate,[13] Nafion-H[14] *etc.* have been used to effect the tetrahydropyranylation of alcohols.

In view of environmental mandates, there is a global effort to replace conventional catalysts by eco-friendly catalysts. In this work, polyaniline salts are used as catalysts in the tetrahydropyranylation of alcohols.

Experimental

Preparation of polyaniline salt catalysts

4.85 g of benzoyl peroxide was dissolved in 150 ml dioxane. To this solution, 1.44 g of sodium lauryl sulfate in 25 ml distilled water was added. 2.4 ml aniline in 30 ml aqueous solution containing acid (hydrochloric acid (18.6 ml), sulfuric acid (9.0 ml) or nitric acid (13.4 ml)) was introduced dropwise into the above solution at 35 °C. The mixture was stirred for 24 h at 35 °C and the precipitated polyaniline salt was filtered off, and then washed with 3 L of distilled water, followed by methanol. The resulting polymer salt was finally dried at 100 °C until a constant mass was reached. The yields of polyaniline salt with the different protonic acids hydrochloric acid, sulfuric acid and nitric acid were 1.11, 1.43 and 1.34 g, respectively. The molecular weight of the polyaniline salts was not determined since they are not soluble in common organic solvents.

Procedure for tetrahydropyranylation

Tetrahydropyranylation of dihydropyran and alcohols was carried out in a 10 ml round bottom flask using a polyaniline salt as catalyst. The reaction mixture was heated at 50 °C for a given time. The reaction mixture was then filtered and washed with hexane to recover the catalyst. The hexane solvent was then evaporated off. The compound was loaded in a column containing silica gel of 60–120 mesh and eluted with ethyl acetate–hexane. The solvent mixture was recovered to obtain the pure product. The products were characterized by FT-IR and ^{1}H NMR spectroscopy. The details of the experimental conditions are given in the Tables.

Results and discussion

Recent advances in the field of electrically conducting polymers have led to a variety of materials with great potential applications. Electrically conducting polymers form a unique class of materials, offering the possibility of controlled electrical conductivity combined with good processing characteristics, low cost and stability. Among them, polyaniline is one of the most interesting materials because of its moderately high conductivity upon doping with acids, well behaved electrochemistry, easy preparation, possible processability and good

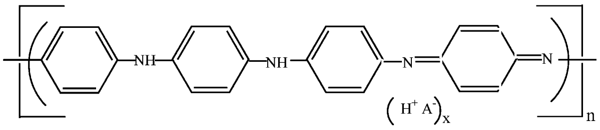
Green Context

While the use of protecting groups may not be expected to feature in the 'ideal synthesis', they remain very widely used in such as peptide, nucleotide, carbohydrate and steroid chemistry. The tetrahydropyranyl group is particularly popular in this context. When protection is to be used then, as with any processes, we want to ensure the greenest, most efficient conditions. Here, the novel use of a polymer more commonly associated with conductive materials than catalysis is described in the tetrahydropyranylation of alcohols. Polyaniline salts are efficient catalysts and they are easily recovered and reused. *JHC*

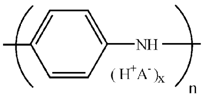
DOI: 10.1039/b205860j

environmental stability.[15] In this work, the application of polyaniline salts as catalysts was attempted. Polyaniline salts such as polyaniline hydrochloride, polyaniline sulfate and polyaniline nitrate were prepared by chemical oxidative polymerization of aniline by benzoyl peroxide in presence of acid.[16]

The general formula of polyaniline salts is as shown below:



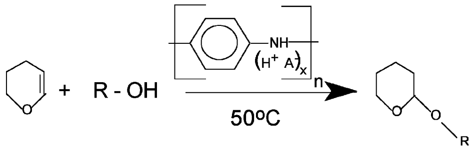
A more simplified formulation of polyaniline salts is represented by:



The dopant group (acid group) per aniline unit present in the polymer chain was calculated from elemental analyses. The percentage of carbon, hydrogen, nitrogen and sulfur was calculated theoretically by varying the acid group from $x = 0.1$ to 0.5 in steps of 0.01. The number of acid groups per aniline unit was found by comparing the experimental value with that of the theoretical value and the results are reported in Table 1.

The number of acid groups (dopant) per aniline unit was found to be 0.27, 0.21 and 0.24 whereas, the amount of acid present in the polyaniline salt was 22.1, 12.4 and 8.6 wt% with respect to dopants sulfuric acid, nitric acid and hydrochloric acid respectively (Table 1).

As shown in Table 2, polyaniline salts can promote the tetrahydropyranylation of behenyl alcohol at 50 °C for 4 h. Polyaniline sulfate salt was efficient in giving the ether in good yield (Table 2, entry 1) when compared to polyaniline nitrate and polyaniline hydrochloride salts (Table 2, entries 2 and 3). The reason as to this may be the higher strength of sulfuric acid.



It is possible to employ different solvents for the tetrahydropyranylation of alcohols (Table 3). For example, behenyl alcohol was tetrahydropyranylated at 50 °C for 4 h using three different solvents. Reasonably good yield was obtained with chloroform as solvent (Table 3, entry 1) while a lower yield resulted with tetrahydrofuran as solvent (Table 3, entry 3). When acetonitrile was used as solvent a 70% yield (Table 3, entry 2) was obtained and no byproduct was observed in the presence of an acid catalyst (polyaniline salt). This result shows that polyaniline salts act as mild polymer solid acid catalysts.

Reusability of the catalyst was checked by the tetrahydropyranylation of behenyl alcohol with polyaniline sulfate salt as catalyst which resulted in a yield of 78%. The polyaniline salt catalyst was recovered and reused three times for tetrahydropyranylation of the alcohol with the ether being obtained in 75–78% yield.

Table 2 Tetrahydropyranylation of behenyl alcohol catalyzed by polyaniline salts[a]

Entry	Polyaniline salt	Yield (%)[b]
1	Polyaniline sulfate	78
2	Polyaniline nitrate	50
3	Polyaniline hydrochloride	47

[a] *Reaction conditions*: 3,4-dihydro-2*H*-pyran (DHP) (10 mmol), behenyl alcohol (10 mmol), chloroform (5 ml), polyaniline salt (1.7 mmol with respect to a single unit of the polyaniline salt *i.e.* 20 wt% based on weight of DHP), temperature: 50 °C, time: 4 h. [b] Isolated product.

Table 3 Tetrahydropyranylation of behenyl alcohol in different solvents catalyzed by polyaniline sulfate salt[a]

Entry	Solvent	Yield (%)[b]
1	Chloroform	78
2	Acetonitrile	70
3	Tetrahydrofuran	50

[a] *Reaction conditions*: 3,4-dihydro-2*H*-pyran (DHP) (10 mmol), behenyl alcohol (10 mmol), solvent (5 ml), polyaniline sulfate salt (1.7 mmol with respect to a single unit of the polyaniline salt *i.e.* 20 wt% based on weight of DHP), temperature: 50 °C, time: 4 h. [b] Isolated product.

After these preliminary examinations, tetrahydropyranylation of functionalized alcohols (primary, secondary, tertiary, allylic, propargylic, benzylic, diols, cyclic) was scrutinized at 50 °C using polyaniline sulfate salt as catalyst without using any solvent.

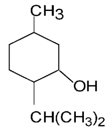
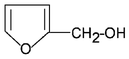
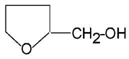
Treatment of 3,4-dihydro-2*H*-pyran with decanol in polyaniline sulfate salt for 8 h at 50 °C afforded the ether (Table 4, entry 1) with a yield of 62%. The reaction was extended to a variety of alcohols (Table 4, entries 2–7, primary, benzylic, allylic, propargylic) which also underwent facile tetrahydropyranylation affording the corresponding ethers. Even the otherwise less reactive tertiary amyl alcohol afforded the corresponding ether in 38% yield (Table 4, entry 8). The polyaniline sulfate salt was employed for tetrahydropyranylation of butoxyethanol which gave the ether in a low yield of 52% (Table 4, entry 9). THP was further extended to diols such as butane-1,4-diol and but-2-ene-1,4-diol. Butane-1,4-diol gave the ether in 63% yield (Table 4, entry 10) and the ratio of mono : di product was 1 : 1.2. But-2-ene-1,4-diol gave the ether in 55% yield (Table 4, entry 11) retaining the same configuration and the ratio of mono : di product was 1 : 1.1. THP of DL-menthol produced the ether in very low yield of 43% (Table 4, entry 12). Tetrahydropyranylation was further extended to furfuryl alcohol which gave a higher yield of 75% (Table 4, entry 13) when compared to tetrahydropyranylation of tetrahydrofurfuryl alcohol which gave a 62% yield (Table 4, entry 14).

For liquid alcohols, tetrahydropyranylation can be carried out using polyaniline salt catalyst with/without using any solvent whereas solid alcohol can be tetrahydropyranylated using solvents.

Table 1 Theoretical and experimental values of the percentage of carbon, hydrogen, nitrogen and sulfur of polyaniline salts

	Theoretical value (%)				Experimental value (%)					
Sample	C	H	N	S	C	H	N	S	No. of acid groups per aniline unit	Dopant (%)
PANI-H_2SO_4	61.3	4.7	11.9	7.4	60.6	4.5	12.5	7.1	0.27	22.1
PANI-HNO_3	67.8	4.9	16.3	10.9	68.2	4.4	15.8	11.5	0.24	12.4
PANI-HCl	73.0	5.3	14.2		73.7	5.0	13.6		0.21	8.6

Table 4 Tetrahydropyranylation of alcohols catalyzed by polyaniline sulfate salt[a]

Entry	Alcohol	Yield (%)[b]
1	$CH_3(CH_2)_9OH$	62
2	$C_6H_5CH_2OH$	59
3	$C_6H_5CH_2CH_2OH$	66
4	$C_6H_5CH{=}CHCH_2OH$	71
5	$Cl(CH_2)_3OH$	65
6	$CH_2{=}CHCH_2OH$	70
7	$CH{\equiv}CCH_2OH$	66
8	$CH_3CH_2C(CH_3)_2OH$	38
9	$CH_3CH_2CH_2CH_2OCH_2CH_2OH$	52
10	$HO(CH_2)_4OH$	63
11	$HOCH_2CH{=}CHCH_2OH$	55
12		43
13		75
14		62

[a] *Reaction conditions*: 3,4-dihydro-2*H*-pyran (DHP) (12 mmol), alcohol (10 mmol), polyaniline sulfate salt (1.7 mmol with respect to a single unit of the polyaniline salt *i.e.* 20 wt% based on weight of DHP), temperature: 50 °C, time: 8 h. [b] Isolated product.

Conclusion

In conclusion, a mild and versatile THP method has been developed based on polyaniline salts. This method has several advantages: the catalytic use of polyaniline salts is practical because of their easy preparation, recovery, reusability and low toxicity. However, the efficiency of the polyaniline salt catalysts in tetrahydropyranylation is found to be low and work is under progress to improve the activity.

References

1 P. T. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, 1998.
2 M. Bodanszky and M. A. Ondehi, *Peptide Synthesis*, Wiley-Interscience, London, 1966, ch. 4.
3 J. H. Van Boom, P. M. J. Burgers, G. R. Owen, C. B. Reese and R. Saffhill, *Chem. Commun.*, 1971, 869.
4 C. Auge, C. D. Warren and R. W. Jeanloz, *Carbohydrate Res.*, 1980, **82**, 85.
5 C. Djerassi, *Steroid Reactions*, Holden-Day, San Francisco, 1963, p. 76.
6 C. B. Reese, *Protective groups in Organic Chemistry*, Plenum Press, London, 1973, ch. 3.
7 (*a*) T. W. Greene and P. G. M. Wuts, *Protective groups in Organic Synthesis*, Wiley, New York, 1991, 2nd edn., p. 31; (*b*) L. A. Paquette, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley & Sons Ltd., Chichester, UK, 1995.
8 M. Miyashita, A. Yoshikoshi and P. A. Grieco, *J. Org. Chem.*, 1977, **42**, 3772.
9 R. D. Johnston, C. R. Marston, P. E. Krieger and G. L. Goe, *Synthesis*, 1988, 393.
10 G. A. Olah, A. Hussain and B. P. Singh, *Synthesis*, 1985, 703.
11 V. Bolitt, C. Mioskowski, D. S. Shin and J. R. Falck, *Tetrahedron Lett.*, 1988, 4583.
12 S. Hoyer, P. Laszlo, M. Orlovic and E. Polla, *Synthesis*, 1986, 655.
13 Y. Morizawa, I. Mori, T. Hiyama and H. Nozaki, *Synthesis*, 1981, 899.
14 G. A. Olah, A. Hussain and B. P. Singh, *Synthesis*, 1983, 892.
15 *Handbook of Organic Conductive molecules and Polymers*, ed. H. S. Nalwa, John Wiley & Sons, Chichester, UK, 1997, vol.1–4.
16 S. Palaniappan, *Indian & US Pat.*, application pending.

Novel calcium based sorbent (Ca-C) for the dehalogenation (Br, Cl) process during halogenated mixed plastic (PP/PE/PS/PVC and HIPS-Br) pyrolysis

Thallada Bhaskar,[a] Toshiki Matsui,[b] Jun Kaneko,[a] Md. Azhar Uddin,[a] Akinori Muto[a] and Yusaku Sakata[a]

[a] *Department of Applied Chemistry, Faculty of Engineering, Okayama University, 3-1-1 Tsushima Naka, 700-8530 Okayama, Japan. E-mail: yssakata@cc.okayama-u.ac.jp*
[b] *Toda Kogyo Co. Ltd, Hiroshima 739-0652, Japan*

Received 17th May 2002
First published as an Advance Article on the web 11th July 2002

A calcium carbonate carbon composite sorbent (Ca-C) was prepared by using 90 wt% of calcium carbonate and 10 wt% phenol resin. The Ca-C sorbent was successfully utilised for the dechlorination and debromination process during halogenated (Cl, Br) mixed waste plastic (PP/PE/PS/PVC/HIPS-Br: 3:3:2:1:1) pyrolysis at 430 °C and produced halogen free liquid products.

Introduction

The disposal of waste plastics is a serious environmental problem as they are not biodegradable. The development of viable recycling technologies for plastic waste materials is becoming increasingly important. Feedstock recycling of waste plastics has more advantages than mechanical recycling or energy recovery, as the energy consumption of the process is very low (only about 10% of the energy content of the waste plastic is used to convert the scrap into petrochemical products). In addition, the volume of harmful gases produced is much lower than that of the incineration process. The degradation of waste plastics into fuel is one of the best methods for preserving valuable petroleum resources in addition to protecting the environment by limiting the volume of non-degradable waste.

Municipal plastic waste (MPW) is a mixture of non-halogenated (PP, PE, PS, PET *etc.*) and halogenated (PVC, HIPS-Br, ABS *etc.*) plastic. Waste from electrical and electronic equipment (WEEE) can contain polybrominated biphenyls, polybrominated diphenyloxides or tetrabromobisphenol-A. High impact polystyrene (HIPS-Br) accounts for more than half of the plastic housing used in domestic electrical and electronic appliances, and acrylonitrile–butadiene–styrene (ABS) plastic is the next most commonly used plastic.[1]

Unlike PE, PP and PS degradation, the MPW polymers pose a serious environmental threat, since, upon thermal degradation, they produce chlorinated hydrocarbons which can be the precursors of toxic emissions such as polychlorinated dibenzodioxins (PCDDs), dibenzofurans (PCDFs) and polychlorobiphenyls (PCBs).[2,3] In addition, PVC and HIPS-Br pyrolysis or combustion presents its own particular problem, due to the formation of highly corrosive HCl and HBr, and it may produce halogenated organic compounds. The presence of such compounds in the liquid products means they cannot be used as fuels, necessitating the removal of the halogen content from the waste plastic derived oil. There has been plethora of research work published[4–10] on the recovery of valuable chemicals and energy recovery from non-halogenated waste plastics and halogenated (chlorinated) waste plastics at higher temperatures using different methods. Recently, Kaminsky and Hartmann[11] highlighted the new pathways in plastic recycling and the current status of plastics recycling. In our earlier studies, we have reported on the thermal and catalytic degradation of polyethylene (PE), polypropylene (PP), PVC and their mixtures into fuel oil.[12–14] However, no studies have been carried out on the recycling of brominated high impact polystyrene (HIPS-Br) and PVC mixed with PP/PE/PS, into halogen free liquid products. Here we report for the first time that a single step process for degradation of PP/PE/PS mixed with PVC and HIPS-Br plastics into halogen-free liquid products using a calcium based sorbent (Ca-C). The halogen-free liquid products can be used as fuel or feed stock in a refinery.

Results and discussion

The thermal degradation of mixed plastics (weight ratio PP/PE/PS/PVC/HIPS-Br = 3:3:2:1:1) was carried out under atmospheric pressure in a batch process at 430 °C and degradation also carried out in the presence of Ca-C. A degradation temperature of 430 °C was chosen from our earlier studies on individual and mixed plastic pyrolysis process.[12–14] The products of mixed plastic degradation were classified into three groups: gas, liquid and degradation residue. Table 1 shows the yield of products such as gas, liquid, residue, average carbon number, and density of liquid products obtained during thermal degradation and also degradation using Ca-C. The thermal degradation yielded liquid products (71 wt%) with average carbon number 13.7 and density of 0.82 g cm^{-3}. The use of Ca-C sorbent in the degradation process decreased the liquid products from 71 wt% to 62 wt% (Ca-C 2 g) and 66 wt% (Ca-C

Green Context

Waste plastic is an enormous potential resource which, if treated properly, could serve a second time as a hydrocarbon raw material, or as a fuel. However, the large amount of halogenated plastics currently used present significant difficulties for second use, with the generation of very corrosive hydrogen halides. This article describes the development of a novel dehalogenation and pyrolysis process which allows the direct formation of usable liquid fuel from these problematic plastics. ***DJM***

DOI: 10.1039/b203745a

4 g). The amount of residue observed with thermal degradation and Ca-C (2 g) was 12 wt%. However, the residue in the degradation process with Ca-C (4 g) was about 9 wt% (Table 1). The density of liquid products did not change in the presence of Ca-C sorbent. The gaseous products, not condensed as liquid products, were passed through the high temperature furnace (900 °C) with the aspirator. During this, the gaseous halogenated organic compounds (if any) were converted into inorganic halogen compounds, which were then passed through the water trap and captured as HBr or HCl (Fig. 1).

It is noteworthy that AED-GC can detect the chlorinated and brominated compounds selectively. The quantitative analysis of chlorine and bromine in the liquid products was by GC-AED and the results are presented in Fig. 2. As can be seen from Fig. 2 the thermal degradation of mixed plastics (weight ratio PP/PE/PS/PVC/HIPS-Br = 3 : 3 : 2 : 1 : 1) produced liquid products with 7300 ppm of bromine and 1120 ppm of chlorine. However, with the use of 2 g of Ca-C in the degradation process, the halogen content drastically decreased (bromine content 320 ppm, chlorine 115 ppm). With an increase of sorbent from 2 g to 4 g in the degradation process, halogen was completely removed from the liquid products. In another process, for comingled plastics containing PVC, lime was added to the input material and the PVC content was reduced to 2–3 wt% in order to avoid adhesion of $CaCl_2$ in the fluidized bed which resulted in blockage in the pipes.[15] In the present study, not only the chlorine but also the bromine content was completely absent at 430 °C.

The liquid products were analyzed by GC-MS to identify the compounds. In our present study, the major hydrocarbons during (thermal and Ca-C) degradation were aromatic hydrocarbons such as benzene, toluene, ethyl benzene, propyl benzene, styrene, 1-methylethyl benzene, butyl benzene, α-methylstyrene, *etc*. In addition to the above compounds, anthracene, naphthalene and substituted derivatives of anthracene and naphthalene were also observed during the thermal degradation.

Table 1 Product yields and properties of liquid products from PP/PE/PS/PVC + HIPS-Br degradation at 430 °C in the absence and presence of Ca-C sorbent (weight ratio: PP : PE : PS : PVC : HIPS-Br = 3 : 3 : 2 : 1 : 1)

Degradation method	Yield of degradation products (wt%) Liquid (L)	 Gas (G)[a]	 Residue (R)	Liquid products C_{np}[b]	 Density/ g cm^{-3}
Thermal	71	17	12	13.7	0.82
Ca-C (2 g)	62	26	12	11.9	0.81
Ca-C (4 g)	66	25	9	12.4	0.81

[a] G = 100 − (L + R). [b] C_{np} = Average carbon number of liquid products based on C-NP gram.

The presence of chlorinated and brominated compounds during both the thermal degradation and also degradation using 2 g of Ca-C was observed. The chlorinated hydrocarbons found during the thermal degradation were 2-chloro-2-phenylpropane, 2-chloro-2-methylpropane, 2-chloro-2-methylpentane and α-chloroethylbenzene while brominated hydrocarbons included bromocyclohexane and 1-bromoethylbenzene.

The formation of $SbBr_3$ was observed in earlier studies on the thermal degradation of polyester flame-retarded with antimony oxide/brominated polycarbonate.[16] However, we have not observed any such compounds in the liquid products obtained from HIPS-Br mixed with PVC/PP/PE/PS at 430 °C.

Richard *et al.*,[17] reported that the high temperature degradation of polybrominated flame retardant materials produced bromobenzenes, bromophenols, polybrominated dibenzodioxins (PBDDs) and polybrominated dibenzofurans (PBDFs), however, they were subsequently destroyed at high temperature (800 °C) . Dioxin formation (PHDD) and furan formation (PHDF) in the thermal treatment of plastics containing polybrominated diphenyl ether with several flame retardants has been reported.[18] Diantimony trioxide and decabromodiphenylene ethers (heating of HIPS for 20 min) produced dioxins at 275 °C. Former test campaigns by the Forschungszentrum Karlsruhe and the Association of Plastic Manufacturers in Europe, in the Karlsruhe TAMARA test facility for waste combustion, focussed on the existence, partitioning, and destruction of bromine and its influence on the formation of bromine containing dibenzo-*p*-dioxins and dibenzofurans.[19,20] In the present study, we have not found any such compounds and the gases (which are not condensed) were passed through the furnace at 900 °C for complete destruction (Fig. 1).

The average carbon number (C_n) of the liquid product decreased in the presence of Ca-C sorbent due to the cracking of higher molecular weight compounds (Table 1 and Fig. 3). The liquid products were characterized by a Normal Paraffin gram (NP-gram) proposed by Murata *et al.*[21] Fig. 3 illustrates the C-NP gram of the liquid products obtained by analyzing their gas chromatogram. The carbon numbers in the abscissa of the NP-gram are equivalent to retention values of the corresponding normal paraffin and the ordinate shows the weight percent of the corresponding hydrocarbons. The amount of higher hydrocarbons decreased in the presence of Ca-C at 430 °C. The amount of C_6–C_{10} hydrocarbons produced during the thermal degradation was 20 wt%, and in the presence of Ca-C (2 or 4 g) degradation produced approximately 30 wt%. However, the amount of C_{16}–C_{20} hydrocarbons was decreased in the presence of Ca-C sorbent (Fig. 3).

X-Ray diffraction studies revealed the presence of $CaCO_3$ phase in the fresh Ca-C sorbent. The X-ray diffraction patterns

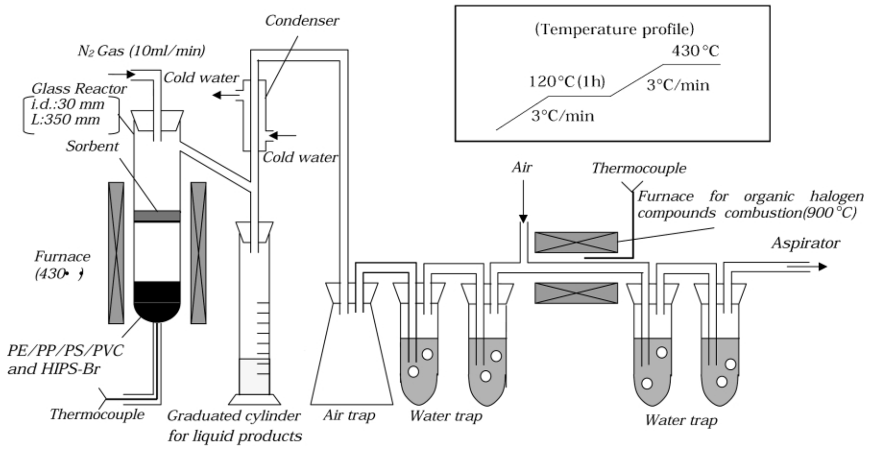


Fig. 1 Schematic experimental setup and temperature profile for PP/PE/PS/PVC + HIPS-Br degradation at 430 °C.

