Green chemistry: challenges and opportunities

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Summary

The green chemistry revolution is providing an enormous number of challenges to those who practice chemistry in industry, education and research. With these challenges however, there are an equal number of opportunities to discover and apply new chemistry, to improve the economics of chemical manufacturing and to enhance the much-tarnished image of chemistry. In this article which is based on his Inaugural Lecture at the University of York in 1998, Professor Clark reviews some of the challenges, considers some of the new and successful "greener" chemistry in practice and uses two areas of chemistry to examine the scale and diversity of current problems and the exciting opportunities for innovative chemistry research and application.

James Clark obtained his BSc and PhD degrees from Kings College, London. After postdoctoral positions in Canada and Exeter he moved to York in 1979. He is currently Professor of Industrial and Applied Chemistry and the Royal Academy of Engineering–EPSRC Clean Technology Fellow in Heterogeneous Catalysis. His research interests cover various aspects of Green Chemistry including clean synthesis and new materials. He was recently appointed as the first director of the RSC Green Chemistry Network.

The challenges to chemists[1]

Sustainable development is now accepted by governments, industry and the public as a necessary goal for achieving societal, economic and environmental objectives. Within this, chemistry has a key role to play in maintaining and improving our quality of life, the competitiveness of the chemical industry and the natural environment. This role for chemistry is not generally recognized by government or the public. In fact chemicals, chemistry and chemists are actually seen by many as causes of the problems.

The European Chemical Industry Council (CEFIC) survey in 1994 showed that 60% of the general public had an unfavourable view of the chemical industry and in the USA, a survey carried out for the Chemical Manufacturers Association (CMA) in 1993 showed that only 26% were favourably disposed towards the industry. The pharmaceutical and plastics sectors scored better than the chemical industry as a whole, possibly because the general public are more aware of their products and their benefits. The chemical industry is consistently regarded less favourably than the petroleum, gas, electricity, lumber and paper industries. The main reasons given for unfavourable opinions of the chemical industry are concerns over adverse environmental impact, transport, safety and waste. Less than one third of those interviewed believed that the chemical industry is concerned about protecting the environment and less than one half believed that the chemical industry is working hard to develop techniques to solve environmental problems.

The negative public opinions of the chemical industry can in some ways be contrasted with the tremendous economic success of the industry. It is one of the most successful and diverse sectors of manufacturing industry in many regions of the world. The range of chemical products is enormous and these products make

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Green Context

This review of Green Chemistry has been written by James Clark whose contribution to the development of the subject in the UK has been recognised in numerous ways; for example he was awarded the SCI Environment Medal and holds a Royal Academy of Engineering/ Engineering and Physical Sciences Research Council Clean Technology Fellowship. It is an authoritative paper reviewing the challenges facing the chemical industry, providing examples of significant advances in manufacturing routes to a number of products as well as drawing attention to the importance of education. In short it explains what green chemistry is all about.

Timothy Lester, Deft Technology and Design.

an invaluable contribution to the quality of our lives with manufacturing plants having capacities ranging from a few tonnes per year in the fine chemicals area to 500,000 tonnes per year in the petrochemicals area. However, these manufacturing processes also lead to millions of tonnes of waste, and the reduction or elimination of this waste is now a central issue for the industry, the authorities, and the general public. There is a danger that if the economic success of the industry is not matched by a clearly perceived improvement in environmental performance then, at best, the industry will be regarded by the general public as a necessary evil.

The challenge for chemists and others is to develop new products, processes and services that achieve the societal, economic and environmental benefits that are now required. This requires a new approach which sets out to reduce the materials and energy intensity of chemical processes and products, minimise or eliminate the dispersion of harmful chemicals in the environment, maximise the use of renewable resources and extend the durability and recyclability of products—in a way which increases industrial competitiveness.

Some of the challenges for chemists include the discovery and development of new synthetic pathways using alternative feedstocks or more selective chemistry, identifying alternative reaction conditions and solvents for improved selectivity and energy minimisation and designing less toxic and inherently safer chemicals. In chemical synthesis, the ideal will be a combination of a number of environmental, health and safety, and economic targets (Fig. 1).
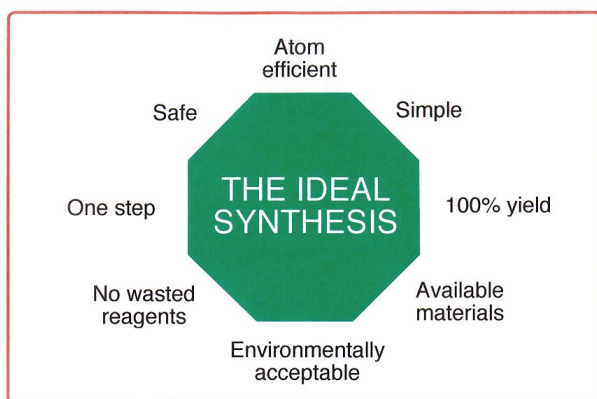

Fig. 1   The ideal synthesis.