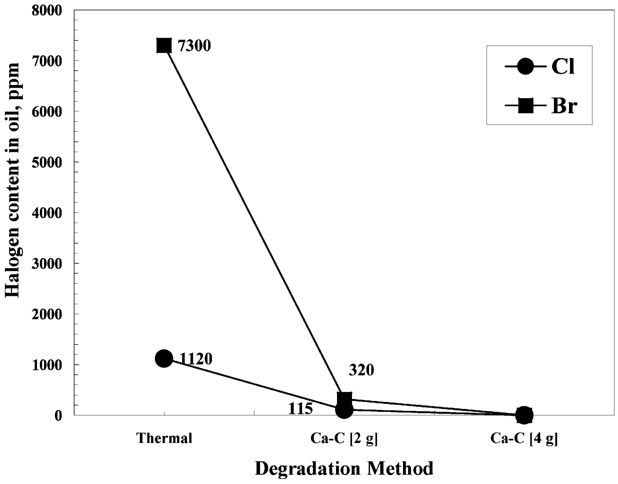


Fig. 2 The effect of Ca-C sorbent for dehalogenation (Cl and Br) during PP/PE/PS/PVC + HIPS-Br degradation at 430 °C

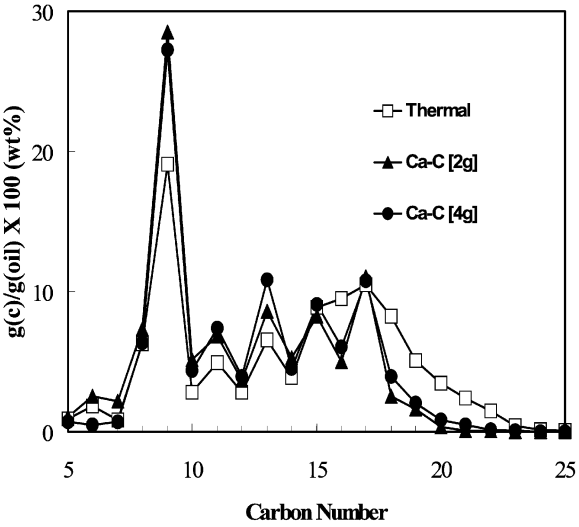


Fig. 3 C-NP gram of liquid products obtained during PP/PE/PS/PVC + HIPS-Br thermal degradation and degradation using Ca-C sorbent.

for the used Ca-C shows that the calcium carbonate was converted to calcium chloride and calcium bromide. This clearly shows that the hydrogen chloride evolved from the PVC and hydrogen bromide evolved from the HIPS-Br reacted with the calcium carbonate sorbent. Detailed investigations about the fate of antimony oxide and the recovery of halogen content and regeneration of Ca-C sorbent are in progress. The applicability of Ca-C sorbent for our waste plastic pyrolysis pilot plant at Mizushima, Japan is underway.

Experimental

Chemicals

HIPS-Br [brominated high impact polystyrene (Br-HIPS) containing 1,2-di(pentabromophenyl)ethane as a flame retardant with antimony trioxide as a synergist; Sb_2O_3: 4.5 wt%, Br: 10.7 wt%; SAYTAX 8010] was obtained from Asahi Chemical Co. Ltd., and PVC (MW: 100 000) from Geon Chemical Co. Ltd., Japan. High density polyethylene (PE) was obtained from Mitsui Chemical Co. Ltd., Japan; polypropylene (PP) from Ube Chemical Industries Co. Ltd., Japan; polystyrene (PS) from Asahi Kasei Industries Co. Ltd., Japan.

Preparation of Ca-C

About 90 wt% of calcium carbonate was mixed with 10 wt% phenol resin by mechanical kneading during which 20% of water was added to the mixture. Subsequent pellet formation was performed using a molding method. The prepared sorbent was calcined at 500 °C for 1 h in a nitrogen atmosphere and during this process the phenol resin was converted into carbon. The addition of phenol resin and calcination led to good mechanical strength and loss of the hygroscopic nature of the sorbent, which are important parameters for the successful use in a pilot plant. The finished sorbent designated as Ca-C [carbon composite of calcium carbonate] had a surface area (BET) of 40 $m^2\ g^{-1}$. Powder X-ray diffraction analysis confirmed the presence of the $CaCO_3$ phase in Ca-C. The calcium carbonate carbon composite (Ca-C) sorbent was cooperatively developed with Toda Kogyo Co. Ltd., Hiroshima, Japan.

Experimental procedure

The thermal degradation of waste plastic was carried out in a glass reactor (length: 32 cm; id 2 cm) under atmospheric pressure by batch operation under identical experimental conditions and temperature program and also using Ca-C sorbent. Briefly, 10 g of mixed plastics [weight ratio (PP/PE/PS/PVC/HIPS-Br: 3:3:2:1:1)] was loaded into the reactor for thermal degradation and also using Ca-C in vapor phase contact. The fresh PP/PE/PS/PVC/HIPS-Br grains used for degradation were well mixed and the solid sorbent (1 mm average diameter) was loaded into the reactor 10 cm above the plastic bed and the plastic sample was kept at the bottom of the reactor (Fig. 1). In a typical run, after setting the reactor, the reactor was purged with nitrogen gas at a flow rate of 10 mL min^{-1} and held at 120 °C for 60 min to remove the physically adsorbed water from the sorbent and plastic sample. The nitrogen flow was then cut off, and the reactor temperature was increased to the degradation temperature (430 °C) at a heating rate of 3 °C min^{-1}. In a similar manner, the thermal degradation of plastics was carried out in the absence of sorbent. A schematic diagram of the experimental setup is shown in Fig. 1. The waste plastic bed temperature was taken as the temperature of the degradation (Fig. 1). The gaseous products were condensed (using a cold water condenser; Fig. 1) to liquid products and trapped in a measuring jar. The hydrogen bromide and hydrogen chloride evolved from the degradation of the plastic mixture were trapped in a flask containing ion-exchanged water. Organic compounds containing chlorine and bromine atoms cannot be trapped (which are not condensed and trapped in a measuring jar) in the above flask, therefore these gases were passed through the furnace at 900 °C with air and converted into inorganic compounds (HBr and HCl) and trapped in ion exchanged water.

Analysis procedure

The quantitative analysis of the liquid products (collected once at the end of formation of liquid products) was performed using a gas chromatograph equipped with a Flame Ionization Detector (FID; YANACO G6800; column, 100% methyl silicone; 50 m × 0.25 mm × 0.25 μm) to obtain the quantity of hydrocarbons and carbon number distribution of the liquid products. The distribution of bromine and chlorine compounds and the level of halogen content (organic) in the liquid products were analyzed by a gas chromatograph equipped with an atomic emission detector (AED; HP G2350A; column, HP-1; cross-linked methyl siloxane; 25 m × 0.32 mm × 0.17 μm). 1-Bromohexane and 1,2,4-trichlorobenzene was used as internal standards for the quantitative determination of bromine and chlorine, respectively, in the GC-AED analysis. The amount of inorganic Br and Cl content was analyzed using an ion chromatograph (DIONEX, DX-120 Ion Chromatograph). The main liquid products were also analyzed by a gas chromatograph with a mass selective detector (GC-MSD; HP 5973; column, HP-1; cross-linked methyl siloxane, 25 m × 0.32 mm × 0.17 μm). The composition of the liquid products was characterized using C-NP grams (C = carbon, NP = normal paraffin) and Br-NP and Cl-NP grams (Br = bromine, Cl = chlorine). The curves were obtained by plotting the weight percent of Br or Cl, in the liquid products against the carbon number of the normal paraffin determined by comparing the retention times from GC analysis using a nonpolar column. In this GC column, peaks for the hydrocarbons appear in the order of increasing boiling points.

Conclusions

The pyrolysis of PVC and HIPS-Br mixed with PP/PE/PS plastics was carried out at 430 °C using a calcium carbonate carbon composite sorbent (Ca-C; 4 g) and produced halogen (dechlorination and debromination) free liquid products in a single-step process. The liquid products can be used as fuel oil or feed stock in refinery.

Acknowledgements

We would like to thank New Energy Development Organization (NEDO), Japan for financial support to carry out this research work under the Chugoku Regional Consortium Project (2000–2003). We are grateful to Dr Katsuhide Murata for his valuable discussions and Takashi Matsukuma for his help to carry out the experiments.

References

1 L. Tange, *Technical workshop report*, on sustainable management for plastics with bromine, Tokyo, 1999.
2 T. Ida, M. Nakanishi and K. Goto, *Polym. Sci., Polym. Chem. Ed.*, 1974, **12**, 737.
3 W. Christmann, D. Kasioke, K. D. Kloppel, H. Partocht and W. Rotard, *Chemosphere*, 1989, **19**, 387.
4 R. Miranda, H. Pakdel, C. Roy and C. Vasile, *Polym. Degrad. Stab.*, 2001, **73**, 47.
5 M. Day, J. Shen and J. D. Cooney, *J. Anal. Appl. Pyrolysis*, 1999, **51**, 181.
6 E. A. Williams and P. T. Williams, *Environ. Technol.*, 1999, **20**, 1109.
7 W. Kaminsky, *Adv. Polym. Technol.*, 1995, **14**, 337.
8 W. Kaminsky, B. Schlesselmann and C. M. Simon, *Polym. Degrad. Stab.*, 1996, **53**, 189.
9 H. Bockhorn, A. Hornung and U. Hornung, *J. Anal. Appl. Pyrolysis*, 1998, **46**, 1.
10 R. Zevenhoven, E. P. Axelsen and M. Hupa, *Fuel*, 2002, **81**, 507.
11 W. Kaminsky and F. Hartmann, *Angew. Chem., Int. Ed.*, 2000, **39**, 331.
12 Y. Sakata, Md. A. Uddin and A. Muto, *J. Anal. Appl. Pyrolysis*, 1999, **51**, 135.
13 Md. A. Uddin, K. Koizumi, K. Murata and Y. Sakata, *Polym. Degrad. Stab.*, 1997, **56**, 37.
14 Y. Sakata, Md. A. Uddin, A. Muto, M. Narazaki, K. Koizumi, K. Murata and K. Mitsuo, *Ind. Eng. Chem. Res.*, 1998, **37**, 2889.
15 W. Kaminsky, *Makromol. Chem. Makromol. Symp.*, 1991, **48/49**, 381.
16 H. Sato, K. Kondo, S. Tsuge, H. Ohtani and N. Sato, *Polym. Degrad. Stab.*, 1998, **62**, 41.
17 C. S. Richard, A. R. Wayne, A. T. Debra and B. Dellinger, *Chemosphere*, 1991, **23**, 1197.
18 H. Kaufer and O. von Quast, *Kunststoffe Plast Europe*, February 1997.
19 J. Vehlow and E. E. Mark, *APME Technical Report*, October 1995.
20 J. Vehlow, B. Bergfeldt, K. Jay, H. Seifert, T. Wanke and E. E. Mark, *Waste Manag. Res.*, 2000, **18**, 131.
21 K. Murata and M. Makino, *Nippon Kagaku Kaishi*, 1975, **1**, 192.

Novel properties of ionic liquids in selective sulfur removal from fuels at room temperature

Shuguang Zhang and Z. Conrad Zhang*

Akzo Nobel Chemicals Inc, 1 Livingstone Ave, Dobbs Ferry, NY 10522, USA.
E-mail: zongchao.zhang@akzonobel.com

Received 28th May 2002
First published as an Advance Article on the web 10th July 2002

The ionic liquids, 1-ethyl-3-methylimidazolium tetrafluoroborate, 1-butyl-3-methylimidazolium hexafluorophosphate and 1-butyl-3-methylimidazolium tetrafluoroborate were found to be effective for the selective removal of sulfur-containing compounds from transportation fuels such as gasoline at room temperature. S-containing compounds with a C_5 aromatic ring are favorably absorbed over C_6 aromatics, while S-containing non-aromatic compounds are poorly absorbed. The ionic liquids are regenerated from absorbed S-containing compounds by distillation or by dissolution in water. These ionic liquids are air- and moisture-stable at low temperature and non-corrosive. Therefore, the ionic liquids can be used in multiple cycles for the removal of S-containing compounds from fuels. The absorption capacity of the ionic liquids for S-containing compounds is sensitive to the structure of both the anion and cation of the ionic liquids, which is manifested by the significant inhibiting effect of methyl group substitution on the aromatic ring.

Introduction

Sulfur removal from transportation fuels has become an increasing technical challenge as oil refineries face growing environmental pressures and strict regulatory requirements. In the United States, the Environment Protection Agency requires that the average concentration of sulfur in gasoline be lowered more than 90%, to 30 parts per million, phased in from by 2004 through 2006.[1] The new on-road diesel regulation specifies a per-gallon sulfur cap of 15 ppm effective mid-2006.[2] The European Union has stringent fuel quality rules that require maximum diesel sulfur content of 50 ppm in 2005 (350 ppm in 2000), and maximum petrol (gasoline) sulfur content of 50 ppm in 2005 (150 ppm in 2000).[3]

The refinery industry utilizes catalytic processes for desulfurization of transportation fuels through hydroprocessing. While the performance of conventional hydroprocessing catalysts have been highly effective for the reduction of sulfur levels, further removal of residual sulfur from the processed fuels is expected to significantly increase the cost of hydroprocessing. These processes are highly energy intensive and consume large amounts of hydrogen. For example, a study based on a typical Co–Mo catalyst shows that either about four times more active catalyst or an increase of 38 °C in reaction temperature is needed to meet the required sulfur reduction of diesel products from 500 to 50 ppm.[4] Therefore, alternative technologies are of particular interest in providing potential solutions for sulfur-free clean fuels.

Ionic liquids have been examined for possible applications related to green chemical processes, such as liquid/liquid extractions, gas separations, electrochemistry and catalysis.[5–13] These liquids are easy to handle because of non-volatility, non-flammability, and high thermal stability. Many ionic liquids, except those containing $AlCl_4^-$, are moisture tolerant.

Even though $AlCl_3$ based ionic liquids are effective for the removal of S-containing compounds,[14] they often form dark precipitates by contacting compounds that contain thiols and cause darkened color in processed fuels.[15] Thus the application of this type of ionic liquid is limited to the absorption of certain aromatic compounds such as dibenzothiophene.

In the present work, the ionic liquids, 1-ethyl-3-methylimidazolium tetrafluoroborate ($EMIM^+BF_4^-$), 1-butyl-3-methylimidazolium hexafluorophosphate ($BMIM^+PF_6^-$) and 1-butyl-3-methylimidazolium tetrafluoroborate ($BMIM^+BF_4^-$), are studied for the absorption of various model components in typical gasoline and diesel fuels. They were also investigated for sulfur removal from real transportation fuels. Unlike $AlCl_3$ based ionic liquids, these ionic liquids are insensitive to the presence of water. $EMIM^+BF_4^-$ is water miscible and $BMIM^+PF_6^-$ is water immiscible.[16] Fig. 1 shows the structures of these three ionic liquids.

The melting points of $EMIM^+BF_4^-$ and $BMIM^+PF_6^-$ are both close to 5 °C. $BMIM^+BF_4^-$ has a melting point about −80 °C. As liquids at room temperature, these compounds are thermally stable up to about 300 °C.[8] For example, Holbrey and Seddon's thermogravimetric study showed that $BMIM^+BF_4^-$

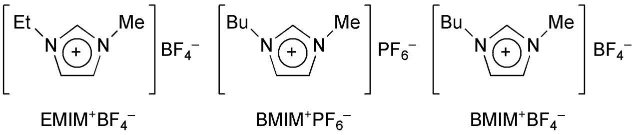


Fig. 1 Structures of ionic liquids.

Green Context

The removal of sulfur-containing impurities from fuels is becoming increasingly challenging as tolerated levels are reduced by legislation. An interesting alternative to hydrodesulfurisation is presented in this article, where the use of ionic liquids as selective adsorbents of S-containing aromatics is described. Considerable structural sensitivity towards absorption is found, but the commonly occurring thiophenes and related compounds are very favourably adsorbed. Recovery and regeneration of the ionic liquid involves simple heating to recover the S-compounds intact.
DJM

DOI: 10.1039/b205170m

had a small weight loss of 3.5 wt% between 280 and 320 °C when heated at 10 °C min^{-1} under nitrogen and no further degradation was observed until 360 °C.[17]

Results and discussion

Absorption capacity of the ionic liquids for model compounds

The absorption capacities of $EMIM^+BF_4^-$, $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$ for eight model compounds are shown in Fig. 2. The three ionic liquids showed little absorption for paraffins and olefins, but absorbed a small amount of aromatics and a relatively larger amount of thiophene and methylthiophene. In the used ionic liquids, the molar ratio of thiophene to ionic liquid was found by NMR analysis to be 0.86 : 1, 3.5 : 1 and 2.2 : 1 for $EMIM^+BF_4^-$, $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$, respectively. These values are consistent with the measured weight loss from the organic phase. No ionic liquid was detected in the organic phase after absorption measurement.

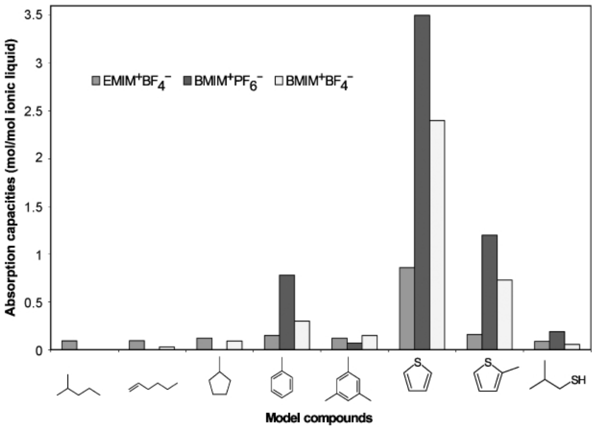


Fig. 2 Absorption capacities of $EMIM^+BF_4^-$, $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$.

The preferred absorption for thiophene, 2-methylthiophene and aromatics by the ionic liquids likely resulted from the interaction of the aromatic ring with the cation of the ionic liquids. It is important to note, however, that the methyl group on the aromatic compounds markedly reduced its absorption capacity. For example, the absorption capacity of $BMIM^+PF_6$ for trimethylbenzene is only about 10% of that for toluene. The absorption capacities of $BMIM^+PF_6$ and $BMIM^+BF_4$ for 2-methylthiophene are about 1/3 of those for thiophene. Methylcyclopentane, a cycloparaffin without aromatic (π charge density, and isobutylmercaptan, which contains sulfur but lacks aromaticity, were only weakly absorbed.

For most aromatic compounds $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$ have higher absorption capacities than does $EMIM^+BF_4^-$. The results suggest that the structure and the size of both cation and anion of an ionic liquid affect absorption. The local structure of the ionic liquids appears to have a significant effect on their interaction with the aromatic compounds. As shown in Fig. 2, the absorption capacity follows the general order: thiophene ≫ methylthiophene > toluene ≫ trimethylbenzene > isobutylthiol, hexene, 2-methylpentane, methylcyclopentane. It appears that absorption is favored for molecules with a higher density of aromatic π electrons. Clearly, those aromatics with a five-membered ring had stronger interaction with the ionic liquids. Sulfur in non-aromatic molecules such as isobutylthiol had weak interaction with the ionic liquids. The specific local structures of the ionic liquids and the chemistry involved in their interaction with the model compounds are under further study.

Absorption of a mixture of thiophene and toluene

When applied to a mixture of thiophene and toluene (weight ratio approximately 1 : 1), $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$ showed strong preferential absorption for thiophene over toluene. The results of NMR analysis are shown in Table 1. As compared with a single model compound, the amount of absorbed thiophene from a model mixture was reduced in both $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$ in the presence of toluene. For the model mixture, $BMIM^+PF_6^-$ again showed higher thiophene absorption than did $BMIM^+BF_4^-$, with a combined (toluene + thiophene) molar ratio of 1.72 : 1. The preferential adsorption of thiophene in both ionic liquids indicates interaction with the ionic liquids favors molecules with higher (π aromatic electronic density.

Table 1 Competitive absorption of thiophene and toluene in $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$

	Composition (mole ratio)	
	Toluene : thiophene : $BMIM^+PF_6^-$	Toluene : thiophene : $BMIM^+BF_4^-$
Whole mixture	6.0 : 7.2 : 1	5.5 : 6.2 : 1
Absorbed	0.65 : 1.07 : 1	0.23 : 0.48 : 1

Removal of sulfur compounds from gasoline samples

Gasoline samples with low and high sulfur level were also treated with these ionic liquids. The concentrations of total sulfur and aromatics in the untreated and treated gasoline are shown in Table 2. Since there is a huge difference in aromatics *vs.* sulfur concentrations in the gasoline samples, comparison was made on the percentage loss of these two components from the gasoline samples following treatment with the ionic liquid. About 10–30 wt% of sulfur was preferentially removed from these samples with little change in the content of the aromatics. Removing sulfur without removing aromatics is desired, as aromatics are important for maintaining octane number in gasoline.

Table 2 Sulfur removal from gasolines

		$EMIM^+BF_4^-$		$BMIM^+PF_6^-$	
Sample		S/ppm	Aromatics[a] (wt%)	S/ppm	Aromatics[a] (wt%)
Low sulfur gasoline	Before treatment	240	33.2	240	33.2
	After treatment	200	33.5	170	33.1
High sulfur gasoline	Before treatment	820	32.6	820	32.6
	After treatment	730	33.0	710	31.7

[a] Toluene, ethylbenzene and xylene.

It is evident that the ionic liquids showed remarkable selectivity for the removal of sulfur compounds over aromatics, particularly from the low sulfur gasoline sample. It should be noted that the absorptive removal of sulfur containing compounds from the gasoline sample represents mainly the removal of aromatic S-containing molecules, even though various saturated sulfur compounds are also present.

Regeneration of ionic liquids and recovery of absorbed S-containing compounds

For a thiophene saturated $EMIM^+BF_4^-$ phase, the absorbed thiophene was released into a separated phase upon addition of water, as $EMIM^+BF_4^-$ is soluble in water. Water was then vaporized from the ionic liquid phase under a nitrogen flow at 110 °C for about 3 h. The $EMIM^+BF_4^-$ ionic liquid was nearly quantitatively recovered.

As $BMIM^+PF_6^-$ has little miscibility with water and may decompose at high temperature (above 80 °C) when water is present, its regeneration was carried out by direct distillation after saturated absorption of thiophene. The ionic liquid was fully regenerated after heating at 110 °C for 3 h under nitrogen. The absorbed thiophene recovered from distillation corresponds to the amount absorbed. NMR analyses indicated that the ionic liquids, $EMIM^+BF_4^-$ and $BMIM^+PF_6^-$, maintained their original structures after the regeneration.

Conclusions

The ionic liquids, $EMIM^+BF_4^-$, $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$ showed remarkable selectivity for the absorption of aromatic S-containing molecules from gasoline. These ionic liquids are moisture insensitive at low temperature, thermally stable under the distillation conditions, and readily regenerated for reuse. The absorbed aromatic S-containing compounds were quantitatively recovered during the regeneration. The preferential absorption of thiophene and methylthiophene over toluene suggests that compounds with higher aromatic π electron density in C_5 rings are favorably absorbed. A methyl group on the aromatic rings was found to reduce the absorption capacity, possibly due to a steric effect. The cation and anion structure and size in the ionic liquids are important parameters affecting the absorption capacity for aromatic compounds.

Experimental

Preparation of ionic liquids

Preparation of $EMIM^+BF_4^-$. Equimolar quantities of 1-ethyl-3-methyl-1*H*-imidazolium chloride (from Aldrich) and lithium tetrafluroborate (from Aldrich) were each dissolved in acetonitrile. These two solutions were gradually mixed together with active stirring. The precipitate, lithium chloride, was separated from the liquid by filtration. The liquid phase was distilled in a three—necked flask at 100 °C to remove acetonitrile from the ionic liquid.

Preparations of $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$. $BMIM^+PF_6^-$ and $BMIM^+BF_4^-$ were prepared following a similar procedure as described above. For $BMIM^+PF_6^-$, 1-butyl-3-methylimidazolium chloride and $LiPF_6$ (Aldrich) were used as starting materials. 1-Butyl-3-methylimidazolium chloride was obtained by refluxing equal molar amounts of 1-methylimidazole and 1-chlorobutane in a flask when heating and stirring at about 70 °C for 48 h.[18] Another sample of $BMIM^+PF_6^-$ was obtained from the laboratory of Professor Robin D. Rogers at the University of Alabama. It was prepared by the reaction of 1-butyl-3-methylimidazolium chloride and HPF_6.[16] The preparation of $BMIM^+BF_4^-$ started from 1-butyl-3-methylimidazolium chloride and $LiBF_4$.

A Varian Inova-500 MHz NMR spectrometer and a JEOL GSX-270 MHz NMR spectrometer were used to verify the structures of the ionic liquids. NMR analyses (^{13}C quantitative and approached proton test) were also conducted to obtain the sulfur content in the ionic liquid phase after absorption.

Measurement of absorption capacity and efficiency

Eight model compounds, 2-methylpentane, 1-hexene, methylcyclopentane, toluene, trimethylbenzene, thiophene, 2-methylthiophene and isobutyl mercaptan were selected to represent typical molecules in gasoline. The absorption capacity of an ionic liquid for a specific compound was measured at room temperature by adding 1 g of the ionic liquid and 2 g of a model compound to a glass vial. After shaking for a few minutes, two phases were formed and excess model compound in the upper phase was carefully removed. The ionic liquid phase was weighed to obtain the amount of the model compound absorbed.

The absorption selectivity of $BMIM^+BF_4^-$ for thiophene from a mixture with toluene was measured by adding 1 g of the ionic liquid to a mixture of 2.12 g of thiophene and 2 g of toluene. After 15 min stirring, the weight loss of the mixture was measured. Concentrations of toluene and thiophene in the ionic liquid phase were measured by NMR spectroscopy after absorption. A similar procedure was applied to $BMIM^+PF_6^-$ but with a mixture of 2.04 g of thiophene and 2 g of toluene.

The sulfur removal efficiencies of $EMIM^+BF_4^-$ and $BMIM^+PF_6^-$ for two gasoline samples were measured. In each case, 2 g of gasoline and 1 g of ionic liquid was mixed in a glass vial and shaken for 15 min. After settling, the upper fuel phase was removed and analyzed. Quantitative elemental analysis of sulfur was conducted on a Bruker S4 Explorer wavelength dispersive X-ray fluorescence spectrometer. Aromatics analysis was carried out on HP 6890 GC/MS using an OV-1 column (30 m × 0.32 mm id × 5 μm) for gasolines.

Recovery of used ionic liquids

The ionic liquids saturated with sulfur containing compounds were readily regenerated by either direct distillation or by successive dissolution in water followed by vaporization of water.

Acknowledgment

We would like to thank Professor R. D. Rogers at the University of Alabama for kindly providing a sample of $BMIM^+PF_6^-$. Analytical support by Drs B. Su, B. Joyce, and G. Darsey at Akzo Nobel is appreciated.

References

1 http://www.epa.gov/otaq/tr2home.html.
2 http://www.petroleumrefining.com/program19.html.

3 http://www.dieselnet.com/standards/eu/ld.html.
4 K. G. Knudsen, B. H. Cooper and H. Topsoe, *Appl. Catal. A: General*, 1999, **189**, 205.
5 K. A. Howard, H. L. Mitchell and R. H. Waghore, *US Pat*., 4,359,596, 1982.
6 D. R. Boate and M. J. Zaworotko, *US Pat.*, 5,220,106, 1993.
7 F. G. Sherif, L. Shyyu and C. C. Greco, *US Pat.*, 5,824,832, 1998.
8 V. R. Koch, C. Nanjundiah and R. T. Carlin, *US Pat.*, 5,827,602, 1998.
9 S. M. Silvu, P. A. Z. Suarcz, R. F. de Souza and J. Doupont, *Polym. Bull.*, 1998, **40**, 401–405.
10 A. J. Carmichael, D. M. Haddleton, S. A. F. Bon and K. R. Seddon, *Chem. Commun*, 2000, 1237–1238.
11 R. T. Carlin and J. S. Wilkes, *J. Mol. Catal.*, 1990, **63**, 125–129.
12 M. Goledzinowski, V. I. Birss and J. Galuszka, *Ind. Eng. Chem. Res.*, 1993, **32**, 1795–1797.
13 J. A. Boon, J. A. Levisky, J. L. Pflug and J. S. Wilkes, *J. Org. Chem.*, 1986, **51**, 480–483.
14 A. Bösmann, L. Datsevich, A. Jess, A. Lauter, C. Schmitz and P. Wasserscheld, *Chem. Commum.*, 2001, 2494–2495.
15 L. Shyu, Z. Zhang and Q. Zhang, International PCT Publication, WO 01/40150 A1, 2001.
16 Professor R. D. Rogers, University of Alabama, http://bama.ua.edu/~rdrogers/.
17 J. D. Holbrey and K. R. Seddon, *J. Chem. Soc., Dalton Trans.*, 1999, 2133–2139.
18 A. E. Visser, R. P. Swatloski and R. D. Rogers, *Green Chem.*, 2000, **2**, 1–4.

Development of a heterogeneous *cis*-dihydroxylation process with hydrogen peroxide as oxidant

A. Severeyns, D. E. De Vos and P. A. Jacobs*

Centre for Surface Chemistry and Catalysis, K.U. Leuven, Kasteelpark Arenberg 23, Leuven 3001, Belgium. E-mail: pierre.jacobs@agr.kuleuven.ac.be; Tel: 32 16 321610

Received 17th April 2002
First published as an Advance Article on the web 11th July 2002

The development of a successful heterogeneous *cis*-dihydroxylation process, using a heterogenized Os-catalyst and H_2O_2 as oxidant, is reported. In the described method, Os^{VI} is reoxidized to Os^{VIII} by *N*-methylmorpholine *N*-oxide (NMO), which is only present in catalytic amounts; NMO is regenerated from *N*-methylmorpholine (NMM) by oxidation with H_2O_2, which is used as a stoichiometric oxidant. To maintain the heterogeneous nature of the Os catalysis, it is necessary to perform the *cis*-dihydroxylation reaction and the regeneration of NMO in two physically separated vessels. A two batch system, with discontinuous circulation of the liquid between the NMO regeneration vessel and the dihydroxylation vessel, was designed. For the oxidation of NMM, two different heterogeneous catalysts, namely Ti-MCM-41 and LDH-WO_4^{2-} (tungstate exchanged layered double hydroxide) are used, both with satisfying results. This innovative system is one of the first attempts to perform heterogeneous *cis*-dihydroxylation reactions with the ecologically friendly oxidant H_2O_2.

1. Introduction

The osmium-catalyzed *cis*-dihydroxylation reaction is a unique process for the preparation of *cis*-1,2-diols.[1] In spite of the excellent results obtained on a laboratory scale with OsO_4 and *N*-methylmorpholine *N*-oxide (NMO) or $K_3[Fe(CN)_6]$ as oxidants,[2–4] industrial application of the process is difficult. The high toxicity and volatility of the homogeneous OsO_4 is a serious obstacle and the used oxidants are expensive and leave a large amount of organic waste after reaction. Much research has been done recently to improve the utility of the osmium-catalyzed dihydroxylation by heterogenization of the catalyst or by developing processes which use ecologically interesting oxidants like hydrogen peroxide or oxygen.[5]

We previously reported a new, truly heterogeneous *cis*-dihydroxylation catalyst with Os immobilized on a modified silica support.[6] The catalyst is prepared through formation of stable Os–diolate esters in the reaction of OsO_4 with silica-linked tetrasubstituted olefins. The central idea is that these tertiary diolate esters are not hydrolyzed during reaction, keeping the catalyst fixed to the support, if the hydrolytic conditions are not too drastic. The *cis*-dihydroxylation reaction can take place at the remaining free binding sites of the Os centre (Fig. 1). Excellent results are obtained for the dihydroxylation of a series of olefins with this catalyst and NMO as oxidant, while catalytic experiments on filtrates of the reaction prove that there is no Os whatsoever leached out from the support under the reaction conditions. Unfortunately, the stoichiometric production of *N*-methylmorpholine (NMM) remains a serious drawback of the system. In view of this, the heterogeneous catalyst would be even more attractive in combination with an environmentally friendly oxidant such as hydrogen peroxide.

It has been known for a long time that the use of H_2O_2 as an oxidant in homogeneous Os-catalyzed *cis*-dihydroxylation leads to low selectivities, due to overoxidation of Os–diolates to hydroxyketones.[7,8] Bäckvall and coworkers dealt with aforementioned problem by using a coupled catalytic system (Fig. 2).[9–11] In this system Os^{VI} is reoxidized to Os^{VIII} by NMO, which is only present in a catalytic amount and has to be regenerated during reaction. H_2O_2 is slowly added to the reaction mixture; it reoxidizes NMM to NMO *via* an electron transfer mediator and is the stoichiometric oxidant in the system. Different types of electron transfer mediators can be used, namely vanadium[10] or organic flavins.[9,11] In this method the excellent chemo- and even enantioselectivity of the Os–NMO reaction is combined with the ecologically favorable properties of H_2O_2. The mechanistic aspects of the enantioselective homogeneous reaction with Os and H_2O_2 have been studied in detail.[11]

This paper reports our efforts to use the heterogenized Os-catalyst with H_2O_2 as oxidant for the *cis*-dihydroxylation of 1-hexene, while maintaining the heterogeneous nature of the catalysis. In first instance, the triple catalytic Bäckvall system is applied with vanadium as electron transfer mediator for the NMM oxidation. This system of coupled catalytic cycles contains three catalysts (Os/NMO/VO(acac)$_2$). Apart from the homogeneous V catalyst for NMM reoxidation, heterogeneous Ti- or W-based materials were used as well. When H_2O_2 was used to reoxidize NMM in the presence of the heterogenized Os catalyst, some Os leaching was frequently observed. However, it is possible to keep the Os dihydroxylation reaction with H_2O_2 as the terminal oxidant strictly heterogeneous, if the reoxidation of NMM is performed with a second heterogeneous catalyst in a separate reactor.

Green Context

It is widely recognised that green chemistry solutions will often require a combination of more efficient chemistry and alternative reactor designs. Phase separation with two parallel reactors can often be useful to avoid end of process separation problems. Here we see the use of a two batch system for a heterogeneous *cis*-dihydroxylation process. The oxygen source is the benign reagent hydrogen peroxide. Of particular value is that any metal catalyst leaching problem is solved by physically separating the oxidant recycling from the organic oxidation. ***JHC***

DOI: 10.1039/b203741f

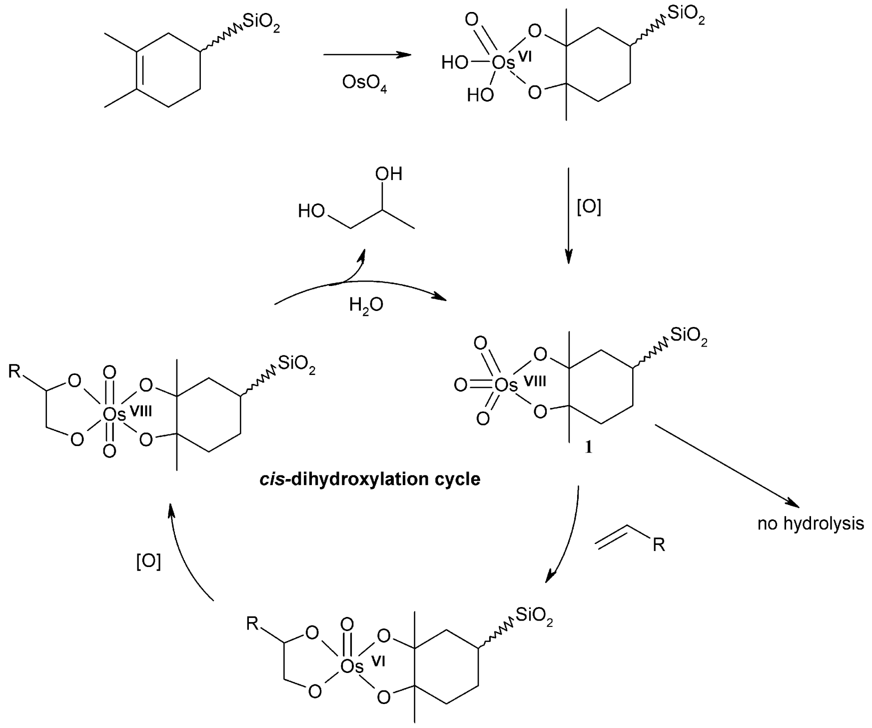


Fig. 1 Immobilization of Os in a stable diolate complex and proposed catalytic cycle for the *cis*-dihydroxylation ([O] = *N*-methylmorpholine *N*-oxide).

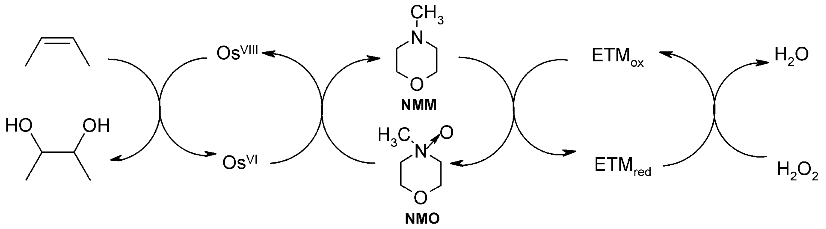


Fig. 2 Triple catalytic system for the Os-catalyzed *cis*-dihydroxylation with H_2O_2 as terminal oxidant (ETM = electron transfer mediator, *e.g.* V, Ti or W).

2. Experimental

2.1 Synthesis of heterogenized Os-catalyst

Silica gel 60 (Fluka), dried at 150 °C, was dispersed in dry toluene and stirred overnight at 60 °C under N_2 with a 9:1 mixture of propyltrimethoxysilane and 3-aminopropyltrimethoxysilane (3 mmol silylating agent per g of silica). The functionalized silica was filtered off, washed with toluene to remove the excess of silylating agent and dispersed in dry toluene. An excess of 3,4-dimethylcyclohex-3-enylcarbonyl chloride (1 mmol per g of silica), prepared according to a reported method,[12] was added and reacted with the grafted amino groups. The mixture was stirred overnight at room temperature while HCl, formed during the reaction, was removed by flushing with N_2. The solid was filtered off, washed with toluene and dried at 60 °C. Finally, the material was loaded with Os by the addition of OsO_4, prepared *in situ* from $K_2(OsO_2(OH)_4)$, on the immobilized double bonds. First, 200 μl water containing 4×10^{-6} mol $K_2(OsO_2(OH)_4)$ and 10 mg NMO were stirred overnight at room temperature with 1 ml CH_2Cl_2. Next, 2 ml *tert*-butyl alcohol was added, 0.1 g of the functionalized support was dispersed in the resulting solution, and stirred for 5 h at room temperature. Excess OsO_4 was removed from the support material by threefold washing, 1 h each time, with dichloromethane–*tert*-butyl alcohol (1:2).

2.2 Reaction conditions

Safety equipment. The reactions with homogeneous and heterogeneous Os catalysts were carried out in a closed glove box, placed in a hood. The box was flushed with nitrogen and the gas leaving the box led through a bottle containing corn oil to trap the hazardous OsO_4, if any was present.

‘Blocking’ of *cis*-dihydroxylation by tetrasubstituted olefins. In the ‘blocking’ test, two homogeneous catalytic reactions were performed with 1-hexene as substrate and NMO as oxidant, one in the presence of 2,3,4-trimethyl-2-pentene; the other without this tetrasubstituted olefin [NMO:1-hexene:(2,3,4-trimethyl-2-pentene):Os = 400:400:(10):1; 20 μl H_2O containing $K_2(OsO_2(OH)_4)$, 1.6 mmol 1-hexene in 3 ml dichloromethane–*tert*-butyl alcohol (1:2), RT]. For the reaction in presence of the tetrasubstituted olefin, 1-hexene was added 4 h after the other reagents. Sampling was performed after 10 h and the samples analyzed on a gas chromatograph (Chrompack CP-Sil-5 column: T_1 = 140 °C; t_1 = 5 min; ramp = 5 °C min^{-1}; T_2 = 290 °C; t_2 = 5 min).

Heterogeneous *cis*-dihydroxylation with NMO as the oxidant. The heterogeneous *cis*-dihydroxylation reaction was performed at room temperature with 1-hexene as substrate and NMO as oxidant in a solvent mixture of dichloromethane and *tert*-butyl alcohol ([0.1 g heterogenized catalyst, 1.6 mmol 1-hexene, 1.6 mmol NMO, 200 µl H_2O in 3 ml dichloromethane : *tert*-butyl alcohol (1 : 2)]. After 24 and 48 h, samples were taken.

Reactions with V-catalyzed NMO regeneration. Homogeneous reactions with V-catalyzed NMM reoxidation were performed at 10 °C with 2×10^{-6} mol OsO_4 (2.5 wt% solution in *tert*-butyl alcohol) as dihydroxylation catalyst. The 1-hexene : NMM : $VO(acac)_2$: H_2O_2 ratio equals 100 : 25 : 2 : 100 with 1.6 mmol 1-hexene in 1.3 ml CH_2Cl_2. Hydrogen peroxide (2 ml of a *tert*-butyl alcohol solution of aqueous H_2O_2 (35 wt%)) was added slowly over 10 h. After 8 h additional stirring, sampling was performed. A reference reaction was performed with slow addition of H_2O_2, without NMM or $VO(acac)_2$ as cocatalysts.

The reactions with the heterogenized catalyst were performed at 20 °C with 0.2 g catalyst (maximally 8×10^{-6} mol Os). The 1-hexene : NMM : $VO(acac)_2$: H_2O_2 ratio equals either 100 : 16 : 1.3 : 100 (procedure 1) or 100 : 16 : 1.3 : 25 (procedure 2) with 1.6 mmol 1-hexene in 1.3 ml CH_2Cl_2. Hydrogen peroxide (2 ml of a *tert*-butyl alcohol solution of aqueous H_2O_2 (35 wt%)) was added slowly to the reaction mixture (10 h for procedure 1 and 20 h for procedure 2). After 10 h additional stirring, sampling was performed.

Reactions with dihydroxylation and NMO regeneration in separate vessels. Two separate reaction vessels were used: one for the regeneration of NMO from NMM and another for the dihydroxylation of 1-hexene. For the oxidation of NMM to NMO, the so-called regeneration of NMO, two different heterogeneous catalysts were used: Ti-MCM-41 and LDH-WO_4^{2-}.[13,14] Ti-MCM-41 was obtained by grafting titanocene dichloride on a previously prepared MCM-41 material (pore diameter = 2.8 nm), followed by calcination at 823 K. The material has a Si/Ti ratio of 11. LDH-WO_4^{2-} was prepared by exchanging a layered double hydroxide (LDH) with a Mg/Al ratio of 2.3 and nitrate ions as interlayer anions with Na_2WO_4, to obtain a material with following composition: $(Mg_{0.7}Al_{0.3}(OH)_2)(NO_3)_{0.262}(WO_4)_{0.019}\cdot nH_2O$.

For the reaction, a mixture of NMM (0.5 mmol), H_2O_2 (0.5 mmol) and 1-hexene (1.6 mmol) in 3 ml CH_2Cl_2 : *t*-BuOH (1 : 2) was placed in the 'NMO regeneration vessel', containing 100 mg Ti-MCM-41 or 50 mg LDH-WO_4^{2-}. After 5 h stirring at room temperature, the mixture was centrifuged and the supernatant transferred into the 'dihydroxylation vessel', containing 100 mg heterogeneous Os-catalyst (max. 4×10^{-6} mol Os). After 24 h of reaction at room temperature, the supernatant was transferred again to the NMO regeneration vessel. 0.5 mmol H_2O_2 was added and a new regeneration–dihydroxylation sequence started. A schematic presentation of the two batch system is given in Fig. 3. After each sequence the conversion of 1-hexene and the selectivity for the 1,2-hexanediol were determined.

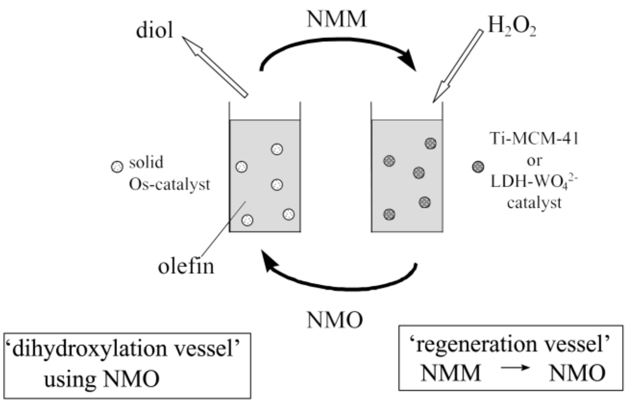


Fig. 3 Schematic representation of the two batch system for the *cis*-dihydroxylation reaction with H_2O_2 as terminal oxidant.

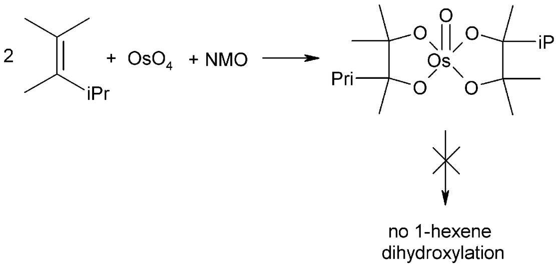
2.3 Filtrate tests to control heterogeneity

For the heterogeneous *cis*-dihydroxylation with NMO, a filtrate test was performed by bringing half of the supernatant of a reaction mixture into another vessel after 10 h reaction time and following the further conversion of 1-hexene in the remaining suspension and in the clear supernatant (method A). Alternatively (method B), the reaction mixture may be split at the end of the reaction with 1-hexene, with fresh NMO (0.5 mmol) and cyclohexene (0.5 mmol) added to the suspension and to the clear supernatant. The conversion of cyclohexene is then monitored in both reaction vessels. Finally, in the two batch system (method C), the suspension was split after three regeneration–dihydroxylation sequences; NMO (0.5 mmol) was added to the suspension and supernatant and the further conversion of 1-hexene monitored.

3. Results and discussion

3.1 Stability of tetrasubstituted Os diolates and heterogeneous *cis*-dihydroxylation using NMO as terminal oxidant

The heterogeneity of the solid Os catalyst critically depends on the stability of the Os–O bonds in the Os–diolate complex of Fig. 1 (**1**). While it is generally recognized that a higher degree of substitution on the diolate decreases its susceptibility to hydrolysis, even tetrasubstituted Os diolate complexes may eventually be hydrolyzed, depending on conditions such as pH, temperature, and the presence of additives such as methyl sulfonamide or tetraethylammonium acetate. Accordingly, the solid Os catalyst should be used under well-defined conditions, which ensure the stability of the Os–diolate bonds. In order to quickly evaluate this stability, a 'blocking' experiment was devised, in which the effect of an added tetrasubstituted olefin on the dihydroxylation of 1-hexene was assessed. The reaction is initiated with the oxidant, OsO_4, and 10 equivalents of 2,3,4-trimethyl-2-pentene (eqn. (1)). After a short reaction time, it is expected that all Os has formed bis diolate complexes with 2,3,4-trimethyl-2,3-pentanediol. Subsequently, 1-hexene was added. If the Os–O bonds in the tetrasubstituted diolate are inert, no Os is available to osmylate the 1-hexene, and a total blockage of the 1-hexene dihydroxylation is expected:



(1)

This is indeed observed: in the presence of 2,3,4-trimethyl-2-pentene, no hexanediol was formed after 10 h, while in the absence of the tetrasubstituted olefin, a 98% conversion was obtained. This proves that under the conditions applied (NMO, water, CH_2Cl_2-*t*BuOH, 293 K), hydrolysis of tetrasubstituted diolates does not occur. Note that a blocking of the catalytic activity is not expected for the heterogeneous catalyst: in contrast with homogeneous Os, the supported Os catalyst only forms monodiolates with the anchored tetrasubstituted olefins. Consequently, free coordination sites remain available for *cis*-dihydroxylation of *e.g.* 1-hexene (Fig. 1).

Heterogeneous *cis*-dihydroxylations were performed with the solid Os catalyst, under the same conditions of solvent, temperature, water concentration *etc*. as the blocking experiment. With NMO as the oxidant, 1-hexene conversions of 66 and 99% were found after 24 and 48 h and the selectivity for the desired diol was 98% in both samples. The result of the filtrate test (method A) is very satisfying. Splitting up after 10 h, at a conversion of 21%, a conversion of 21% was found in the clear supernatant 20 h later, while 60% of the 1-hexene was converted in the suspension. This test proves that the catalyst is truly heterogeneous, as a zero-activity was observed in the filtrate.

3.2 Dihydroxylations with V-catalyzed *in situ* regeneration of NMO

The results for the homogeneous and heterogeneous Os catalysts are summarized in Table 1. For the homogeneous reaction performed with the triple catalytic system (Os/NMO/VO(acac)$_2$), a conversion of 83% and a selectivity of 95% are obtained for the *cis*-dihydroxylation of 1-hexene (entry 1). While the high selectivity evidences that the Os was reoxidized by NMO and not by H_2O_2, only 25 mol% of NMM and no NMO at all were initially present in the reaction mixture. This means that the NMM has participated in at least three or four consecutive oxidation–reduction cycles, as shown in Fig. 2. To exclude the possibility that the slow addition of H_2O_2 alone is enough to obtain such a high selectivity, the reference reaction without NMM and VO(acac)$_2$ was performed (entry 2). In this reaction 83% of the 1-hexene has reacted, but the selectivity was rather low (60%).