Although many chemists, and some large and smaller companies, are actively pursuing 'green chemistry' there are still many barriers to progress. These include a general lack of awareness and training in schools, universities and industry and a management perception that green chemistry is a cost without benefits.

The drive towards clean technology in the chemical industry with an increasing emphasis on the reduction of waste at source will require a level of innovation and new technology that the chemical industry has not seen in many years. Mature chemical processes, that are often based on technology developed in the first half of the 20th century, may no longer be acceptable in these environmentally conscious days. 'Enviro-economics' will become the driving force for new products and processes. This can be seen by considering the ever-escalating and various 'costs of waste' (Fig. 2).

The costs of waste can truly be enormous. It has been estimated that compliance with existing environmental laws will cost new EU member states $130 billion. In the US, $115 billion was spent in 1992 on waste treatment and disposal. New European legislation and tighter national laws will make matters worse.

Industry and academe are now reacting to these challenges and many are seeing the opportunities—be they in winning research funding, unprecedented opportunities for translating new, greener chemistries from the research bench to the production plant or in gaining commercial advantage from the application of new low-waste processes or the marketing of new environmentally friendly products or technologies. The rapidly growing interest in green chemistry is partly witnessed by the growth in relevant conferences with regular events now being held in the USA, Europe and Asia. The Gordon Green Chemistry conferences (held alternately in the USA and Europe since 1995) along with other recent international meetings are good examples of effective meetings of industrial, academic and governmental chemists and engineers with a variety of backgrounds, interests and areas of expertise but with the common goal of seeing the application of green chemistry throughout the chemical and allied industries.[2]

Additionally, the emergence of Green Chemistry organisations in the USA, Italy and the UK are indications of the growing interest in the concept and the recognition of the value of networking such diverse activities. It is particularly significant to note that many of these organisations place education as high on their agenda as research—the long term future of the subject and indeed of the industry will depend on future generations. In the US, a particularly important and strategic development was the emergence of the Presidential Green Chemistry Challenge awards. These have had numerous benefits, not least the open disclosure of many new and exciting products and processes that will be of real benefit to the environment and to the image of chemistry.

Green chemistry in practice

Through the US Presidential Green Chemistry Challenge awards, other promotional initiatives and a general increase in public awareness, an increasing number of headlines have drawn attention to scientific and commercial breakthroughs in reducing the environmental impact of chemical products and processes. These include: new marine antifoulant to replace tributyltin oxide (Rohm and Haas); environmentally friendly high solid coating reduces VOCs (Bayer); new route to a steroidal intermediate involving catalytic oxidation with no heavy metal waste (Pharmacia and Upjohn); new microemulsion based solvent for industrial cleaning (Dow); full plant trials for a new polymerisation catalyst that gives a 90% reduction in waste (GE Plastics); new commercial hydrogenation process based on supercritical fluid technology promises to be greener and safer than existing processes (Thomas Swan); new environmentally friendly route to herbicide intermediate (Monsanto); envirocats launched as environmentally friendly replacements for hazardous reagents and catalysts (Contract Chemicals).

Some individual case studies can be used to illustrate the environmental advantages that are being achieved in some chemical processes.[1]

Disodium aminodiacetate (DSIDA) is a key intermediate in the manufacture of Roundup™, the environmentally friendly herbicide. The traditional manufacturing route to DSIDA was based on old Strecker chemistry and suffered from numerous serious environmental and health and safety problems: the use of the highly toxic hydrogen cyanide which requires special handling and gives rise to operator, environmental and local community risks; the exothermic generation of unstable intermediates requires special care to avoid runaway reactions; the process gen-
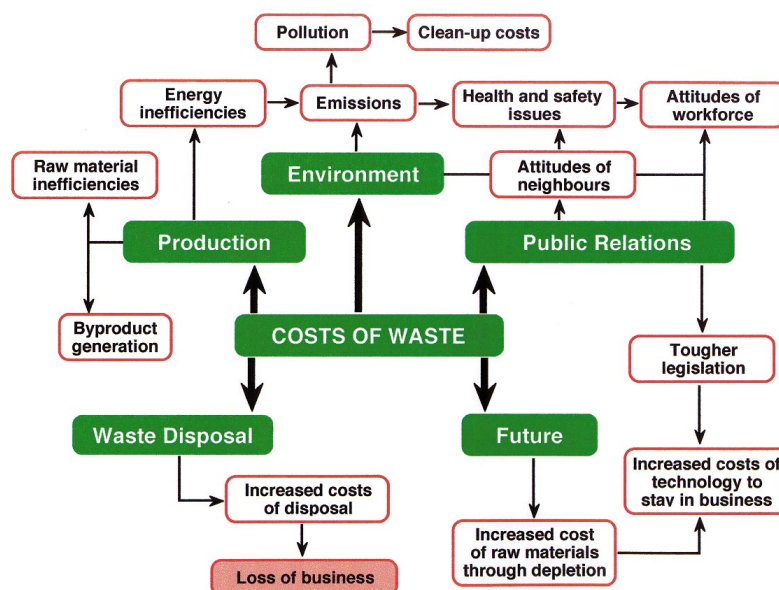
Fig. 2 The costs of waste.