When the heterogeneous Os catalyst was used in the *in situ* V-catalyzed reoxidation of NMM, a conversion of 27% and a selectivity of 93% were obtained (entry 3). The high selectivity indicates again that Os^{VI} is reoxidized by NMO and not by H_2O_2. The conversion is rather low, due to the intense decomposition of H_2O_2 in the reaction mixture. Unfortunately, the heterogenized Os-catalyst is leaching active species into solution during the reaction: the performed filtrate test (method B) shows that 42% of the cyclohexene, added to filtrate and suspension after splitting the reaction mixture at the end of the reaction, was converted in the filtrate and 48% in the suspension, 24 h after splitting (entry 4). Apparently, the tertiary diolate esters of the Os-catalyst are hydrolyzed under the reaction conditions applied, even though these conditions are similar to those of the successful heterogeneous dihydroxylations with NMO. However, H_2O_2 is a stronger nucleophile than NMO, and it seems that H_2O_2 not only reacts with the homogeneous VO(acac)$_2$ catalyst, but also with the solid Os catalyst. To protect the catalyst from such direct exposure to H_2O_2, the reaction was repeated with a much slower oxidant addition (procedure 2). If the H_2O_2 reacts exclusively and quickly with the V catalyst, the reaction medium should not contain any free H_2O_2. With slow hydrogen peroxide addition, a conversion of 17% and a selectivity of 95% are obtained (entry 5). From the filtrate test (method B), however, it is clear that the catalyst is losing Os species to solution, as cyclohexene conversions of 47 and 57% are determined in the filtrate and suspension, respectively, 24 h after splitting (entry 6). Thus even low concentrations of H_2O_2, in direct contact with the Os-catalyst, seem to cause leaching.

3.3 Reactions with dihydroxylation and NMO regeneration in separate vessels

The results obtained with the *in situ* reoxidation of NMM necessitate a change in the reaction protocol in such a way that any contact between the solid Os catalyst and H_2O_2 is avoided. Table 2 presents the catalytic results of the adapted coupled system, with physically separated NMO regeneration and dihydroxylation steps. As heterogeneous catalysts for NMM reoxidation, a Ti- and a W-containing material were selected. Ti-MCM-41, like many other Ti molecular sieves, has been known for a long time to oxidize amines with H_2O_2;[13,15] peroxotungstate on an LDH has recently been reported to oxidize tertiary amines to amine *N*-oxides.[14,16]

The overall conversion of 1-hexene in the reaction mixture after the successive regeneration–dihydroxylation sequences is also given in Fig. 4. For instance after three sequences, 32 and 23% of the 1-hexene has reacted for the NMO regeneration with Ti-MCM-41 and LDH-WO_4^{2-}, respectively. Obviously, a higher conversion can be obtained by raising the number of sequences, or by using larger H_2O_2 doses. The high selectivity, typical for the reaction with NMO, is preserved. The results of the filtrate tests are very satisfying. Starting from a 1-hexene conversion of 32%, after three cycles with Ti-MCM-41 as NMO regeneration catalyst and performing the filtrate test according to method C, conversions of 34 and 84% are obtained after 24 h in the filtrate and the suspension, respectively. With LDH-WO_4^{2-} as the regeneration catalyst, the 1-hexene conversion at the splitting point was 23%; a conversion of 23% was determined in the filtrate after 24 h, while a conversion of 77% was found in the suspension. This filtrate test is graphically presented in Fig. 5. The zero activity of the filtrates proves the heterogeneity of the Os catalyst in this two batch system. Clearly, the consumption of H_2O_2 during the recycling step is practically complete; Os leaching by direct contact between H_2O_2 and the solid catalyst is thus avoided.

4. Conclusions

A successful heterogeneous *cis*-dihydroxylation process has been developed, with H_2O_2 as terminal stoichiometric oxidant. The leaching problem, encountered when directly exposing the heterogenized Os catalyst to H_2O_2 in the Bäckvall protocol, is

Table 1 *cis*-Dihydroxylation of 1-hexene in the coupled catalytic system of Bäckvall (Os/NMO/VO(acac)$_2$)

Entry	Catalyst	Conditions[a]	Time/h	Conversion of 1-hexene (%)	Conversion of cyclohexene (%)	Selectivity (%)
1	OsO_4	—	18	83	—	95
2[b]	OsO_4	—	18	83	—	60
3	Het. Os-catalyst	1	20	27	—	93
4[c]	Het. Os-catalyst	1	24 h, filtr.	—	42	—
			24 h, susp.	—	48	—
5	Het. Os-catalyst	2	30	17	—	95
6[c]	Het. Os-catalyst	2	24 h, filtr.	—	47	—
			24 h, susp.	—	57	—

[a] Reactions with the coupled Bäckvall system and the heterogenized Os catalyst were performed under different conditions as described in the experimental section. 1 = normal H_2O_2 addition rate; 2 = slow addition. [b] Homogeneous reaction with slow addition of H_2O_2 and without NMM and VO(acac)$_2$. [c] Filtrate test, performed as described in the experimental section (method B).

solved by physically separating the NMM oxidation and the dihydroxylation reaction.

Table 2 *cis*-Dihydroxylation of 1-hexene in the two batch system with the heterogenized Os-catalyst as dihydroxylation catalyst and Ti-MCM-41 or LDH-WO_4^{2-} as NMO recycling catalyst

Entry	Recycling catalyst	Number of sequences[a]	Conversion[b] (%)	Selectivity (%)
1	Ti-MCM-41	1	11	89
2	Ti-MCM-41	2	22	96
3	Ti-MCM-41	3	32	96
4	LDH-WO_4^{2-}	1	8	87
5	LDH-WO_4^{2-}	2	16	97
6	LDH-WO_4^{2-}	3	23	96

[a] Number of recycling–dihydroxylation sequences. [b] Total conversion of 1-hexene after successive recycling–dihydroxylation sequences.

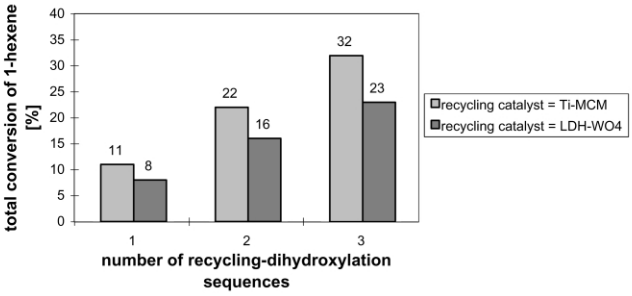


Fig. 4 *cis*-Dihydroxylation with the two batch system: total conversion of 1-hexene after successive recycling–dihydroxylation sequences.

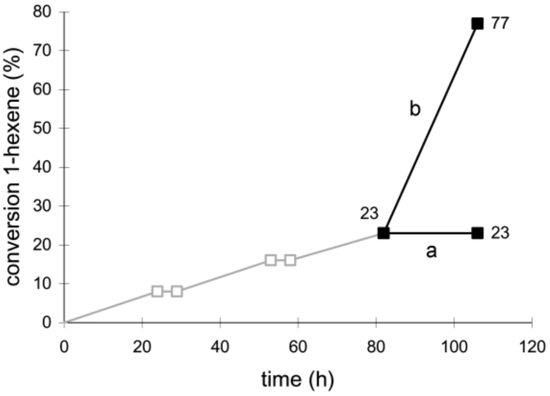


Fig. 5 Filtrate test (method C) for the *cis*-dihydroxylation of 1-hexene in the two batch system with heterogenized Os-catalyst as dihydroxylation catalyst and LDH-WO_4^{2-} as recycling catalyst: (☐) conversions of 1-hexene in three successive recycling–dihydroxylation sequences; (■) = filtrate test: (a) conversion of 1-hexene in filtrate, (b) conversion of 1-hexene in suspension.

For the oxidation of NMM to NMO with H_2O_2, two different heterogeneous catalysts were used, both with satisfying results. The catalysts Ti-MCM-41 or LDH-WO_4^{2-} allow to perform the recycling at room temperature. While other methods have been proposed for NMM reoxidation, even in the absence of a metal catalyst, these methods are not suitable for the coupled system because they need elevated temperatures (50–100 °C).[17,18]

The procedure in the present form is interesting on a laboratory scale. On a larger scale, one may envisage the use of two coupled catalytic reactors, a NMO recycling reactor and a dihydroxylation reactor, thus combining heterogeneous Os catalysis with H_2O_2 as the oxidant.

Acknowledgements

This work was supported by the Belgian Federal Government in the frame of an Interuniversitary Attraction Pole on Supramolecular Catalysis. A. S. thanks FWO (Vlaanderen) for a Ph.D. grant. We thank Prof. J. Bäckvall for inspiring discussions. P. A. J. and D. E. D. V. are indebted to FWO (Vlaanderen) for a research grant (G.0334.99).

References

1 M. Schröder, *Chem. Rev.*, 1980, **80**, 187.
2 V. VanRheenen, R. C. Kelly and D. Y. Cha, *Tetrahedron Lett.*, 1976, **23**, 1973.
3 M. Minamoto, K. Yamamoto and J. Tsuji, *J. Org. Chem.*, 1990, **55**, 766.
4 J. S. Mayell, *Ind. Eng. Chem. Prod. Res. Dev.*, 1968, **7**, 130.
5 A. Severeyns, D. E. de Vos and P. A. Jacobs, *Top. Catal.*, 2002, **19**, 125.
6 A. Severeyns, D. E. De Vos, L. Fiermans, F. Verpoort, P. J. Grobet and P. A. Jacobs, *Angew. Chem.*, 2001, **113**, 606.
7 N. A. Milas and S. Sussman, *J. Am. Chem. Soc.*, 1936, **58**, 1302.
8 N. A. Milas and S. Sussman, *J. Am. Chem. Soc.*, 1937, **59**, 2345.
9 K. Bergstad, S. Y. Jonsson and J.-E. Bäckvall, *J. Am. Chem. Soc.*, 1999, **121**, 10424.
10 A. H. Éll, S. Y. Jonsson, A. Börje, H. Adolfsson and J.-E. Bäckvall, *Tetrahedron Lett.*, 2001, **42**, 2569.
11 S. Y. Jonsson, K. Färnegård and J. E. Bäckvall, *J. Am. Chem. Soc.*, 2001, **123**, 1365.
12 J. Monnin, *Helv. Chim. Acta*, 1958, 2112.
13 M. Ramakrishna Prasad, G. Kamalakar, G. Madhavi, S. J. Kulkarni and K. V. Raghavan, *Chem. Commun.*, 2000, 1577.
14 B. M. Choudary, B. Bharathi, Ch. Venkat Reddy, M. Lakshmi Kantam and K. V. Raghavan, *Chem. Commun.*, 2001, 1736.
15 J. S. Reddy and P. A. Jacobs, *Catal. Lett.*, 1996, **37**, 213.
16 B. M. Choudhary, N. S. Chowdari, S. Madhi and M. L. Kantam, *Angew. Chem.*, 2001, **113**, 4756.
17 K. G. Massonne, M. D. Sandison, G. E. Moffitt, L. E. James and J. Banger, *US Pat.*, 5502188, 1995.
18 R. L. Zimmerman, *US Pat.*, 5216154, 1992.

Novel biomass gasification method with high efficiency: catalytic gasification at low temperature

Mohammad Asadullah,[a] Tomohisa Miyazawa,[a] Shin-ichi Ito,[a] Kimio Kunimori,[a] Muneyoshi Yamada[b] and Keiichi Tomishige*[a]

[a] *Institute of Materials Science, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8573, Japan. E-mail: tomi@tulip.sannet.ne.jp*

[b] *Department of Applied Chemistry, Graduate School of Engineering, Tohoku University, Aoba, Aramaki, Aoba-ku, Sendai 980-8579, Japan*

Received 10th May 2002
First published as an Advance Article on the web 11th July 2002

The gasification of biomass (wood powder) has been found to proceed completely by the combination of an excellent catalyst ($Rh/CeO_2/SiO_2$) with a fluidized bed reactor at 823–973 K. This temperature range is much lower than conventional gasification methods (973–1073 K for catalytic and 1073-1223 K for non-catalytic). The commercial steam reforming catalyst G-91 and dolomite have also been used in this investigation. At 873 K, the carbon conversion on $Rh/CeO_2/SiO_2(60)$, G-91 and dolomite and in the non-catalyzed gasification is 95, 75, 63 and 44%, respectively. Above 873 K, no tar was formed on $Rh/CeO_2/SiO_2(60)$, however, a small amount of char (1–5% C-based) was formed. Therefore, the catalyst activity is quite stable during the reaction. Comparison among the catalysts with respect to the carbon conversion and gas, tar and char formation, shows that this novel catalyst exhibited high efficiency.

Introduction

Biomass is a plant derived ligno-cellulosic material, which is renewable and abundantly available in the world and some times causes disposal problems. As an agricultural and forestry product it stores solar energy that can be converted to electricity and fuels. It can be used as a solid fuel, or converted into liquid or gaseous fuels for the production of electric power and heat. The gaseous product, syngas, can potentially be used in the synthesis of clean liquid transportation fuels such as methanol,[1] dimethyl ether,[2] and Fischer–Tropsch oils,[3–5] hydrogen or many other chemicals. Since plants naturally recycle CO_2 from the atmosphere during their growth and the biomass derived fuels in various forms are super clean, the increased use of biomass as an energy resource would lead to a decrease of CO_2, NO_x, SO_x, and particulate matters in the atmosphere.[6–9] Furthermore, biomass based technology would reduce the dependence of foreign petroleum and also result in new markets for agricultural and forestry products in rural areas.

The principal part of the effort to meet the goal of biomass based technology for energy production is related to biomass gasification to produce fuel gases or synthesis gases.[10,11] However, the gasification process is challenging. The most severe difficulty is the formation of tar (a complex mixture of liquid hydrocarbons) and char (solid carbonaceous materials) during the gasification process. The most reported works on biomass gasification describe two-step processes in which biomass is thermochemically converted to a low or medium-energy-content gas. The first step is gasification, which provides mainly gas products with substantial amounts of tar and char.[12–17] On cooling, the vaporized tars condense either onto cool surfaces or into aerosols of small droplets. In the catalytic conversion of syngas to useful liquid fuels or chemicals, the tar droplets deposit on the catalyst surface and cause catalyst deactivation.[18–20] Thus, in the second step the removal of tars and char is essential for end use of the gas products. Since char is a solid material, it can be removed completely by filtration, however, even using complex filtration methods only 90% of the tar can be removed from the gas product.[11]

Biomass derived tars can be removed from the gas stream by catalytic cracking and efforts in this direction have been continued for more than two decades.[21–30] A variety of metallic and non-metallic catalysts have been investigated either in the gasifier itself or in separate reactors downstream from the gasifier. Attempts to use catalyst in the primary gasifier started in the early 1980s and have continued intermittently since then.[21] Most work has focused on dolomite and nickel based catalysts.[31–39] Tars are rapidly cracked to gas molecules on the catalyst surface at around 1023–1173 K. Although this conceptual approach has potential advantages, the process does not appear to be an effective approach for complete tar removal by cracking in large-scale systems due to sudden deactivation of the catalyst over time of the reaction due to deposition of carbon on the catalyst surface. Extensive research has been carried out using catalysts in a secondary reactor downstream from the gasifier. The non-metallic catalysts such as dolomite, zeolite, and calcite and also nickel based commercial catalyst for petrochemical industry have been investigated for tar cracking in the secondary reactor. The extent of tar cracking is a function of the catalytic activity as well as temperature. Catalysts in the secondary reactor showed better results, however, deactivation of the catalyst in a matter of hours still makes the process

Green Context

One of the most important development areas for green chemistry is the increasing use of renewable biomass. One of the ways of utilising biomass is *via* conversion to synthesis gas which can be used for a variety of applications including the synthesis of hydrogen and methanol for fuels. This paper describes a novel catalytic system for biomass gasification. In particular, the process operates at unusually low temperatures and with very high conversion efficiencies. ***JHC***

DOI: 10.1039/b204536m

problematic. We have investigated various types of support materials and supported metal catalysts in the primary gasifier for cellulose gasification, a model compound of real biomass, at 773–873 K, where CeO_2 exhibited high performance for tar and char conversion to gas. Loading of Rh on the CeO_2 surface drastically improved the catalytic activity for tar and char cracking in the primary bed reactor. Almost complete conversion of cellulose to gas product was achieved at as low as 823 K.[40] However, in both the batch and continuous feeding systems, catalyst deactivation was observed within a rather short reaction time.[41] Transmission electron microscopy (TEM) images of fresh and used catalysts showed that the CeO_2 was sintered and the particle sizes became larger during reaction. Furthermore, Brunauer–Emmett–Teller (BET) analysis of these particles showed that the surface area of the catalyst drastically decreased from 60 to 10 $m^2\ g^{-1}$ within these short reaction times. In order to prevent the sintering of the catalyst, we have further modified the catalyst, where CeO_2 was first loaded on high surface area SiO_2 (380 $m^2\ g^{-1}$) by the incipient wetness method and then the Rh was loaded on CeO_2/SiO_2 by simple impregnation. The catalytic activity of $Rh/CeO_2/SiO_2$ was improved and it was quite stable over longer reaction times.[42] TEM images and BET analysis of this catalyst showed that the particle size and surface area remain intact during reaction. In this paper, the $Rh/CeO_2/SiO_2$ catalyst is applied to the gasification of real biomass (cedar powder). We compared the gasification performance of $Rh/CeO_2/SiO_2$ to a commercial steam reforming catalyst, dolomite, and non-catalyst systems. This comparison shows that the novel $Rh/CeO_2/SiO_2$ catalyst is much more efficient than conventional systems.

Experimental

Cedar powder (C 45.99 wt%, H_2O 10 wt%, H 5.31 wt%, O 38.25 wt%, N 0.11 wt%, Cl 0.01 wt% and S 0.02 wt%) was used for gasification in a continuous-feeding fluidized-bed reactor in the temperature range 823–973 K. The reactor system is shown in Fig. 1. The gasifier is a quartz tube of 66 cm height. The reactor consisted of a fluidized-bed section of 5 cm height and 15 mm internal diameter and located at the middle of the reactor. The internal diameter of the upper part of the reactor just after the fluidized bed section is larger (30 mm) so that the gas turbulence suddenly decreases in this region and the catalyst particles easily return to the fluidized bed section. The biomass feeder consisted of a glass vessel with a small pore at the bottom of about 0.5 mm diameter, allowing continuous feeding by vibrating the vessel with an electric vibrator. The vibration rate controlled the feeding rate. Biomass particles were transported to the catalyst bed by the flow of N_2 gas through an inner tube of 8.5 mm i.d. Air was introduced from the bottom of the reactor as a gasifying agent and it also fluidized the catalyst particles. The bed temperatures at different points were measured by thermocouples. Samples of the product gas were collected from the sampling port by a microsyringe and analyzed by gas chromatography (GC). CO, CO_2, CH_4, H_2, and H_2O were formed as the products. The concentration of CO, CO_2 and CH_4 was determined by FID-GC and the concentration of hydrogen was determined by TCD-GC. The carbon-based conversion to gas (C-conv) is calculated using the relation:

$$[(\text{formation rate of CO} + CO_2 + CH_4)/(\text{rate of carbon feeding in biomass}) \times 100]$$

The amount of char was determined by the amount of gas (mainly CO_2) formed after stopping the feed of biomass under the air flowing at the reaction temperature. The amount of char is calculated using the relation:

$$(\text{total } CO_2 + CO \text{ formed after stopping the feed})/(\text{total carbon amount in fed biomass}) \times 100$$

The amount of tar is defined as (100 − C-conv (%) − char (%)).

CeO_2/SiO_2 was prepared by the incipient wetness method using an aqueous solution of $Ce(NH_4)_2(NO_3)_6$ and SiO_2 (Aerosil, 380 $m^2\ g^{-1}$). CeO_2 loading was 60 wt% (denoted in parenthesis). After drying at 393 K for 12 h, the catalyst was calcined at 773 K for 2 h and 873 K for 1 h under an air atmosphere. The Rh was loaded on CeO_2/SiO_2 by impregnation of the support with an acetone solution of $Rh(acac)_3$. After evaporating the acetone solvent, the catalyst was dried at 393 K for 12 h. The final catalyst was pressed, crushed and sieved to 44–149 μm particle size. The loading amount of Rh was 1.2×10^{-4} mol g^{-1} of catalyst. In each run, 3 g of catalyst was used and pretreated by a hydrogen flow at 773 K for 0.5 h. The composition of the commercial steam reforming catalyst (TOYO CCI, G-91) was 14 wt% Ni, 65–70 wt% Al_2O_3, 10–14 wt% CaO and 1.4–1.8 wt% K_2O. The composition of the dolomite was 21.0 wt% MgO, 30.0 wt% CaO, 0.7 wt% SiO_2, 0.1 wt% Fe_2O_3 and 0.5 wt% Al_2O_3. Before reaction the dolomite was calcined at 773 K for 3 h followed by a hydrogen treatment at 773 K for 0.5 h. Chemisorption experiments were carried out in a high-vacuum system by volumetric methods. Research grade H_2 gas (H_2: 99.99%, Takachiho Trading Co. Ltd.) was used without further purification. Before H_2 adsorption measurement, the catalysts were treated in H_2 at 773 K for 0.5 h. H_2 adsorption was performed at room temperature. The gas pressure at adsorption equilibrium was about 1.1 kPa while the sample weight was about 0.2 g. The dead volume of the apparatus was about 60 cm^3. The fresh (after H_2 treatment) and used catalysts were also characterized by BET analysis with a Gemini (Micrometrics) system.

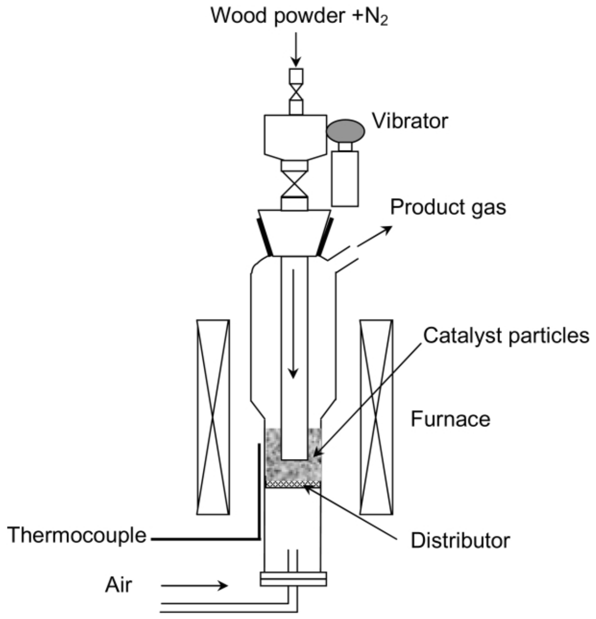


Fig. 1 Diagram of the continuous-feeding fluidized-bed reactor.

Results and discussion

The cedar powder has been gasified in a continuous feeding fluidized bed reactor at 873 K on $Rh/CeO_2/SiO_2(60)$ catalyst. Fig. 2 shows the carbon conversion to gas (C-conv) and gas formation rate with respect to the time on stream. Since catalyst deactivation is a severe problem in the catalytic gasification of biomass,[21] the catalyst stability is very important in this system. Fig. 2 shows that C-conv is quite stable at about the 95% level during the reaction time (20 min) at such a low temperature. The formation of hydrogen and CO with an H_2/CO ratio of 1.7 is also stable. When the feeding of biomass was stopped, CO_2 and a small amount of CO were formed. This CO_2 and CO formation can be assigned to the combustion of carbonaceous materials deposited on the catalyst during the reaction. The total amount of CO_2 + CO represents the amount of char. As shown in Table 1, the amount of char deposited on $Rh/CeO_2/SiO_2(60)$ was much smaller than that on other catalysts. This is related to the oxidation activity of the catalyst. In a previous report, we also have found that the combustion activity of methane on this type of catalyst is very high.[42] Under these reaction conditions, the CO_2 formation rate is higher than that of CO. This can be explained by the conversion of unreactive tar and char on the catalyst surface by combustion to form CO_2, and this realizes high C-conv. Furthermore, some secondary reactions such as hydrogenation of CO to produce methane and the water–gas shift reaction can proceed on $Rh/CeO_2/SiO_2(60)$ and these all contribute to the decrease of CO and increase of CO_2. Fig. 2 also shows that a substantial amount of methane was formed constantly.

The gasification test was also carried out on the commercial steam reforming catalyst (G-91) and dolomite at different temperatures under the same flowing conditions. Non-catalytic gasification was also carried out and the results are compared with the catalytic reactions in Table 1. The C-conv at different temperatures in various reaction systems is shown in Fig. 3(a) which shows that the order of C-conv is as follows: $Rh/CeO_2/SiO_2(60)$ > G-91 > dolomite > non-catalyst. The C-conv on $Rh/CeO_2/SiO_2(60)$ is higher than 95% at 873–973 K. In the case of G-91 C-conv does not reach 95% even at 973 K while for dolomite and non-catalytic conditions C-conv does not reach 95% even at 1173 K. From the comparison of char amounts listed in Table 1, high C-conv is related to small amounts of char. $Rh/CeO_2/SiO_2(60)$ exhibits very high performance in char removal, in addition, the formation of tar on $Rh/CeO_2/SiO_2(60)$ is much lower than for the other systems. This also indicates that $Rh/CeO_2/SiO_2(60)$ has a much higher activity for tar conversion to gas.

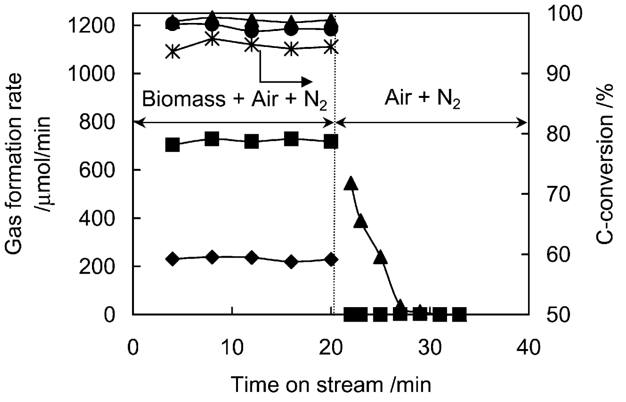


Fig. 2 Dependence of gas formation rate on time on stream in the gasification of wood powder on $Rh/CeO_2/SiO_2(60)$ at 873 K: carbon conversion (★), hydrogen (●), CO (■), CO_2 (▲) and methane (◆). *Conditions*: catalyst: 3 g, biomass feeding rate: 60 mg min^{-1} (H_2O: 10%, C: 2299 μmol min^{-1}, total H: 3852 μmol min^{-1}, total O: 1767 μmol min^{-1}); air: 100 ml min^{-1} (N_2: 3274 μmol min^{-1} and O_2: 818 μmol min^{-1}) from the bottom, N_2: 50 ml min^{-1} from the top.

Fig. 3(b) shows the temperature dependence of CO + H_2 formation rate for each system. In terms of the product gas being used for fuel synthesis (Fischer–Tropsch, methanol and dimethyl ether), CO and H_2 are useful products. In the case that the products are used for the power generation, CO, H_2 and CH_4 are useful products. However, here we have counted only the CO + H_2 as the main product for the liquid fuels and chemical production. The tendency of the total formation rate is similar to that of C-conv. The formation of useful products on $Rh/CeO_2/SiO_2(60)$ can be attained at much lower temperature than that on other systems. The total formation rate on dolomite and non-catalyst at 1173 K does not reach the level on $Rh/CeO_2/SiO_2(60)$ at 823 K. This indicates that $Rh/CeO_2/SiO_2(60)$ leads to a highly energy efficient system in biomass gasification. The difference in the total formation rate between $Rh/CeO_2/SiO_2(60)$ and G-91 seems to be smaller than that in C-conv. As shown in Table 1, a considerable amount of CH_4 is formed on $Rh/CeO_2/SiO_2(60)$, and not on G-91. Methane formation ($CO + 3H_2 \rightarrow CH_4 + H_2O$) consumes CO and H_2 significantly. This is why the difference in total formation rate is apparently small.

The char amount on G-91 is much larger than on $Rh/CeO_2/SiO_2(60)$ and deposition of char-like carbon can cause catalyst deactivation in the syngas production process.[43,44] The commercial steam reforming catalyst G-91 is deactivated much more easily than $Rh/CeO_2/SiO_2(60)$. Since the char or coke like materials are known to be deposited on the adsorbent surface, the yield of them in the non-catalyzed system is low due to lack

Table 1 Product distribution for biomass gasification on various catalysts at different temperatures

		Formation rate/μmol min^{-1}						
Catalyst	*T*/K	CO	H_2	CO_2	CH_4	C-conv (%)	Char (%)	Tar (%)
$Rh/CeO_2/SiO_2(60)$	823	536	883	1155	255	85	10	5
	873	676	1116	1240	254	95	5	0
	923	890	1117	1095	272	98	2	0
	973	945	1207	1097	238	99	1	0
G-91	823	487	795	1081	57	71	20	9
	873	494	1131	1130	95	75	19	6
	923	695	1300	1188	85	85	10	5
	973	975	1385	1025	57	90	5	4
Dolomite	823	353	156	1011	40	61	23	16
	873	380	298	1008	67	63	20	17
	923	490	353	1036	133	72	16	12
	973	618	412	912	176	74	15	11
	1073	569	615	979	209	77	12	11
	1173	655	720	935	245	80	8	12
Non-catalyst	823	285	66	420	38	32	12	54
	873	365	105	545	99	44	6	48
	923	470	111	660	108	54	6	40
	973	705	141	559	123	60	5	35
	1073	710	250	598	201	65	4	31
	1173	818	378	757	217	78	2	20

Conditions: catalyst: 3 g, biomass: 60 mg min^{-1} (H_2O: 10%, C: 2299 μmol min; H: 3852 μmol min^{-1}; O: 1767 μmol min^{-1}), air 100 ml min^{-1} (N_2: 3274 μmol min^{-1} and O_2: 818 μmol min^{-1}, ER = 0.31) from the bottom, N_2: 50 ml min^{-1} from the top. Number in parenthesis is CeO_2 loading, wt%.

Table 2 Properties of various catalyst

Catalyst	Metal loading/ 10^{-4} mol g^{-1}	H_2 adsorption/ 10^{-6} mol g^{-1a}	Dispersion^b (%) H/Rh	Dispersion^b (%) H/Ni	Surface area/m^2 g^{-1} Fresh	Surface area/m^2 g^{-1} Used
$Rh/CeO_2/SiO_2(60)$	1.2	9.7	16.2	—	123	118
G-91	23.7	14.6	—	1.2	33	31
Dolomite	—	—	—	—	1.1	0.9

^{a} Hydrogen chemisorption at 298 K. ^{b} Dispersion of reduced metal: (H consumption/total metal atom) × 100.

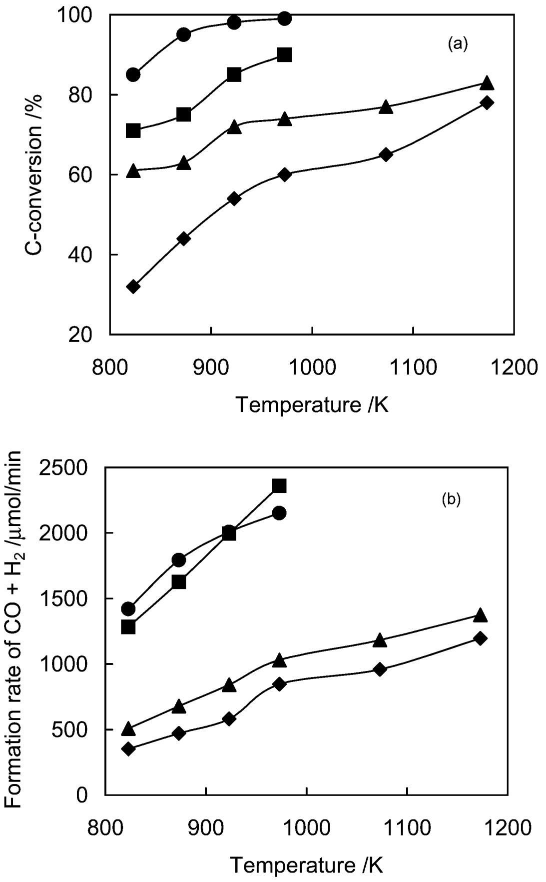


Fig. 3 Effect of temperature on (a) carbon conversion and (b) CO + H_2 formation rate in biomass gasification on (●) $Rh/CeO_2/SiO_2(60)$, (■) G-91, (▲) dolomite and (◆) non-catalyst. *Conditions*: Catalyst: 3 g, biomass feeding rate: 60 mg min^{-1} (H_2O: 10%, C: 2299 µmol min^{-1}, total H: 3852 µmol min^{-1}, total O: 1767 µmol min^{-1}); air: 100 ml min^{-1} (N_2: 3274 µmol min^{-1} and O_2: 818 µmol min^{-1}) from the bottom, N_2: 50 ml min^{-1} from the top.

of adsorption of them in the bed. Instead they deposited on the cooling zone at the top of the reactor and were not burned.

The properties of various catalysts are shown in Table 2. The BET surface areas of the used and fresh catalysts are almost the same. This means that the sintering of CeO_2 for the $Rh/CeO_2/SiO_2$ catalyst is prohibited by SiO_2 under the reaction conditions unlike for the Rh/CeO_2 catalyst where this was a severe problem. Furthermore, the same $Rh/CeO_2/SiO_2(60)$ catalyst was used at various temperatures for the gasification of cedar powder and no deactivation was observed. This also means that poisonous materials such as S and Cl present in the biomass did not affect the catalyst activity. The amount of H_2 consumption corresponds to the amount of surface metal atoms on the basis of H/metal on the surface = 1. The total amount of surface metal atoms of G-91 is larger than that of $Rh/CeO_2/SiO_2(60)$, and so this can not explain the excellence of $Rh/CeO_2/SiO_2(60)$. This indicates that the synergetic effect of Rh and CeO_2 is very important in this reaction.

In conclusion, $Rh/CeO_2/SiO_2(60)$ efficiently catalyzes the gasification of biomass at temperatures as low as 823–923 K in a fluidized bed continuous feeding reactor, resulting about 98% C-conv. Since this catalyst is highly active both in reforming and combustion reactions, the tar was completely gasified with very small amount of char. The content of the sulfur and chlorine in the biomass did not affect the catalyst activity at these low levels. No deactivation was observed even over longer reaction times. The BET surface area of the $Rh/CeO_2/SiO_2(60)$ catalyst remained constant during the gasification reaction. The combination of this catalyst with the fluidized-bed reactor will provide a novel system for syngas production from biomass at low temperature with a high-energy efficiency.

Acknowledgements

This research was supported by the Future Program of Japan Society for the Promotion of Sciences under the Project ‘Synthesis of Ecological High Quality of Transportation Fuels’ (JSPS-RFTF98P01001).

References

1 H. Schulz, *Appl. Catal. A: General*, 1999, **186**, 3.
2 C. Yaning, N. Yuqin and C. Zhenghua, *Fuel Process. Technol.*, 1997, **50**, 163.
3 K. L. Ng, D. Chadwick and B. A. Toseland, *Chem. Eng. Sci.*, 1999, **54**, 3587.
4 Y. Huang, Q. Ge, S. Li and F. Qiu, *Appl. Catal. A: General*, 1998, **167**, 23.
5 T. Shikada, Y. Ohno, M. Ono, M. Mizuguchi, K. Tomura and K. Fujimoto, *Stud. Surf. Sci. Catal.*, 1998, **119**, 515.
6 J. M. Ogden, *Annu. Rev. Energy Environ.*, 1999, **24**, 227.
7 M. Steinberg, *Int. J. Hydrogen Energy*, 1999, **24**, 771.
8 K. Pehr, P. Sauermann, O. Traeger and M. Bracha, *Int. J. Hydrogen Energy*, 2001, **26**, 777.
9 Z. Dülger and K. R. Özçelik, *Int. J. Hydrogen Energy*, 2000, **25**, 895.
10 T. A. Milne, C. C. Elam and R. J. Evans, *Hydrogen from Biomass: State of the Art and Research Challenges*, IEA/H2/TR-02/001. National Renewable Energy Laboratory, Golden, CO, 2001.
11 D. J. Stevens, *Hot Gas Conditioning: Recent Progress with Larger-Scale Biomass Gasification Systems. Update and Summary of Recent Progress*, NREL/SR-510-29952, National Renewable Energy Laboratory, Golden, CO, 2001.
12 I. Narváez, A. Orío, M. P. Aznar and J. Corella, *Ind. Eng. Chem. Res.*, 1996, **35**, 2110.
13 P. Vriesman, E. Heginuz and K. Sjöström, *Fuel*, 2000, **79**, 1371.
14 C. D. Blasi, G. Signorelli and G. Portoricco, *Ind. Eng. Chem. Res.*, 1999, **38**, 2571.
15 J. Gil, M. P. Aznar, M. A. Caballero, E. Francés and J. Corella, *Energy Fuels*, 1997, **11**, 1109.
16 A. A. C. M. Beenackers, *Renewable Energy*, 1999, **16**, 1180.
17 F. Miccio, O. Moersch, H. Spliethoff and K. R. G. Hein, *Fuel*, 1999, **78**, 1473.
18 K. Maniatis and A. A. C. M. Beenackers, *Biomass Bioenergy*, 2000, **18**, 1.
19 N. Abatzoglou, N. Barker, P. Hasler and H. Knoef, *Biomass Bioenergy*, 2000, **18**, 5.
20 H. A. M. Knoef and H. J. Koele, *Biomass Bioenergy*, 2000, **18**, 55.

21 L. Mudge, E. G. Baker and D. G. Mitchell, *Investigations on Catalyzed Steam Gasification of Biomass*, PNL-3695, Pasific Northwest National Laboratory, Richland, WA, 1981.

22 C. Ekstrom, N. Lindman and R. Petterson, *Catalytic Conversion of Tars, Carbon Black, and Methane from Pyrolysis/Gasification of Biomass. Proceedings of the Fundamentals of Thermochemical Conversion of Biomass Conference*, ed. R. P. Overend, T. A. Milne and L. K. Mudge, Elsevier Applied Press, London, 1982, p. 601.

23 A. A. C. M. Beenackers and K. Maniatis, *Gas Cleaning in Electricity Production via Gasification of Biomass. Conclusions of the Workshop. Advances in Thermochemical Biomass Conversion*, ed. A. V. Bridgewater, Blackie Academic Press, London, 1994, p. 540.

24 A. V. Bridgwater, *Appl. Catal.*, 1994, **116**, 5.

25 P. Simell, E. Kurkela and P. Ståhlberg, *Formation and Catalytic Decomposition of Tars from Fluidized Bed Gasification. Advances in Thermochemical Biomass Conversion*, ed. A. V. Bridgwater, Blackie Academic Press, London, 1994, p. 265.

26 N. Abatzoglou, P. Legast, P. Delvaux, D. Bangala and E. Chornet, *Gas Conditioning Technologies for Biomass and Waste Gasification. Proceedings of the Third Biomass Conference of the Americas*, ed. R. P. Overend and E. Chornet, Elsevier Science Ltd., Oxford, 1997, p. 599.

27 M. P. Aznar, J. Corella, J. Gil, A. Martin, M. A. Caballero, A. Olivares and P. Perez, *Biomass Gasification with Steam and Oxygen Mixtures at Pilot Plant Scale and Catalytic Gas Upgrading, Part I. Developments in Thermochemical Biomass Conversion*, ed. A. V. Bridgwater and D. G. B. Boocock, Blackie Academic and Professional, London, 1997, p. 1194.

28 T. A. Milne, N. Abatzoglou and R. J. Evans, *Biomass Gasifier 'Tars': Their Nature, Formation, and Conversion*, NREL/TP-570-25357. National Renewable Energy Laboratory, Golden, CO, 1998.

29 M. A. Caballlero, M. P. Aznar, J. Corella, J. Gil and J. A. Martin, *Proceedings of the Fourth Biomass Conference of the Americas*, ed. R. P. Overend and E. Chornet, Pergamon, Oxford, 1999, p. 979.

30 J. Corella, M. A. Caballero, M. P. Aznar and J. Gil, *Proceedings of the Fourth Biomass Conference of the Americas*, ed. R. P. Overend and E. Chornet, Pergamon, Oxford, 1999, p. 933.

31 P. Pérez, M. P. Aznar, M. A. Caballero, J. Gil, J. A. Martín and J. Corella, *Energy Fuel*, 1997, **11**, 1194.

32 J. Corella, *Fuel Energy Abstr.*, 1997, **38**, 163.

33 J. Delgado, M. P. Aznar and J. Corella, *Ind. Eng. Chem. Res.*, 1997, **36**, 1535.

34 M. A. Caballero, J. Corella, M. P. Aznar and J. Gil, *Ind. Eng. Chem. Res.*, 2000, **39**, 1143.

35 J. Corella, A. Orio and J. M. Toledo, *Energy Fuels*, 1999, **13**, 702.

36 J. Corella, A. Orio and P. Aznar, *Ind. Eng. Chem. Res.*, 1998, **37**, 4617.

37 M. P. Aznar, M. A. Caballero, J. Gil, J. A. Martin and J. Corella, *Ind. Eng. Chem. Res.*, 1998, **37**, 2668.

38 M. A. Caballero, M. P. Aznar, J. Gil, J. A. Martin, E. Frances and J. Corella, *Ind. Eng. Chem. Res.*, 1997, **36**, 5227.

39 I. Narváez, J. Corella and A. Orio, *Ind. Eng. Chem. Res.*, 1997, **36**, 317.

40 M. Asadullah, K. Tomishige and K. Fujimoto, *Catal. Commun.*, 2001, **2**, 63.

41 M. Asadullah, K. Tomishige and K. Fujimoto, *Ind. Eng. Chem. Res.*, 2001, **25**, 5894.

42 M. Asadullah, S.-I. Ito, K. Kunimori, M. Yamada and K. Tomishige, *J. Catal.*, 2002, **208**, 255.

43 K. Tomishige, Y. Chen and K. Fujimoto, *J. Catal.*, 1999, **187**, 91.

44 K. Tomishige, Y. Himeno, Y. Matsuo, Y. Yoshinaga and K. Fujimoto, *Ind. Eng. Chem. Res.*, 2000, **39**, 1891.

Microwave enhanced synthesis of acridines. A new aspect in the Bernthsen reaction

Julio A. Seijas,* M. Pilar Vázquez-Tato,* M. Montserrat Martínez and Jacobo Rodríguez-Parga

Departamento de Química Orgánica, Universidad de Santiago de Compostela, Facultad de Ciencias, Aptdo. 280, 27080- Lugo, Spain. E-mail: qoseijas@lugo.usc.es or pilarvt@lugo.usc.es

Received 1st May 2002
First published as an Advance Article on the web 12th July 2002

The Bernthsen reaction is studied using microwaves as the heat source. This leads to acridines with aromatic and aliphatic substituents in position 9, shortening reaction times and increasing yields, with a reduction in Lewis acid catalyst ($ZnCl_2$), allowing a more environmentally friendly reaction.

Introduction

Acridines are a well known group of compounds[1] with a wide variety of biological properties[2] as DNA intercalating agents, anticarcinogenics, bactericides, antimalarials, insecticides and antifungics.

Although there are several approaches to their synthesis, the Bernthsen reaction is one of the classical methods. It consists of heating diphenylamine in the presence of zinc chloride and a carboxylic acid, at 200–210 °C with reaction times of several hours.[3]

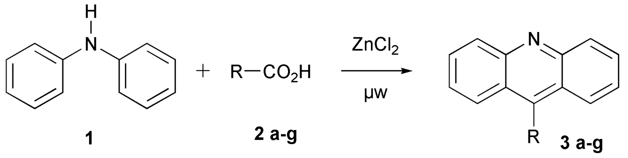
In our group we are interested in the application of microwave heating to organic synthesis,[4] usually this reactions can be carried out in a domestic pulsed microwave oven,[5] inside test tubes open to the air, in the absence of solvent and the reaction times are often shortened. These features make this MORE (Microwave Organic Reactions Enhancement) chemistry a very attractive option to improve some aspects of classical reactions. In this sense, the Bernthsen reaction can be an ideal candidate to be enhanced by microwave heating, particularly from a green chemistry point of view, since at present it uses a heavy metal such as zinc—in a considerable excess—as acid catalyst, with the consequent environmental problem for disposal of the reaction residues. We have already stated this principle in a preliminary communication for the synthesis of 9-phenylacridine.[6]

Results and discussion

As a first approach, the reactants (diphenylamine, zinc chloride and benzoic acid) were mixed in the stoichiometry used in literature for the conventional heating (1 : 5 : 1), and after 5 min of irradiation 34% of 9-phenylacridine was obtained, slightly lower than the yield reported by classical method (40%). This yield was improved by modifying the reaction stoichiometry, lowering the zinc chloride amount to two equivalents, the yield (risen to 80%) can be further improved to 98% with 1 : 1 : 1 reagents ratio after 2.5 min of irradiation.[6] In order to determine the scope of this reaction, the behaviour of other benzoic acids (*ortho*-, *meta*- and *para*-toluic acids) were studied. The best yields were obtained when the carboxylic acid amount was two-fold and the yields were 73, 60 and 64% for each of the toluic acid isomers (Table 1, entries 2–4). *p*-Phenylbenzoic acid with diphenylamine and zinc chloride were also irradiated with microwaves for 11 min to yield 88% of the corresponding acridine **3e** (Table 1, entry 5).

Aliphatic carboxylic acids were also employed. Thus, enantic acid gave 57% yield of 9-hexylacridine and lauric acid 75% of 9-undecylacridine (Table 1, entries 6–7).

Table 1



a: Ph; **b**: *o*-MeC_6H_4; **c**: *m*-MeC_6H_4; **d**: *p*-MeC_6H_4; **e**: *p*-PhC_6H_4; **f**: $CH_3(CH_2)_5$; **g**: $CH_3(CH_2)_{10}$

Entry	R	Time/ min	Stoichiometry **1**:$ZnCl_2$[a]:**2**	Micro- wave yield (%)	Conven- tional yield (%)
1	Ph	2.5	1:1:1	98	48[8]
2	*o*-MeC_6H_4	7	1:1:2	73	50[9]
3	*m*-MeC_6H_4	12	1:1:2	60	53[9]
4	*p*-MeC_6H_4	7	1:1:2	64	40[9]
5	*p*-PhC_6H_4	11	1:1:2	88	41[10]
6	$Me(CH_2)_5$	5	1:1:2	57	18[b]
7	$Me(CH_2)_{10}$	6	1:1:2	75	20[11]

[a] See ref. 7. [b] Prepared by the authors following Bernthsen's general procedure.

Green Context

There are several organic chemistry reactions which involve 'catalysts' that are actually required in very large quantities if reasonable product yields are to be obtained. The Bernthsen reaction is an important method for the synthesis of acridines which have various applications as bioactive compounds. The traditional route employs greater than stoichiometic amounts of zinc chloride. Here we see how microwave activation can lead to a substantial reduction in the required amount of $ZnCl_2$ ***JHC***

DOI: 10.1039/b204243f

Parallel to the work presented in this paper and after our preliminary communication concerning the microwave enhancement of the Bernthsen reaction, a report by Toma and coworkers[12] has just appeared on the application of microwave heating to the synthesis of 9-substituted acridines. The authors report similar reaction times, but they still claim that an excess of zinc chloride is required. Furthermore, only aliphatic carboxylic acids are used, whereas in the present paper the scope of the reaction was extended not only to aliphatic carboxylic acids, but also to aromatic ones.

To summarize, irradiation in a microwave oven proved to be a good way to optimise the Bernthsen reaction both for aromatic and aliphatic carboxilic acids, shortening the reaction time and reducing the amount of zinc chloride, which is a non-negligible aspect in environmental concerns. Use of microwaves also considerably raised the yields compared to the 'classical' method (see Table 1).

Experimental

General procedure for the synthesis of acridines. Synthesis of 9-(4-biphenyl)acridine (3e)

A mixture of *N*,*N*-diphenylamine (100 mg, 0.592 mmol), 4-phenylbenzoic acid (234 mg, 1.183 mmol) and recrystallised zinc chloride (81 mg, 0.59 mmol) was irradiated in a domestic microwave oven (at 80% of a total output of 1000 W) for 11 min (the reaction was monitored by TLC). The crude product was dissolved in dichloromethane (20 ml) and washed with 10% aqueous NaOH and water. The organic layer was dried (Na_2SO_4), evaporated and the residue crystallised yielding 9-(4-biphenyl)acridine (**3e**) (172 mg, 88% yield), mp 224–226 °C (toluene–hexane), lit.[10] mp 234–236 °C.

Acknowledgements

DGES (PB96-0937) and Xunta de Galicia (PR405A 98/59-0 and PGIDT01PXI26203PR) are thanked for financial support.

Notes and references

1 *Acridines. The Chemistry of Heterocyclic Compounds*, ed. R. M. Acheson, Interscience Publishers Inc., New York, 1956.

2 A. W. McConnanghis and T. C. Jenkins, *J. Med. Chem.*, 1995, **38**, 3488–3501; A. Lorente, M. Fernández Saiz and J. F. Espinosa, *Tetrahedron Lett.*, 1995, **36**, 5261–5264; M. Lourdan, J. García and J. Lhommen, *Biochemistry*, 1999, **38**, 14205–213; S. Bonse, C. Santelli-Rouvier, J. Barbe and R. L. Krauth-Siegel, *J. Med. Chem.*, 1999, **42**, 5448–5454; S. A. Gamage, J. A. Spicer, G. J. Atwell, G. J. Finlay, B. C. Baguley and W. A. Denny, *J. Med. Chem.*, 1999, **42**, 2383–2393; J. Lhomme, *J. Med. Chem.*, 1997, **40**, 3346–3352; W. A. Denny, *J. Med. Chem.*, 1996, **39**, 2508–2517; S. R. Kirk, N. W. Luedtke and Y. Tor, *J. Am. Chem. Soc.*, 2000, **122**, 980–981.

3 A. Bernthsen, *Justus Liebig's Ann. Chem.*, 1884, **224**, 1.

4 M. P. Vázquez-Tato, *Synlett*, 1993, 506; J. A. Seijas, M. P. Vázquez-Tato, M. M. Martínez and G. Núñez-Corredoira, *J. Chem. Res. (S)*, 1999, 420–421; J. A. Seijas, M. P. Vázquez-Tato and M. M. Martínez, *Tetrahedron Lett.*, 2000, **41**, 2215–2217; J. A. Seijas, M. P. Vázquez-Tato, C. González-Bande and B. Pacios-López, *Spanish Pat. Appl.*, P200002113, 22 August 2000; J. A. Seijas, M. P. Vázquez-Tato, C. González-Bande and B. Pacios-López, *Synthesis*, 2001, 999–1000; J. A. Seijas, M. P. Vázquez-Tato and M. M. Martínez, *Synlett*, 2001, 875–877.

5 Domestic microwave ovens are suitable for many microwave enhanced reactions, since most of them are performed in absence of solvent and non-flammable reagents are used. For a discussion on this subjet by researchers on this field, see the discussion list on the last ECSOC-5 *Symposium on Microwave Assisted Synthesis* (http://www.mdpi.net/ecsoc-5/).

6 J. A. Seijas, M. P. Vázquez-Tato, M. M. Martínez and J. Rodríguez-Parga, *Chem. Abstr.*, 2001, **135**, 46075; *Communication a0068, Fourth Electronic Conference on Synthetic Organic Chemistry (ECSOC-4)*, September 2000. (http://www.unibas.ch/ecsoc-4/a0068/a0068.htm).

7 Zinc chloride performance in the reaction is improved when purified by recrystallysation from dioxane: *Purification of Laboratory Chemicals*, ed. D. D. Perrin and W. L. F. Armarego, Pergamon Press, Oxford, UK, 3rd edn, 1988.

8 Buu-Hoï and J. Lecocq, *Compt. Rend.*, 1944, **218**, 794–794.

9 A. Schmid and H. Decker, *Ber. Dtsch. Chem. Ges.*, 1906, **39**, 933–939.

10 G. Jones II, M. S. Farahat, S. R. Greenfield, D. J. Gosztola and M. R. Wasielewski, *Chem. Phys. Lett.*, 1994, **224**, 40–46; M. S. Farahat, *Ph. D. Dissertation*, Boston University, 1993.

11 Buu-Hoï and J. Lecocq, *Recl. Trav. Chim. Pays Bas*, 1945, **64**, 250–253.

12 E. Veverkova, M. Noskova and S. Toma, *Synth. Commun.*, 2002, **32**, 729–773.

Waste elimination in condensation reactions of industrial importance

G. J. Kelly,* F. King and M. Kett

Synetix, PO Box 1, Belasis Avenue, Billingham Avenue, Cleveland, UK TS23 1LB

Received 25th February 2002
First published as an Advance Article on the web 15th July 2002

Industrial condensation reactions are usually homogeneously catalysed by strong caustic. Recent work has demonstrated the practical application of heterogenised base catalysts, which enhance selectivity and eliminate the generation of organically contaminated waste caustic streams. A number of successful systems have been developed and the combination of base and hydrogenation functionality has been explored.

Introduction

Industrially, condensation reactions are of great importance in the production of a number of key compounds. These include 2-ethylhexanol, methyl isobutyl ketone (MIBK) and Guerbet alcohols. Over 1.5 million tonnes of these chemicals are produced worldwide every year using homogeneous bases such as NaOH and $Ca(OH)_2$.[1] 2-Ethylhexanol is predominately converted to diethylhexyl phthalate (generally known as dioctyl phthalate (DOP), which is used as a plasticiser for PVC. DOP, obtained by reacting 2-ethylhexanol with phthalic anhydride is an excellent, physiologically harmless, standard plasticizer used by the plastics industry. More recently DOP has been used as a dielectric liquid for capacitors, where it replaces toxic polychlorinated diphenyls. Other esters of 2-ethylhexanol, in particular with aliphatic dicarboxylic acids, are employed as hydraulic oils or as components of synthetic lubricants. 2-Ethylhexanol is, in addition, oxidised to 2-ethylhexanoic acid. This acid can also be manufactured by oxidation of 2-ethylhexanal produced by selective hydrogenation of 2-ethylhexenal with Pd catalysts. 2-Ethylhexanoic acid is used for modifying alkyd resins while 2-ethylhexanal can also be used as a raw material for perfumes. MIBK is the largest volume aldol reaction product of acetone and is an excellent solvent for cellulose and resin based coating systems and also for vinyl, epoxy and acrylic resins. Guerbet alcohols are saturated primary alcohols that possess two linear chains. They are used in a variety of applications such as cosmetics, textiles, metal processing, lubricants and surfactants. It has been estimated for these compounds that 30% of the selling price is product purification, recovery and waste treatment.[2] For every 10 tonnes of product formed the current homogeneous catalysts generate about 1 tonne of spent catalyst.[2] High capital costs are also associated with the handling of strong homogeneous bases such as 30% caustic.

Industrial production of 2-ethylhexanol

At present most 2-ethylhexanol producers start from the hydroformylation of propene to form *n*-butanal. The *n*-butanal is then converted to 2-ethylhexenal by a base catalysed aldol condensation reaction. Hydrogenation of 2-ethylhexenal produces 2-ethylhexanol. This process is shown in the following chemical equations (Fig. 1).

The industrial manufacture of 2-ethylhexanol involves very high capital cost plants. Major problems are associated with the safe handling of the 30% caustic that is required for the reaction and the treatment of organically contaminated caustic containing waste streams.

At present nearly all *n*-butanal is produced from propylene with various phosphine modified rhodium catalysts in a hydroformylation reaction.[3] Various technologies have been developed by companies such as Union Carbide/Davy-McKee/Johnson-Matthey, Celanese, BASF, Mitsubishi Chemicals and Ruhrchemie/Rhone-Poulenc. Step 2, the aldol condensation process has been greatly developed by Mitsubishi Chemical.[4] In Step 2 *n*-butanal is converted almost quantitatively into 2-ethylhexenal in the presence of caustic or a basic ion-exchanger at 80–100 °C. The hydrogenation, Step 3, can be carried out in the gas phase over either Ni or Cu catalysts. If required, a further hydrogenation can be conducted in the liquid phase.[1] The pure product is obtained from a three-step distillation. The overall selectivity of the process is about 95% (based on *n*-butanal) with side-products such as C_3-C_7 hydrocarbons and heavy ends produced.[1] Typical catalysts and conditions for each of these steps are shown in the Table 1.

Shell[5] and Exxon both developed single-step process producing 2-ethylhexanol directly from propylene by adding co-catalysts such as compounds of Zn, Sn, Ti, Al, or Cu or KOH, to the original ‘oxo’ catalyst. Besides using KOH as a co-catalyst, Shell also uses a ligand-modified hydroformylation catalyst, $HCo(CO)_3PR_3$, in their ‘Aldox’ process. These processes have several disadvantages over the three-step process outlined above *i.e.* (i) a large excess of CO is required which entails large gas recovery facilities, (ii) a relatively low liquid space velocity in the hydroformylation, (iii) a low selectivity to the C_8 alcohol product and (iv) an increased capital investment.

Green Context

Strong bases such as metal hydroxides are used in a range of industrially important condensation reactions. In order to eliminate the salt waste generated as a consequence of neutralisation after reaction, heterogeneous systems are being investigated. This paper describes some new approaches to these reactions, and to the incorporation of the second step (catalytic hydrogenation) into a single step system. Comparisons with existing proceses are informative.
DJM

DOI: 10.1039/b201982p

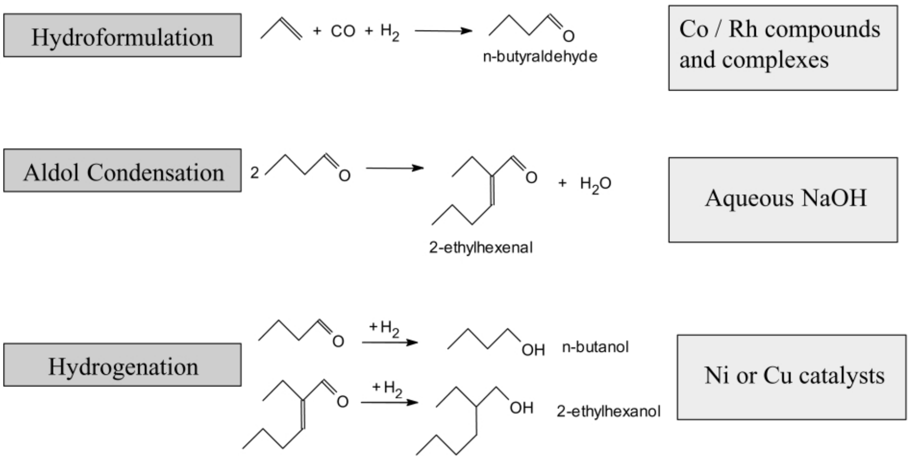


Fig. 1 Industrial production of 2-ethylhexanol.

Table 1 Typical catalysts and conditions for 2-ethylhexanol production

	Catalyst	Temp./°C	Pressure
STEP 1	Rh phosphine	90–120	7–25 bar
STEP 2	NaOH aqueous	80–100	atm
STEP 3	CuO/ZnO or Ni/ Al_2O_3	135–170 or 100–150	5 bar

Industrial production of MIBK

MIBK is traditionally manufactured *via* a three-step reaction scheme as follows (Fig. 2).[2] (i) Base catalysed aldol condensation of acetone in the liquid phase to diacetone alcohol (DAA), (ii) acid catalysed dehydration of DAA to mesityl oxide (MO) using H_2SO_4 or H_3PO_4 at 100 °C, (iii) hydrogenation of MO to mesityl isobutyl ketone (MIBK) and further to methyl isobutyl carbinol using Cu or Ni catalysts at 15–200 °C and 3–10 bar.

These processes are complicated and the operating costs are high. The condensation equilibrium in step (i) does not favour aldol formation. In step (ii) acetone can be formed by the reaction of mesityl oxide with water and in step (iii) the less useful methyl isobutyl carbinol has to be separated by distillation. There is also a corrosive problem due to the use of liquid acids and bases.

Recently, a one-step process from acetone to MIBK has become commercially feasible and several catalytic systems have been claimed for this process. They mainly consist of palladium supported catalysts, for example, on KOH–Al_2O_3, MgO–SiO_2,[6] CaO–MgO–SrO–Al_2O_3,[7] Nb_2O_5,[8] $ZrO(OH)_2$–carbon,[5,9] Ce, Hf and/or Ta oxides or hydroxides–carbon[10] and cation exchange resins.[2] Very high selectivities to MIBK ($>90\%$) are described in the 80–160 °C range and acetone conversions are near 40%. Nevertheless high operating pressures, typically 10–100 atm are a disadvantage of the single-step process. More recently, the development of catalysts, which operate efficiently in the gas phase at atmospheric pressure, has been the main target of the one-step process. These have included Pd/SAPO-34,[11] Pd/KH-ZSM-5,[12] Ni/MgO,[13] Ni/ALPON,[14] Na/Pd/MgO,[15] Ni/Al_2O_3[16] and Pd or Ni supported on Mg/Al hydrotalcites.[17]

Industrial production of Guerbet alcohols

Guerbet alcohols (2-alkyl-1-alkanols) are saturated primary alcohols which possess two linear alkyl chains and have the general chemical structure shown in Fig. 3.

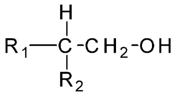


Fig. 3 Structure of Guerbet alcohols.

Examples of Guerbet alcohols are compounds such as 2-butyloctanol and 2-hexyldecanol. Traditionally Guerbet alcohols are produced[6] by the dimerisation of alcohols at >200 °C at elevated pressures over alkali hydroxides or alkoxides. This method however produces significant amounts of fatty acids. More recently by-product formation has been minimised by

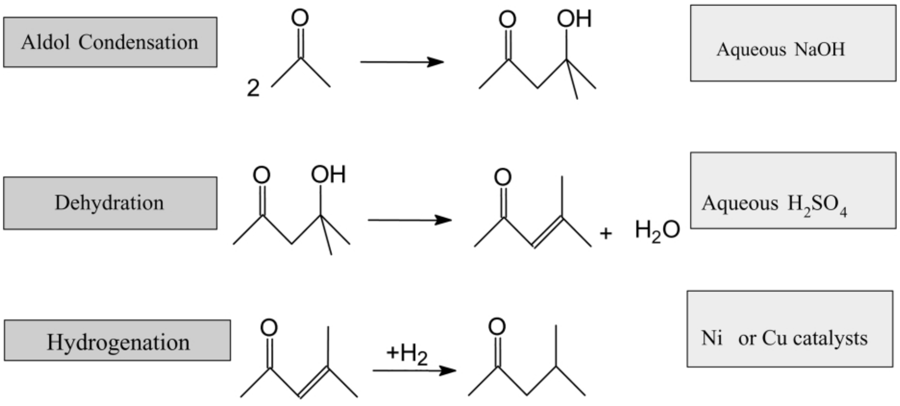


Fig. 2 Industrial production of MIBK.

using $MgO–K_2CO_3–CuC_2O_2$ at high temperatures or Rh, Pt or Ru complexes at lower temperatures.

Solid base catalysts

Solid base catalysts have a number of advantages over conventional homogeneous (NaOH, KOH, $Ca(OH)_2$) systems as follows:[18,19]

- High catalytic activity and selectivity are often observed
- Solid base catalysts do not corrode reaction vessels or reactors
- Repeated use is possible
- Easier separation from the products
- Less waste than produced from stoichiometric reagents
- Lower operation and maintenance costs
- No acid or base containing waste streams
- Lower energy synthesis
- Solid base catalysts do not catalyse cracking reactions
- In the presence of solid base catalysts there are no strong adsorption complexes as found between acid sites and N- and O-functionalized organic compounds. Desorption energy is lower allowing reactions to occur at lower temperatures

Most industrial condensation products also pass through a fixed-bed hydrogenation step after the homogeneous condensation step.[1] The use of solid base catalysts also allows the easier integration of the condensation step with any subsequent hydrogenation steps. Despite the many possible advantages of using solid base catalysts there are in fact very few solid base catalysts currently in use commercially. According to a recent review of industrial acid and base catalysis[20] of the 127 processes identified only 10 were solid base catalysed. Although solid base catalysts have a much lower environmental impact than conventional liquid systems, this alone is often not enough to persuade users to switch from liquid to solid systems, due to factors such as:

- The capital already invested in to the process
- The understanding and confidence that users have with liquid systems
- The 'cheapness' and availability of some of the liquid acids and bases
- The cost that would be incurred by modifying existing systems
- To switch from a liquid based system to a solid system the user has to see the advantages of using solid systems in terms of quality of product, selectivity of process and the overall process economics and for new plants in reduced capital. Solid base catalysis is an area of chemistry that offers an opportunity for exploitation if suitable catalysts and processes can be identified and developed. On a manufacturing site an acid/base balance has to be maintained in the effluent streams to ensure neutrality. Eliminating caustic containing waste streams would also be a driver for the application of processes that eliminate acid waste streams. Overall there would be a reduction in the amounts of salt put to waste.

Solid base selection

A suitable solid base must have the appropriate base strength for the reaction under investigation. If the initial reaction step is the removal of a proton from a reactant of the form $R_1CH_2R_2$ then the acidity of the proton to be removed depends on the identity of the R_1 and R_2 groups[21] (Table 2). The solid base selected should have sufficient base strength to carry out the reaction but should not have excessive base strength as this may lead to rapid catalyst deactivation (due to carbon laydown for instance) or to side-product formation. For aldehyde and ketone condensation reactions therefore with a pK_a of 19.7–20 a strong base is required but not a superbase material.[22] Caustic can be used to carry out reactions with reactants with the removable proton having a pK_a of up to around 20. For less acidic protons stronger bases such as aluminium *tert*-butoxide are usually required to give sufficient rate of reaction.[23]

Table 2 Base strength required to remove proton from $R_1CH_2R_2$ reactant molecule

R_1	R_2	pK_a	Base required	
CH_3	CH_3	42	SUPER BASE	
CH_3	$CH{=}CH_2$	35.5		
C_6H_5	H	35		
C_6H_5	C_6H_5	33		
CH_3	CN	25	STRONG BASE	
CH_3	COOR	24.5		
CH_3	$COCH_3$	20		NaOH
CH_3	COH	19.7		
COOR	COOR	11.5	MEDIUM BASE	
CN	CN	11.2		
CH_3	NO_2	10.6		
COR	COR	9		
NO_2	COOR	5.8	MILD BASE	
COH	COH	5		
NO_2	NO_2	3.6		

The strength of surface base sites on solids can be measured by the use of Hammett indicators[24] and expressed in terms of the acidity function (H_-) proposed by Paul and Long.[25] There are a number of mild base materials ($H_- = 10–5$) such as hydrotalcites, alkali doped zeolites and aluminophosphates oxynitrides (ALPON) available[26] and at the other extreme a number of super basic materials ($H_- > 26$) such as alkaline earth oxides (CaO, MgO) and alkaline metal based catalysts ($Na/NaOH/Al_2O_3$, Na/MgO *etc.*).[22] There are few available solid base materials, however, in the strong solid base area ($H_- = 20–25$) that would be suitable for the aldol condensation of aldehydes (Fig. 4). One example of a recently developed strong basic catalyst is a Cs/SiO_2 material developed for a new route for producing methyl methacrylate from the reaction of methyl propionate ester with formaldehyde.[27] According to Table 2 the Cs/SiO_2 catalyst has sufficient base strength to remove protons of $pK_a = 24.5$.

Besides having the appropriate base strength to carry out the reaction a solid base catalyst also requires active sites which are

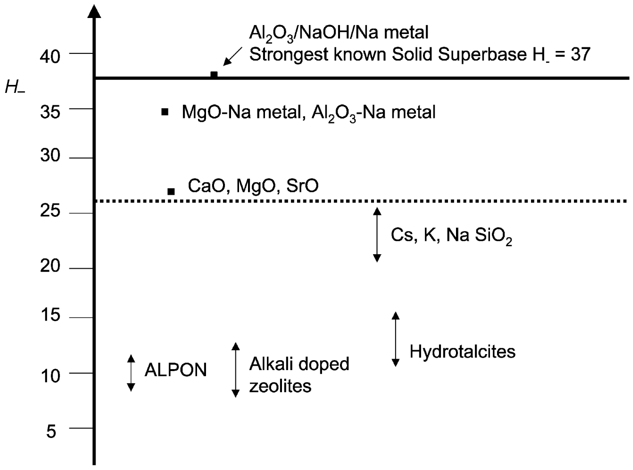


Fig. 4 Strength of solid base catalysts (H_- scale).

accessible to the reactants and the required density of active sites for sufficient reaction rate. Mass transport and diffusion limitations are of particular concern in liquid phase reactions and for bulky reactants and products.

Condensation reactions of aldehydes and ketones using solid base catalysts

A series of condensation reactions were performed in the gas phase over fixed-bed solid base catalysts. The organic feeds tested were *n*-butanal and butanone as model compounds for aldehyde and ketone condensation reactions. The solid base catalysts were all based on alkali doped silica materials. A Pd doped Na/SiO_2 catalyst was tested for combined base/selective hydrogenation properties. Dual bed experiments using base catalysts followed by CuO/ZnO hydrogenation catalysts in a single tube were also carried out.

Reactions networks

The product from the aldol condensation of *n*-butanal is usually an α,β-unsaturated aldehyde (Fig. 5), 2-ethylhexenal, from the dehydration of the aldol product. The choice of product formed on the hydrogenation of 2-ethylhexenal depends largely on the metal function used. Pd catalysts can be used to selectively hydrogenate the –C=C– as Pd is often inactive with regard to the carbonyl group at the temperatures required for –C=C– hydrogenation. This is the case in the gas or liquid phase and for saturated and unsaturated carbonyls.[28] Promoted Pt or Ru catalysts can be used to selectively hydrogenate the carbonyl to produce α-unsaturated alcohols.[28] Cu or Ni catalysts are the conventional catalysts for fully hydrogenating the α-unsaturated aldehyde through to the saturated alcohol.[29]

Regioselective reactions of asymmetric ketones are of fundamental importance in organic synthesis, the most familiar reactions being α-alkylations, Michael additions and aldol condensations. In the presence of a base, butanone is capable of losing a proton from the adjacent methylene group or the terminal methyl group. Tautomerisation of the two possible carbanions formed from the proton abstraction leads to two regioisomeric enolates (Fig. 6).

The terminal enolate **1** is formed by irreversible kinetic control, whereas those reactions under thermodynamic control usually yield the internal enolate **2**.[30] In more favourable cases one regioisomer can greatly predominate in the equilibrium mixture but often the equilibrium constant is not sufficiently high enough to achieve an acceptable regioselectivity. The enolates formed can then attack a polarised carbonyl group to form a carbon–carbon bond (Fig. 7) to form two aldol products.

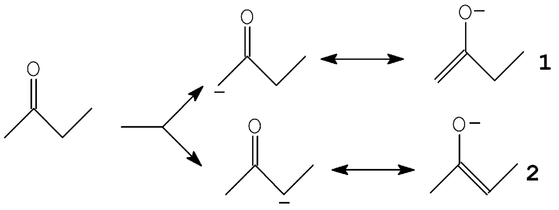


Fig. 6 Formation of regioisomeric enolates from butanone.

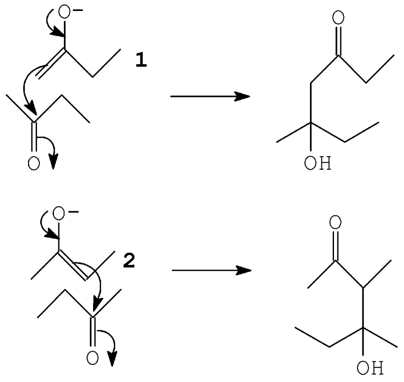


Fig. 7 Formation of aldol products from butanone.

Under our reaction conditions rapid dehydration of the aldol product occurs resulting in the formation of unsaturated carbonyl compounds. Starting from butanone the point of proton abstraction and the direction of dehydration can lead to a wide range of possible products. Possible products from the aldol-condensation of butanone are given in Table 3.

As Table 3 clearly demonstrates, a number of products can be produced in this reaction, and this does not account for any double-bond migration induced by the base catalyst.

Experimental

Catalyst preparation

A 4 wt% Na/SiO_2 catalyst and a 4 wt% Cs/SiO_2 catalyst were prepared by an impregnation method using nitrate salts. Fuji Q10 silica spheres (2–3 mm) were used which have a surface area of 359 $m^2\ g^{-1}$ and a pore volume 1.01 $cm^3\ g^{-1}$. A Pd doped

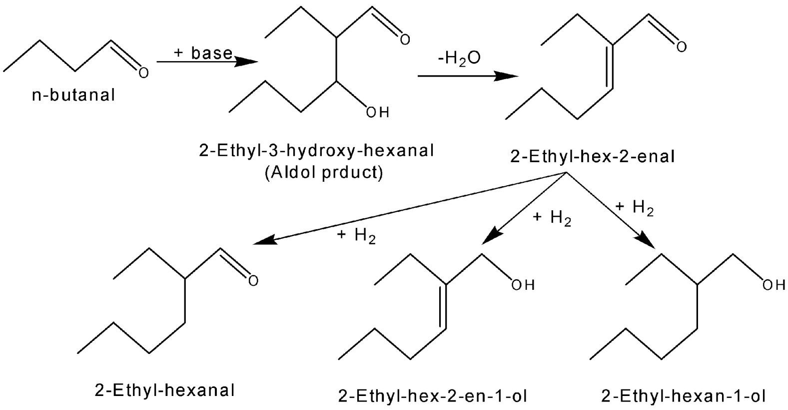
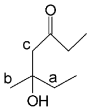
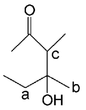


Fig. 5 *n*-Butanal condensation/ hydrogenation reaction scheme.

Table 3 Possible products from the aldol condensation of butanone

Intermediate	Terminal proton $CH_3CH^a{}_2C(OH)(CH^b{}_3)$-$CH_2COCH_2CH_3$	Internal proton $CH_3CH^a{}_2C(OH)(CH^b{}_3)CH^c$-$(CH_3)COCH_3$
Structure		
Proton a	*cis*-5-Methyl-5-hepten-3-one *trans*-5-Methyl-5-hepten-3-one	*cis*-3,4-Dimethyl-4-hexen-2-one *trans*-3,4-Dimethyl-4-hexen-2-one
Proton b	5-Methyleneheptan-3-one	3-Methyl-4-methylenehexan-2-one
Proton c	*cis*-5-Methyl-4-hepten-3-one *trans*-5-Methyl-4-hepten-3-one	*cis*-3,4-Dimethyl-3-hexen-2-one *trans*-3,4-Dimethyl-3-hexen-2-one

version of the Na/SiO_2 catalyst was also prepared by co-impregnating the Fuji Q10 silica with a mixture of Na and Pd nitrates to produce a catalyst of the following formulation 0.1 wt% Pd/4 wt% Na/SiO_2. All catalysts were dried overnight at 100 °C after impregnation and calcined at 450 °C for 3 h. A CuO/ZnO hydrogenation catalyst was prepared by co-precipitation and contained 35 wt% CuO.

Catalyst testing

Reaction testing was carried out in a stainless steel fixed bed microreactor system that allowed testing at a range of pressures and organic feed rates. The catalysts were crushed to a particle size of 0.6 to 1 mm before testing. To carry out the experiments the catalysts were brought up to reaction temperature in a flow of carrier gas (H_2 or N_2; 50 ml min^{-1}) before initiating the organic feed. Before commencing testing, the CuO/ZnO hydrogenation catalyst, where used, was reduced in a 10% H_2/N_2 flow at 160 °C over a period of 24 h. The organic feed was controlled using a HPLC pump. Reaction products were analysed off-line using a combination of GC and GC-MS. The analysis was based on the use of internal standards and suitable calibrants. Typically a 98% mass balance was achieved. Catalyst temperature was recorded from a thermocouple in the catalyst bed. Where two beds were in place a thermocouple was inserted into each of the beds. In the single bed experiments with aldehyde a 3 ml bed of catalyst was used. In the dual bed experiment with the aldehyde the two 3 ml beds of catalyst were separated by ~ 10 cm. In the single bed experiments with ketone a 4 ml bed of catalyst was used. In the dual bed experiment with the ketone two 2 ml beds of catalyst were used which were touching. Table 4 summarises the range of experiments carried out on the *n*-butanal and butanone feeds. The experimental error on the activities and selectivities was estimated at ± 5% of the measured value.

Table 4 Condensation reaction of *n*-butanal and butanone

Run	Feed	Catalyst 1st bed	Catalyst 2nd bed	Carrier gas
1	*n*-Butanal	4 wt% Na/SiO_2		H_2
2	*n*-Butanal	0.1 wt% Pd/4 wt% Na/SiO_2		H_2
3	*n*-Butanal	4 wt% Na/SiO_2	CuO/ZnO	H_2
4	Butanone	4 wt% Na/SiO_2		N_2
5	Butanone	4 wt% Cs/SiO_2		N_2
6	Butanone	4 wt% Na/SiO_2	CuO/ZnO	H_2

Results and discussion

Aldehyde reactions

The aldol condensation reaction of *n*-butanal was carried out over the 4 wt% Na/SiO_2 and the 0.1 wt% Pd/ 4 wt% Na/SiO_2 catalysts under near identical conditions (Table 4, runs 1 and 2). The system was run at 7 barg and a *n*-butanal liquid feed of 0.05 ml min^{-1}. At 50 ml min^{-1} hydrogen carrier flow this equates to a contact time of 2.8 s, an inlet reactant to catalyst ratio of 0.019 mol h^{-1} $g_{cat}{}^{-1}$ and an organic partial pressure of 1.59 bar. The start up procedure used would reduce the Pd present in the 0.1 wt% Pd/ 4 wt% Na $/SiO_2$ catalyst to Pd metal. The results are shown in Tables 5 and 6.

Although the 0.1 wt% Pd containing catalyst initially has a higher conversion of *n*-butanal it undergoes a more rapid deactivation than the Na/SiO_2 catalyst (Fig. 8).

The other major difference between the two catalysts is in the product spectrum achieved. The Na/SiO_2 catalyst produces almost exclusively (>99%) the α,β-unsaturated aldehyde despite carrying out the reaction in a hydrogen carrier stream. Less than 0.5% of the *n*-butanal feed was hydrogenated to *n*-butanol. The 0.1 wt% Pd containing catalyst produces a high selectivity towards the saturated aldehyde product 2-ethylhexanal (max 94.9%) with less than 2% of the butanal feed hydrogenated to either *n*-butanol or 2-ethylhexanol.[29] This demonstrates the selective hydrogenation activity that can be achieved with Pd. No lights (C_1, C_2 or C_3 by-products) were produced over either of these catalysts. The reason for the more rapid deactivation of the $Pd/Na/SiO_2$ catalyst are not clear but may be due to catalyst poisoning by the branched saturated aldehyde product itself. The 2-ethylhexanal product has a replaceable proton of a similar acidity to the *n*-butanal feed. The adsorption of the 2-ethylhexanal on to the solid base surface and removal of this proton may form an unreactive intermediate that leads to catalyst deactivation. This theory will require further investigation.

During both runs 1 and 2 the H_2 flow rate was dropped by half after *ca.* 24 h on line. The drop in the H_2 flow rate, and the

Table 5 Reaction of *n*-butanal over Na/SiO_2 catalyst

					Product spectrum		
Time/h	Temp./°C	H_2 flow rate/ ml min^{-1}	Conversion (%)	Selectivity (%)	% 2-Ethylhexenal	% 2-Ethylhexanal	% 2-Ethylhexanol
2	350	42	45	72	99.0	0.5	0.5
4	350	42	58	86	98.4	1.3	0.3
6	350	42	50	89	99.5	0.2	0.3
22	350	42	38	99	99.2	0.6	0.2
30	350	21	40	91	100	0.0	0.0
46	350	21	41	92	99.5	0.5	0.0
53	400	21	43	100	99.8	0.2	0.0
70	400	21	40	89	99.6	0.2	0.2
72	450	21	47	79	99.7	0.3	0.0

Table 6 Reaction of *n*-butanal over Pd/Na/SiO_2 catalyst

					Product spectrum		
Time/h	Temp./°C	H_2 flow rate/ ml min^{-1}	Conversion (%)	Selectivity (%)	% 2-Ethylhexenal	% 2-Ethylhexanal	% 2-Ethylhexanol
4	350	50	82	81	30.2	69.2	0.6
6	350	50	58	92	13.6	86.0	0.4
8	350	50	49	94	7.0	92.5	0.5
24	350	50	42	100	4.5	94.9	0.6
31	350	25	39	96	6.6	92.6	0.8
48	350	25	34	100	10.6	88.6	0.8
55	400	25	40	86	12.2	87.0	0.8
72	400	25	32	92	16.2	83.1	0.7
77	450	25	38	75	25.4	73.9	0.7

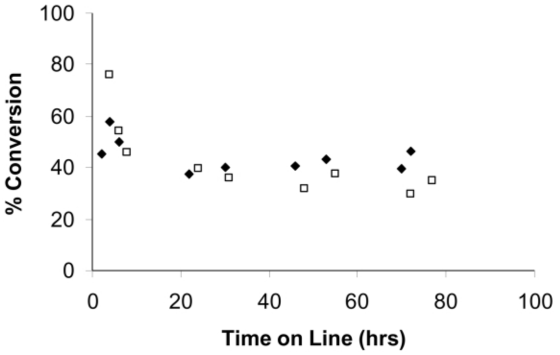


Fig. 8 Reaction on *n*-butanal over 4 wt% Na/SiO_2 catalyst (◆) and 0.1 wt% Pd/4 wt% Na/SiO_2 catalyst (☐).

associated increase in contact time to ~5 s did not appear to give any beneficial advantage in terms of activity or selectivity. Raising the temperature of the catalysts to 400 °C did not give any significant improvement in conversion. Raising the temperature of the catalysts to 450 °C had a marked negative impact on selectivity on both catalysts.

The reactions of *n*-butanal were carried out over dual-bed reactor systems with 4 wt% Na/SiO_2 catalysts followed by a bed of a CuO/ZnO hydrogenation catalyst loaded into a single reaction tube. The reaction is shown in Table 7. The Na/SiO_2 bed was held at 350 °C and the CuO/ZnO bed at 130 °C. The reaction products in this case were only 2-ethylhexanol and *n*-butanol. It can be seen that the proportion of 2-ethylhexanol increases as the pressure increases and as the hydrogen feed is decreased. At a constant hydrogen to butanal ratio, the proportion of 2-ethylhexanol increases as the *n*-butanal feed decreases, *i.e.* as the space velocity decreases.

Ketone reactions

The aldol condensation reaction of butanone was carried out over the 4 wt% Na/SiO_2 and the 4 wt% Cs/SiO_2 catalysts (Table 7, runs 4 and 5) at 5 barg, a butanone liquid feed of 0.05 ml min^{-1} and a nitrogen flow rate of 50 ml min^{-1}. This equates to a contact time of 2.9 s, an inlet reactant to catalyst ratio of 0.019 mol h^{-1} g$_{cat}$$^{-1}$ and an organic partial pressure of 1.20 bar. Run 4 in Table 7 was ran in the temperature range 325–400 °C in the following order 375–400–325–350 °C. Run 5 in Table 7 was ran in the same temperature range but in the following order 350–375–400–325 °C. The catalysts were held for 3-4 h at each temperature before sampling. Fig. 9 reveals how conversion varies with temperature and shows little difference in performance for the Na and Cs based systems with similar conversions over the temperature range 325–375 °C. A drop in performance for the Cs/SiO_2 system was observed at 400 °C. It should be noted that overall the conversions achieved with these base catalysts was much lower for butanone than for *n*-butanal. This is due to the higher pK_a value of the protons on the ketone as compared with the aldehyde (Table 2).

Table 7 Reaction of *n*-butanal over Na/SiO_2 catalyst followed by CuO/ZnO catalyst

Pressure/ barg	H_2 flow rate/ ml min^{-1}	*n*-Butanal flow rate/ml liquid min^{-1}	2-Ethylhexanol/ *n*-butanol (%)	% Conversion of *n*-butanal to aldol products
3	80	0.05	14.9	22.9
5	80	0.05	19.9	28.4
7	80	0.05	23.3	31.7
5	80	0.025	17.3	25.7
5	40	0.025	21.5	30.0
5	100	0.025	9.8	16.3

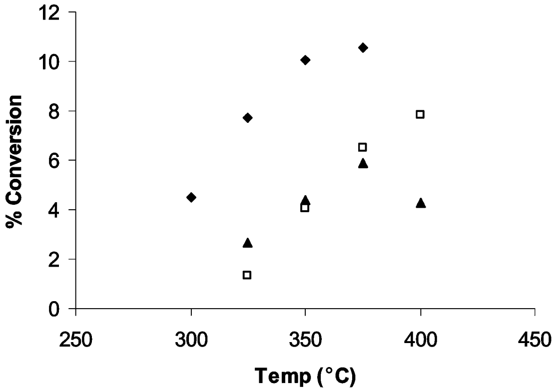


Fig. 9 Aldol condensation of *n*-butanone over 4 wt% Na/SiO_2 (☐), 4 wt% Cs/SiO_2 (▲) and 4 wt% Na/SiO_2 followed by CuO/ZnO catalyst (◆).

The selectivities for the Na and Cs/SiO_2 catalysed reactions are given in Tables 8 and 9. For these experiment the major product was 5-methyl-4-hepten-3-one, with both isomers being formed. This indicates an initial proton abstraction from the terminal methyl group of MEK. Only very low levels of the comparable 3,4-dimethyl-4-hexen-2-one product formed *via* the abstraction of the internal proton were detected. Two major unidentified condensation products with molecular weight of 126 were detected.

The reaction of butanone over a dual bed reactor stream with a 4 wt% Na/SiO_2 catalyst followed by a bed of CuO/ZnO hydrogenation catalyst in a H_2 carrier flow produces essentially two main components; 5-methylheptan-3-one and 5-methylheptan-3-ol (Table 10).

The former is merely the partially hydrogenated form of the latter and therefore both compounds can be regarded as being derived from the kinetically controlled aldol product 5-methyl-4-hepten-3-one (Fig. 10). It can be also inferred from this result that the two unidentified aldol products with molecular weight 126 produced over the Na and Cs/SiO_2 catalysts are *cis*- and *trans*-5-methyl-5-hepten-3-one because subsequent hydrogen-

Table 8 Reaction of butanone over 4 wt% Na/SiO_2

	Selectivity (%)			
Component	325 °C	350 °C	375 °C	400 °C
3,4-Dimethyl-4-hexen-2-one	1.0	1.3	1.5	1.5
5-Methyleneheptan-3-one	2.1	3.1	3.5	3.5
Unknown 1 (126)	10.5	14.1	14.9	12.2
5-Methyl-4-hepten-3-one (a)	15.5	19.2	19.9	19.3
Unknown 2 (126)	14.9	19.7	20.2	18.0
5-Methyl-4-hepten-3-one (b)	24.4	32.0	31.0	33.0
3-Methyl-3-hepten-2-one	4.3	0.9	0.1	0.0
Unknown 3 (126)	8.9	0.6	0.0	0.0
Unknown 4 (180)	0.9	2.8	6.5	10.9
Unknown 5 (180)	7.5	2.3	0.9	0.5
Unknown 6 (180)	9.9	4.0	1.6	1.1

Table 9 Reaction of butanone over 4 wt% Cs/SiO_2

	Selectivity (%)			
Component	325 °C	350 °C	375 °C	400 °C
3,4-Dimethyl-4-hexen-2-one	1.1	1.3	1.4	1.5
5-Methyleneheptan-3-one	2.8	3.1	3.1	3.2
Unknown 1 (126)	12.9	14.2	14.0	14.3
5-Methyl-4-hepten-3-one (a)	18.7	19.4	19.2	19.4
Unknown 2 (126)	18.4	20.3	18.6	18.5
5-Methyl-4-hepten-3-one (b)	30.2	31.5	32.6	31.7
3-Methyl-3-hepten-2-one	2.1	0.0	0.0	0.0
Unknown 3 (126)	1.1	0.0	0.0	0.0
Unknown 4 (180)	4.3	8.9	10.5	11.0
Unknown 5 (180)	3.4	0.6	0.3	0.3
Unknown 6 (180)	5.0	0.7	0.2	0.0

Table 10 Reaction of butanone over 4 wt% Na/SiO_2 followed by CuO/ZnO catalyst

	Selectivity (%)			
Component	300 °C	325 °C	350 °C	375 °C
3,4-Dimethylhexan-2-one	0.4	0.6	0.8	1.0
5-Methylheptan-3-one	16.5	24.4	31.6	44.6
5-Methylheptan-3-ol	80.9	73.4	65.1	54.3
Unknown 1 (126)	0.5	0.5	0.6	0.0
Unknown 2 (126)	0.6	0.6	0.9	0.0
Unknown 3 (126)	1.1	0.5	1.1	0.1

ation of these compounds results in the formation of 5-methylheptan-3-ol. The dual bed reactor system appears to be more active than the base catalysts alone (Fig. 9). To investigate this observation further a blank experiment was run using 4 ml of the CuO/ZnO catalyst. The catalyst was pre-reduced as described above but prior to introduction of the MEK the reactor was purged of hydrogen and the reaction was performed under an inert nitrogen atmosphere. The products showed little evidence of aldol condensation compounds.[31] A reason for the increased activity of the sequential bed remains to be determined.

Conclusions

The viability has been demonstrated for solid fixed-bed basic materials to carry out industrially important aldol condensations. This gives the opportunity to eliminate the use of 30% caustic solution and dramatically reduce the amount of organically contaminated waste caustic produced. The solid base catalysts can be run continuously on-line for hundreds on hours at high conversions and selectivities. The use of solid base catalysts also allows the easier integration of the condensation step with any subsequent hydrogenation steps. By selection of the hydrogenating metal a range of products can be selectively produced. The reaction of an aldehyde over a Na/SiO_2 solid base catalyst produces an α,β-unsaturated aldehyde intermediate. This can be selectively hydrogenated to the saturated aldehyde by the addition of small amounts of Pd to the solid base catalyst or fully hydrogenated to an alcohol over a conventional CuO/ZnO hydrogenation catalyst. With the reaction of butanone there is a high selectivity (max >96%) for reaction at the terminal position of the unsymmetrical ketone.

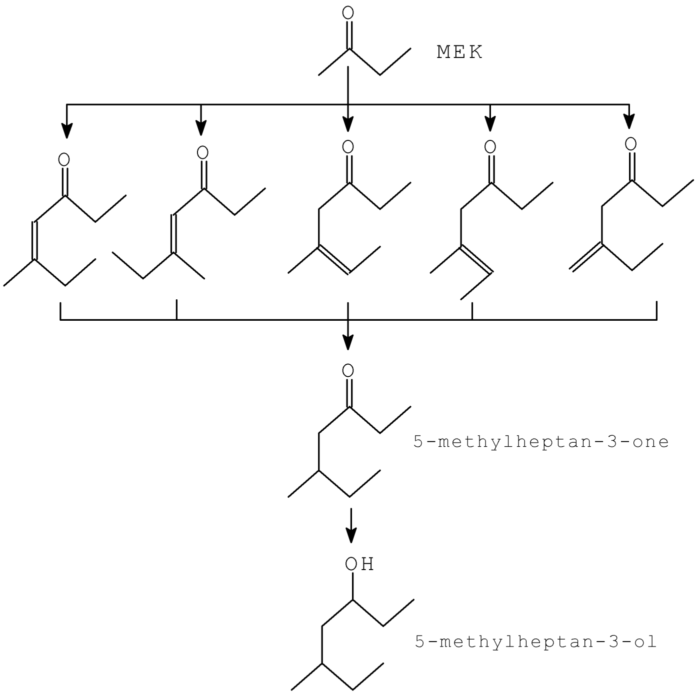


Fig. 10 Butanone condensation/hydrogenation reaction scheme.

The combination of aldol condensation and hydrogenation offers the possibility of the removal of a process step and consequent capital saving.

References

1 K. Weisssermel and H.-J. Arpe, *Industrial Organic Chemistry*, 3rd edn., Wiley, 1997.
2 J. J. Spivey and M. R. Gogate, Research Triangle Institute, US EPA Grant, Pollution Prevention in Industrial Condensation Reactions, 1996.
3 *SRI Reports*, 1978, 1986: OXO Alcohol Process.
4 M. Tomoyuki, O. Yasukazu, F. Koichi, E. Hiroki and T. Akio, *Jpn. Pat.*, 11269118 (May 10, 1999), Mitsubishi Chemical Corp.
5 C. R. Greene, *US Pat*., 3278612, (Oct. 11, 1966), Shell Oil Co.
6 *Kirk-Othmer Encyclopaedia of Chemical Technology*, Wiley, New York, 4th edn., 1991, vol. 1, p. 911.
7 Y. Too and T. Nakayama, *Jpn. Pat*., 62 258,335 (Nov. 10, 1987), Sumitomo Chemical Co., Ltd.
8 T. Maki, T. Yokoyama and Y. Sumino, *Jpn. Pat*., 63 68,538 (Mar. 28, 1988), Mitsubishi Chemical Industries Co., Ltd.
9 T. Maki, T. Yokoyama and Y. Sumino *Jpn. Pat*. 63 96,147 (Apr. 27, 1988), Mitsubishi Chemical Industries Co., Ltd.
10 T. Maki, T. Yokoyama and Y. Sumino, *Jpn. Pat*., 63 68,146 (Apr. 27, 1988), Mitsubishi Chemical Industries Co., Ltd.
11 K. D. Olson, *US. Pat*., 4 704 478 (Nov. 03, 1987), Union Carbide Corp.
12 P. Y. Chen, S. J. Chu, C. C. Chen, N. S. Chang, W. C. Lin and T. K. Chaung, *US. Pat*., 5 059 724 (Oct. 22, 1991), Industrial Technology Research Institute.
13 L. M. Gandia and M. Montes, *Appl. Catal. A: General*, 1993, **101**, L1–L6.
14 L. M. Gandia, R. Malm, R. Marchand, R. Conanec, Y. Laurent and M. Montes, *Appl. Catal. A: General*, 1994, **114**, L1–L7.
15 K. Lin and A. Ko, *Appl. Catal. A: General*, 1996, **147**, L259–L265.
16 S. Narayanan and R. Unnikrishnan, *Appl. Catal. A: General*, 1996, **145**, 231–236.
17 Y. Z. Chen, C. M. Hwang and C. W. Liaw, *Appl. Catal. A: General*, 1998, **169**, 207–214.
18 K. Tanabe, *Solid Acids and Bases*, *Kodansha*, Tokyo and Academic Press, New York, London, 1970.
19 H. Hattori, *Heterogeneous Catalysis and Fine Chemicals III*, Elsevier, Amsterdam,1993.
20 K. Tanabe and W. F. Hoelderich, *Appl. Catal. A: General*, 1999, **181**, 399–434.
21 A. J. Gordon, *The Chemists Companion*, Wiley, New York, 1972.
22 K. Tanabe, *Catalysis by Acids and Bases*, Elsevier Science Publishers B.V., Amsterdam, 1985.
23 J. March, *Advanced Organic Chemistry*, McGraw-Hill, Kogakusha, 2nd edn., 1977.
24 L. P. Hammett, *Physical Organic Chemistry*, McGraw-Hill, New York, 1940.
25 M. A. Paul and F. A. Long, *Chem. Rev*., 1957, **57**, 1.
26 M. J. Climnet, A. Corma, R. Guil-opez, S. Iborra and J. Primo, *Catal. Lett*., 1999, **59**, 33–38.
27 S. D. Jackson, D. W. Johnson, J. D. Scott, G. J. Kelly and P. B. Williams, *World Pat. Appl.*, WO 99/52628, Oct. 1999.
28 V. Ponec, *Appl. Catal. A: General*, 1997, **149**, 27–48.
29 G. J. Kelly, *World Pat. Appl.*, WO 00/31011, June 2000.
30 J. March, *Advanced Organic Chemistry*, McGraw-Hill, Kogakusha, 2nd edn., 1977, p. 694.
31 G. J. Kelly, *World Pat. Appl.*, WO 01/87812, Nov 2001.

1-*n*-Butyl-3-methylimidazolium ([bmim]) octylsulfate—an even 'greener' ionic liquid

Peter Wasserscheid,* Roy van Hal and Andreas Bösmann

Institut für Technische Chemie und Makromolekulare Chemie der RWTH Aachen, Worringer Weg 1, D-52074 Aachen, Germany. E-mail: Wasserscheid@itmc.rwth-aachen.de

Received 5th June 2002
First published as an Advance Article on the web 18th July 2002

Ionic liquids are considered as green solvents mainly due to their lack of vapour pressure. In fact, environmental and safety problems arising through the volatility of organic solvents can be avoided by the use of these innovative liquids. However, typical ionic liquids consist of halogen containing anions (such as $[AlCl_4]^-$, $[PF_6]^-$, $[BF_4]^-$, $[CF_3SO_3]^-$ or $[(CF_3SO_2)_2N]^-$) which in some regard limit their 'greenness'. The presence of halogen atoms may cause serious concerns if the hydrolysis stability of the anion is poor (*e.g.* for $[AlCl_4]^-$ and $[PF_6]^-$) or if a thermal treatment of spent ionic liquids is desired. In both cases additional effort is needed to avoid the liberation of toxic and corrosive HF or HCl into the environment. In this context, we present here the synthesis and application of 1-*n*-butyl-3-methylimidazolium ([bmim]) [n-$C_8H_{17}OSO_3$] which represents a halogen-free and relatively hydrolysis-stable ionic liquid. Moreover, the technical availability and the well documented toxicology of the octylsulfate anion make this ionic liquid a highly interesting candidate for industrial application.

Introduction

Ionic liquids (ILs) are low melting (< 100 °C) salts which represent a new class of non-molecular, ionic solvents.[1] In the past years the range of known and available ILs has been expanded so that many different candidates are accessible and even commercially available today.[2] Typically, the ionic liquid systems used in the literature consist of halogen containing anions such as $[AlCl_4]^-$, $[PF_6]^-$, $[BF_4]^-$, $[CF_3SO_3]^-$ or $[(CF_3SO_2)_2N]^-$ which are usually combined with imidazolium or pyridinium cations to form the ionic liquid.

For good reasons, these ionic liquids are often discussed as 'green solvents'. In contrast to volatile organic solvents and extraction media, they have no measurable vapour pressure. Therefore there is no loss of solvent through evaporation. Environmental and safety problems arising through the use of volatile organic solvents can be avoided. For catalytic applications, where a transition metal catalyst is dissolved in the ionic liquid, two additional aspects are of interest. Firstly, the special solubility characteristics of an ionic reaction medium enables a biphasic reaction procedure in many cases. Exploitation of the miscibility gap between the ionic catalyst phase and the products allows, in this case, the catalyst to be isolated effectively from the product and reused many times. Secondly, the non-volatile nature of ionic liquids enables a more effective product isolation by distillation. Again, the possibility arises to reuse the isolated ionic catalyst phase. In both cases, the total reactivity of the applied catalysts is increased and catalyst consumption relative to the generated product is reduced. For example, all these advantages have been convincingly demonstrated for transition metal catalysed hydroformylation.[3]

As mentioned above, almost all ionic liquids described currently in the literature for catalytic and other solvent applications contain halogen atoms such as Cl or F. However, with regard to the environmental impact of technical processes using these ionic liquids, their presence may cause—under certain conditions—serious concerns. This would be explicitly the case for the relatively hydrolysis labile anions $[AlCl_4]^-$ and $[PF_6]^-$ if water is present. In this case, significant amounts of HCl (or HF) would be liberated under reaction conditions. However, this would be the case as well for the potential disposal of technical amounts of spent ionic liquid by thermal treatment. In both cases additional efforts and costs have to be considered to avoid the liberation of toxic and corrosive HF or HCl into the environment. The aspect of ionic liquid disposal gets even more important since disposal alternatives such as the treatment of spent ionic liquid in biological waste water treatment is equally effected by the presence of halogen atoms in the ionic liquid.

Bearing these aspects in mind, we decided to look for new, even 'greener' ionic liquids for industrial catalytic applications, which should meet the following, technically desired combination of properties: (a) melting point or glass point below 40 °C; (b) hydrolysis stable in neutral aqueous solution up to 80 °C; (c) temperature of thermal decomposition above 250 °C; (d) possible disposal by combustion without formation of HF or HCl; (e) possible biodegradation of the used anion in ordinary waste water treatment; (f) synthesis from cheap, technical available raw materials *e.g.* alkali-metal salts.

A number of halogen-free ionic liquids are known from the literature. However, none of these systems fulfil all the above

Green Context

The replacement of volatile organic compounds as solvents for organic reactions is one of the most important areas of green chemistry. It is very important that in developing alternatives we do not create a new problem by shifting the environmental burden to another stage in the process or product life cycle. Ionic liquids are subject to an enormous research effort due to their involatility and interesting solvent properties, but they do have 'hidden' problems including the hydrolytic instability of halogen-containing anions, which can lead to halide waste. Here we see a new halogen-free ionic liquid. The octylsulfate anion is cheap and widely available and has a well-documented toxicology. The article also shows that the new substance is a very promising solvent for some transition metal catalysts. *JHC*

DOI: 10.1039/b205425f

mentioned, complex combination of properties. Ionic liquids with nitrate,[4] nitrite,[4] sulfate,[4] benzenesulfonate[5] and toluenesulfonate[6] anions have been described but their reported melting points are usually higher than 40 °C. Hydrogensulfate and hydrogenphosphate ionic liquids lose their protons in aqueous solution to form acidic solutions.[7] Ionic liquids with methylsulfate and ethylsulfate anions show significant hydrolysis in aqueous solution at 80 °C. Hydrogensulfate is formed together with the corresponding alcohol.[8]

In this paper we present in detail the synthesis and some important physico-chemical properties of the ionic liquid 1-butyl-3-methylimidazolium ([bmim]) [n-$C_8H_{17}OSO_3$]. We demonstrate that [bmim][n-$C_8H_{17}OSO_3$] is a first ionic liquid candidate that fulfills the above mentioned, complex combination of technical criteria in a promising manner. Moreover, a first example for the successful application of this new ionic liquid will be presented, namely its use as catalyst solvent in the Rh-catalysed hydroformylation of 1-octene.

Results and discussion

Ionic liquid quality

It is well known that impurities in an ionic liquid can have large effects on the physico-chemical properties of the material under investigation.[9] In the case of [bmim][n-$C_8H_{17}OSO_3$] the following potential sources for impurities were identified: (a) organic volatiles (*e.g.* traces of methylimidazole from the synthesis of the chloride salt); (b) halide impurities from incomplete metathesis reaction; (c) other ionic impurities resulting from the Na[n-$C_8H_{17}OSO_3$] that was applied in technical grade or from some solubility of Na[n-$C_8H_{17}OSO_3$] in the ionic liquid product; (d) water.

In order to obtain reliable data for physico-chemical properties of [bmim][n-$C_8H_{17}OSO_3$] we took maximum care to either eliminate the impurities completely during synthesis (in case of impurities a–c) or to investigate a material with a clearly defined amount of the impurity (in case of water).

To achieve this we checked for volatile impurities (*e.g.* methylimidazole) in the [bmim]Cl prior to its application in synthesis *e.g.* using the method described earlier by Holbrey, Seddon and Wareing.[10] The amount of chloride in the final product was checked by titration with $AgNO_3$ from an acidic aqueous solution ([bmim][n-$C_8H_{17}OSO_3$] is water soluble). Using the synthetic method described in detail in the Experimental section, [bmim][n-$C_8H_{17}OSO_3$] could be easily obtained in a chloride-free quality. This is not only important for the determination of physico-chemical data but also crucial for the application of the material in hydroformylation catalysis.

Apart from chloride impurities, it is important to consider that the synthesis of [bmim][n-$C_8H_{17}OSO_3$] from technical grade [bmim]Cl and Na[n-$C_8H_{17}OSO_3$] may also result in contamination of the final products with other ionic impurities. Two main sources of such contamination have to be considered here in particular, namely the fact that Na[n-$C_8H_{17}OSO_3$] shows significant solubility in [bmim][n-$C_8H_{17}OSO_3$] and the fact that the applied technical grade Na[n-$C_8H_{17}OSO_3$] contains inorganic salts (mainly Na_2SO_4) in considerable amounts.

While ionic impurities such as Na^+ or SO_4^{2-} may not be a problem for some catalytic applications of the ionic liquid (such as *e.g.* Rh-catalysed hydroformylation) it is of great relevance for the determination of physico-chemical properties of the melt.

Fortunately, [bmim][n-$C_8H_{17}OSO_3$] shows highly preferential solubility in methylene chloride in a water/CH_2Cl_2 mixture and all relevant ionic impurities are highly water soluble. Therefore, these can be efficiently eliminated from the product by careful washing of a product solution in CH_2Cl_2 with water. After this procedure CH_2Cl_2 is removed from the product, collected and can be reused for further purification steps.

Concerning the amount of water in [bmim][n-$C_8H_{17}OSO_3$] we found it very difficult to reduce the latter in large samples to less than 200 ppm by evaporation at 80 °C under high vacuum (10^{-3} bar). This reflects the highly hygroscopic nature of 'dry' [bmim][n-$C_8H_{17}OSO_3$] and gives rise to the question whether anybody would really use such an ionic liquid under absolute dry conditions. Therefore, we decided to determine our set of physico-chemical data for [bmim][n-$C_8H_{17}OSO_3$] not in absolute "dry" form but with an ionic liquid material of defined, low water content.

We found that the water content in [bmim][n-$C_8H_{17}OSO_3$] can be adjusted quite reproducibly to 1000 ± 100 ppm (0.1 ± 0.01 mass%) after a defined drying procedure of the material [80 °C; 3 h, high vacuum (10^{-3} bar)]. This water content was checked by coulometric Karl–Fischer titration prior to the measurements and the catalytic experiments.

Thermal properties

At room temperature [bmim][n-$C_8H_{17}OSO_3$] is often obtained as a sub-cooled melt which slowly crystallises at temperatures below 5 °C. The melting point of crystalline [bmim][n-$C_8H_{17}OSO_3$] was determined by DSC to be 34–35 °C. The heat of fusion was found to be 12.7 ± 0.5 kJ mol^{-1}. Furthermore the thermal decomposition point was determined by TGA to be 341 °C.

Viscosity and density

In our viscosity measurements, [bmim][n-$C_8H_{17}OSO_3$] showed no deviation from Newtonian behaviour in the investigated temperature range. The viscosity data have been determined for the sub-cooled liquid below the melting point as well as for the ionic liquid above its melting point in a temperature range between 20 and 100 °C. (Table 1, Fig. 1).

To compare the viscosity of [bmim][n-$C_8H_{17}OSO_3$] to other known solvent systems it may be of interest to note that [bmim][n-$C_8H_{17}OSO_3$] at about 45 °C reaches the viscosity of [bmim][PF_6] at room temperature [$\eta_{25\,°C}$([bmim][PF_6]) = 207 cP according to a paper by Bright and coworkers[11]] and at 100

Table 1 Absolute viscosity of [bmim][n-$C_8H_{17}OSO_3$] at different temperatures (mPa s = cP)

T/°C	20	30	40	50	60	70	80	90	100
η/mPa s	874.5	447.9	262.3	152.3	97.7	64.2	45.9	30.7	23.3

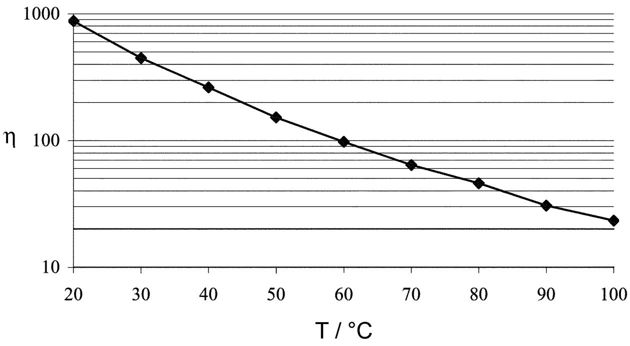


Fig. 1 Absolute viscosity of [bmim][n-$C_8H_{17}OSO_3$] at different temperatures (mPa s = cP).

°C is close to the room temperature viscosity of ethanediol [$\eta_{25\,^\circ C}$(ethanediol) = 16.1 cP according to ref. 12].

The density of [bmim][n-$C_8H_{17}OSO_3$] was determined to be ρ = 1.0601 g cm^{-3} at 25 °C.

Hydrolysis stability

The lower homologues of alkylsulfate anions, namely methanesulfate and ethanesulfate, are known for their sensitivity towards hydrolysis. In the presence of water these anions form the corresponding alcohol and hydrogensulfate at elevated temperatures. Obviously, this process is undesired for most applications since the ionic liquid system changes dramatically in its properties and an acidic proton is formed that may be a reactive species in many applications.

For alkylsulfates with longer alkyl groups the sensitivity towards hydrolysis is much lower. This becomes very obvious taking into account that alkylsulfates with 8–18 carbon atoms are used on a multi-million ton scale in detergents, cosmetics and in many other applications where water is omnipresent.

To confirm the expected hydrolysis stability of [bmim][n-$C_8H_{17}OSO_3$], we stirred the ionic liquids with the same mass of water at 80 °C for several hours, and took samples in regular intervals. The pH-values of the aqueous samples were recorded to monitor the extent of hydrolysis of the ionic liquid. While [bmim][$MeOSO_3$] and [emim][$EtOSO_3$] showed quick hydrolysis under the conditions of this experiment (within the first 30 min), no decrease of pH-value was determined for [bmim][n-$C_8H_{17}OSO_3$] during 8 h.

Rh-catalyzed hydroformylation of 1-octene using [bmim][n-$C_8H_{17}OSO_3$] as solvent

Biphasic catalysis is a well-established method for effective catalyst separation and recycling in Rh-catalyzed hydroformylation. This principle has been technically realised in the Ruhrchemie–Rhône–Poulenc-process, where water is used as the catalyst phase.[13–15] Unfortunately, this process is limited to C_2–C_5-olefins due to the low water solubility of higher olefins (1-octene solubility in water is only in the range of 0.0001 mol% at 25 °C[15]). Nevertheless, the hydroformylation of *e.g.* 1-octene is of technical interest for the synthesis of nonanals. The latter are used *e.g.* as intermediates for the production of plasticiser alcohols. In Fig. 2, general aspects of the 1-octene hydroformylation are summarised.

Already in 1995, Chauvin *et al.* described the first Rh-catalyzed biphasic hydroformylation using room-temperature liquid ionic liquids.[3a,b] The group investigated in detail the hydroformylation of 1-pentene with [$Rh(CO)_2(acac)$]/triarylphosphine in *e.g.* [bmim][PF_6].

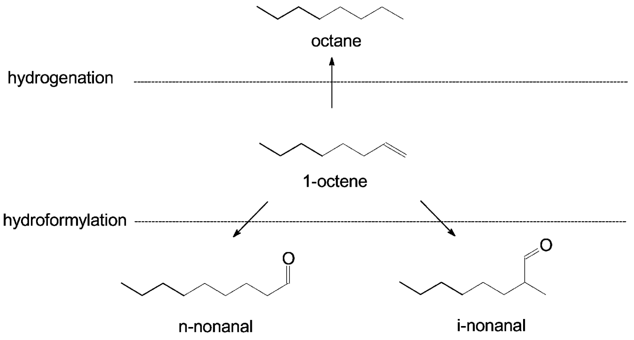
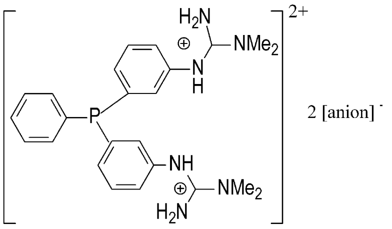


Fig. 2 Hydroformylation of 1-octene.

Since the use of a simple triarylphosphine resulted in significant leaching of the Rh-catalyst into the product layer, most research efforts in the following years were dedicated to improve the immobilisation of phosphine ligands in the ionic liquids *e.g.* by using ionic phosphine ligands with cobaltocenium,[3d] guanidinium,[3e,f] or imidazolium and pyridinium[3f,g] groups.

While all this research was carried out using halogen-containing ionic liquids (mostly hexafluorphosphate ionic liquids), Andersen and coworkers published a communication in 1998 describing the use of some phosphonium tosylates in the rhodium catalyzed hydroformylation of 1-hexene.[6] However, all ionic liquids described in this publication melt at temperatures > 70 °C which causes serious limitations for a continuous processing of the biphasic reaction with these systems.

From all this it appeared highly interesting to us to test [bmim][n-$C_8H_{17}OSO_3$] as solvent for the Rh-catalysed hydroformylation of 1-octene. For the catalyst system we used an $Rh(CO)_2(acac)$ precursor in combination with the earlier described[3e] phenylguadinium modified triphenylphosphine ligand precursor **1**. Under reaction conditions the anion attached to the ligand precursor **1** is readily exchanged by the anion of the ionic liquid.



1

The results of the hydroformylation experiments are given in Table 2. Surprisingly, we found that at room temperature [bmim][n-$C_8H_{17}OSO_3$] does show a miscibility gap with 1-octene but does not form a biphasic system any more with the hydroformylation products. Consequently, the reaction mixture becomes monophasic during reaction when 1-octene conversion is high. Therefore an additional experiment with added cyclohexane as extraction solvent was carried out (entry b, Table 2). With cyclohexane being used as additional extraction solvent, the biphasic reaction system was maintained even at very high 1-octene conversion, and the ionic catalyst solution could be easily separated from the colourless product layer by simple decantation.

For all examples displayed in Table 2 the ratio between linear and branched hydroformylation products was found in the range between 2 and 3 which is the expected value for triphenylphosphine derived ligands in Rh-catalyzed hydroformylation under the applied conditions. It is however somewhat unexpected and very interesting, that the activity of the Rh-catalyst is significantly higher with [bmim][n-$C_8H_{17}OSO_3$] when compared with the commonly used hexafluorophosphate and tetrafluoroborate ionic liquids with the same cation (comparison examples c and d in Table 2). This observation is explained by the higher 1-octene solubility in [bmim][n-$C_8H_{17}OSO_3$] in comparison to the corresponding hexafluorophosphate and tetrafluoroborate ionic liquids.

Thus our preliminary studies demonstrate that [bmim][n-$C_8H_{17}OSO_3$] is a very interesting solvent for Rh-catalyzed hydroformylation. Taking into account the much lower cost of the ionic liquid, the better hydrolysis stability and the wider disposal options related to the octylsulfate ionic liquid in comparison to [bmim][PF_6] or [bmim][BF_4], there is no real reason to centre future hydroformylation research around hexafluorophosphate and tetrafluoroborate ionic liquids.

Table 2 Comparison of results in the hydroformylation of 1-octene using different ionic liquid systems

Entry	Solvent	Reaction	TOF[a]/h^{-1}	$n:i$-Ratio[b]
a	[bmim][n-$C_8H_{17}OSO_3$]	Monophasic	892	2.9
b	[bmim][n-$C_8H_{17}OSO_3$] + cyclohexane	Biphasic	862	2.5
c	[bmim][PF_6]	Biphasic	276	2.0
d	[bmim][BF_4]	Biphasic	317	2.6

[a] Turnover frequency (TOF) in mol of 1-octene converted per mol of Rh per h. [b] Ratio of linear to branched aldehyde products; *general conditions*: 1-octene/Rh *ca*. 1000; CO/H_2 = 1; $p(CO/H_2)$ = 28 bar; T = 100 °C; L/Rh = 2; Rh-precursor: $Rh(CO)_2(acac)$; ligand precursor **1** ([anion] = [PF_6]$^-$); t = 1 h.

From all our results so far we conclude that [bmim][n-$C_8H_{17}OSO_3$] shows great promise to be applied as an ‘even greener’ ionic liquid in a whole range of applications. Due to the fact that its anion source Na[n-$C_8H_{17}OSO_3$] is a very cheap bulk chemical which is used in multi-thousand ton scale as an ingredient in detergents and cosmetics, this new ionic liquid is clearly characterised by its high technical availability (at relatively low cost) and by its well documented toxicology and biodegradation (at least for the anion part). This makes [bmim][n-$C_8H_{17}OSO_3$] a particularly interesting candidate for expected future, industrial, bulk applications of ionic liquids (*e.g.* as high performance lubricant, thermofluid, solvent for extraction and extractive distillation *etc.*). Moreover, our results demonstrate that [bmim][n-$C_8H_{17}OSO_3$] is even a highly promising solvent for transition metal catalysis if the electrophilicity of the catalytic centre is moderate.

Experimental

Synthesis of [bmim][n-$C_8H_{17}OSO_3$]

84.55 g (0.484 mol) 1-butyl-3-methylimidazolium chloride ([bmim]Cl, commercial grade > 98% purity from Solvent Innovation GmbH, Cologne/Germany[16]) and 101.1 g (≥0.379 mol) Na[n-$C_8H_{17}O$-SO_3] (commercial grade; ≥87% purity from Cognis, Düsseldorf/Germany,[17] main impurities are inorganic water soluble salts *e.g.* Na_2SO_4) were dissolved in 200 ml hot water (60 °C). The water was slowly removed under vacuum and a white solid precipitated. 200 ml CH_2Cl_2 was added to extract the product from the mixture and the white solid filtered off. The clear, slightly yellow filtrate was washed several times with 30 ml water, up to the point where the washing water was chloride-free (test with $AgNO_3$ from acidic solution). The solvent was removed under vacuum. 111.0 g (0.319 mmol) of the chloride-free product was obtained in form of a slightly yellow oil which corresponds to 73% of the theoretical yield. The oil slowly crystallised in the fridge at 4 °C.

NMR spectrum of [bmim][n-$C_8H_{17}OSO_3$] recorded on a Bruker DPX-300 FT-spectrometer:^{1}H NMR (300 MHz, d_6-DMSO): δ 9.16 (s, 1H, NCHN), 7.80, 7.72 (two s, 2 × 1H, NCH), 4.18 (t, J = 7.1 Hz, 2H, NCH_2), 3.86 (s, 3H, NCH_3), 3.71 (t, J = 6.6 Hz, 2H, $SOCH_2$), 3.71 (qnt, J = 7.3 Hz, 2H, NCH_2CH_2), 1.47 (m, 2H, $NCH_2CH_2CH_2$), 1.22 (m, 12H, $SOCH_2(CH_2)_6$), 0.81–0.90 (two t, 2 × 3H, CH_3).

^{13}C NMR (75 MHz, d_6-DMSO): δ 136.9, 123.9, 122.6, 66.0, 55.2, 48.8, 36.0, 31.8, 31.6, 29.4, 29.1, 25.9, 22.4, 19.1, 14.2, 13.5.

Determination of water content

After synthesis the ionic liquid was dried under high vacuum (10^{-3} bar) at 80 °C for 3 h. The water content was determined by coulometric Karl–Fischer titration using a Metrohm 756 KF Coulometer with a Hydranal® Coulomat AG reagent.

Thermal properties

The decomposition temperature was determined by thermogravimetry using a Netzsch STA 409 C instrument. The determined decomposition temperature corresponds to the minimum in the differential thermogravimetrical curve.

Melting point and heat of fusion were determined using a DSC 204/1/G instrument from Netzsch. Samples were first cooled to −60 °C (10 K min^{-1}), then heated to 150 °C (5 K min^{-1}). The determined melting point corresponds to the onset temperature of the heating curve.

Viscosity

Viscosities were measured on a RS 100 viscometer by Haake. Temperature control was maintained by an external thermostat. Viscosity measurements were always carried out with samples of defined water content (1000 ± 100 ppm) that was determined directly prior to the measurement by coulometric Karl–Fischer titration.

Density

Density was measured in a 10 ml pyknometer.

Hydrolysis stability

Mixtures of 5 g of ionic liquid and 5 g of water were heated to 80 °C. Samples were taken at 15 min intervals and the pH-value of the solution was checked with a pH-indicator from Macherey & Nagel.

Rh-catalyzed hydroformylation of 1-octene

Hydroformylation experiments were carried out in a 75 ml stainless steel autoclave equipped with a magnetic stirring bar, a burst disc, a manometer, a side-outlet and a 20 ml dropping funnel with pressure equalisation. The catalyst-precursor $Rh(acac)(CO)_2$ and the ligand were weighed in a Schlenk-tube, purged with argon for several minutes and dissolved in 5 ml of ionic liquid with stirring and gentle heating. The ionic catalyst solution was transferred to the autoclave *via* canula. 1-Octene (Rh/1-octene = 1:1000) and dibutyl ether (as internal standard) were filled in the dropping funnel. After briefly flushing with syngas (CO/H_2 = 1:1) the autoclave was pressurised and stirred at reaction temperature for 30 min to ensure catalyst preformation. The reaction was started by opening the valve of the dropping funnel. Defined reaction times were obtained by quickly cooling the autoclave to room temperature in an ice/water bath after the reaction time was over. After deflating in the fume hood, the autoclave was opened and the contents were analysed by gas chromatography.

Acknowledgements

We wish to thank Solvent Innovation GmbH, Cologne[16] for the donation of [bmim]Cl and Cognis, Düsseldorf/Germany[17] for donation of Na[n-$C_8H_{17}OSO_3$].

References

1 (*a*) H. Olivier-Bourbigou and L. Magna, *J. Mol. Catal. A: Chemical*, 2002, **182–183**, 419; (*b*) R. Sheldon, *Chem. Commun.*, 2001, 2399; (*c*) C. M. Gordon, *Appl. Catal. A: General*, 2001, **222**, 101; (*d*) P. Wasserscheid and W. Keim, *Angew. Chem.*, 2000, **112**, 3926; P. Wasserscheid and W. Keim, *Angew. Chem., Int. Ed.*, 2000, **39**, 3772; (*e*) T. Welton, *Chem. Rev.*, 1999, **99**, 2071; (*f*) J. D. Holbrey and K. R. Seddon, *Clean Prod. Processes*, 1999, **1**, 223.

2 A list of actual commercial suppliers of tetrafluoroborate and hexafluorophosphate salts includes (with no garantee for completeness): Solvent Innovation GmbH, Köln (www.solvent-innovation.com), Sachem Inc. (www.sacheminc.com); Fluka (www.fluka.com), Acros Organics (www. acros.com), Wako (www.wako.com).

3 (*a*) Y. Chauvin, L. Mussmann and H. Olivier, *Eur. Pat.*, EP 776880 (to IFP), 1997; (*b*) Y. Chauvin, L. Mußmann and H. Olivier, *Angew. Chem.*, 1995, **107**, 2941; Y. Chauvin, L. Mußmann and H. Olivier, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2698; (*c*) W. Keim, D. Vogt, H. Waffenschmidt and P. Wasserscheid, *J. Catal.*, 1999, **186**, 481; (*d*) C. C. Brasse, U. Englert, A. Salzer, H. Waffenschmidt and P. Wasserscheid, *Organometallics*, 2000, **19**, 3818; (*e*) P. Wasserscheid, H. Waffenschmidt, P. Machnitzki, K. W. Kottsieper and O. Stelzer, *Chem. Commun.*, 2001, 451; (*f*) F. Favre, H. Olivier-Bourbigou, D. Commereuc and L. Saussine, *Chem. Commun.*, 2001, 1360; (*g*) D. J. Brauer, K. W. Kottsieper, C. Liek, O. Stelzer, H. Waffenschmidt and P. Wasserscheid, *J. Organomet. Chem.*, 2001, **630**, 177.

4 J. S. Wilkes and M. J. Zaworotko, *J. Chem. Soc., Chem. Commun.*, 1992, 965.

5 H. Waffenschmidt, *PhD Thesis*, RWTH Aachen, 2000.

6 N. Karodia, S. Guise, C. Newlands and J.-A. Andersen, *Chem. Commun.*, 1998, 2341.

7 W. Keim, W. Korth, and P. Wasserscheid, *World Pat.*, WO 0016902 (to BP Chemicals Limited, UK; Akzo Nobel NV; Elementis UK Limited), 2000.

8 P. Wasserscheid, A. Bösmann and R. van Hal, unpublished results.

9 K. R. Seddon, A. Stark and M.-J. Torres, *Pure Appl. Chem.*, 2000, **72**, 2275.

10 J. D. Holbrey, K. R. Seddon and R. Wareing, *Green Chem.*, 2001, **3**, 33.

11 S. N. Baker, G. A. Baker, M. A. Kane and F. V. Bright, *J. Phys. Chem. B*, 2001, **105**, 9663.

12 *Handbook of Chemistry and Physics*, ed. D. R. Linde, CRC Press, New York, 82nd edn., 2001, pp. 6–182.

13 E. G. Kuntz, *Fr. Pat.*, 2314910, 1975, to Rhone-Poulenc.

14 E. G. Kuntz, *CHEMTECH*, 1987, 570.

15 B. Cornils and W. A. Herrmann, *Aqueous-Phase Organometallic Catalysis*, Wiley-VCH, Weinheim, 1998.

16 Solvent Innovation GmbH, Cologne; http:\\www.solvent-innovation.com.

17 Cognis Deutschland GmbH & Co. KG, Düsseldorf/Germany; http:\\www.cognis.com.