erates at least 1 kg of waste per 7 kg of product; the waste contains cyanide and formaldehyde and needs treatment prior to disposal.

The new DSIDA manufacturing process is cleaner and safer. It is based on the catalytic dehydrogenation of diethanolamine and involves: less toxic and less volatile starting materials; endothermic and inherently safer chemistry; a 'zero waste' route: after removal of the catalyst, no further purification is required before the intermediate is used in the next stage of the herbicide manufacture; a new active and reusable solid catalyst which has applications wider than in this process.

Overall the new catalytic process gives higher product yields and involves fewer process steps.

The classical route to hydroquinone, a very useful intermediate in the manufacture of polymeric materials, suffers from very poor atom utilisation (*i.e.* a small fraction of the atoms consumed in the process end up in the final product) and leads to the production of enormous volumes of waste. The manufacturing method is shown in Fig. 3.

As can be seen, the production of one mole of hydroquinone leads to the production of mole equivalents of ammonium sulfate and iron(II) oxide and more alarmingly 4 mole equivalents of manganese sulfate. This is an example of a process with a poor environmental acceptability factor (high waste to product ratio)[3] made worse by the hazardous nature of the waste.[4] The poor atom efficiency of the process is best illustrated by some simple atom economy calculations (Table 1).

The new Upjohn route is a great improvement (Fig. 4). Overall only 3 kg of acetone waste are produced per 10 kg of hydroquinone product, and there are no significant amounts of salt waste.

4-Isobutylacetophenone is a key intermediate in the manufacture of the bulk active pharmaceutical ibuprofen. The conventional method of preparation is based on a Friedel–Crafts acylation, which uses greater than stoichiometric quantities of $AlCl_3$. To produce 1000 tonnes of 4-isobutylacetophenone, 760 tonnes of $AlCl_3$ are required and a corresponding amount of aluminium waste in the form of aluminous water is generated when the product–catalyst (Lewis base–Lewis acid) complex is broken down by quenching with a large volume of water. In addition, large amounts of acidic gaseous emissions have to be scrubbed
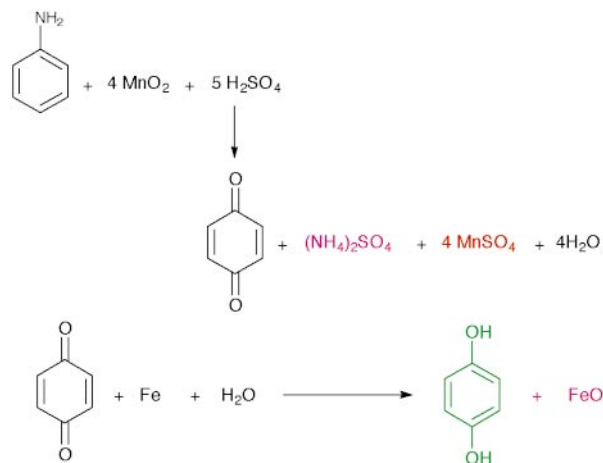
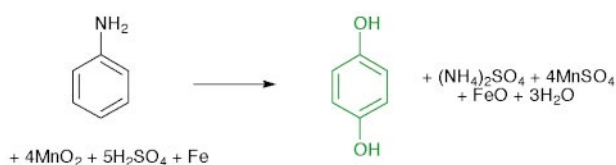Overall the chemistry involved can be represented as:

Fig. 3 The classical route to hydroquinone.

from the off-gas stream. Later stages in the process involve cyanide and elemental phosphorus (which does not end up in the final product) making the whole manufacturing process extremely hazardous and wasteful (Fig. 5).

Increasing pressure from generic competition (as the product came off patent) and to reduce the environmental impact led to Boots, in collaboration with Hoechst Celanese, developing a new cleaner process based on the use of HF as the Friedel–Crafts catalyst. Hydrogen fluoride is extremely corrosive and requires quite expensive plants for safe handling. The dangers resulting from any escape into the environment are also considerable. However, while the use of HF presents serious difficulties, unlike $AlCl_3$ it can be separated and recycled and the process is run continuously with complete containment. The total removal of cata-

Table 1 Atom accounts for the classical route to hydro-quinone

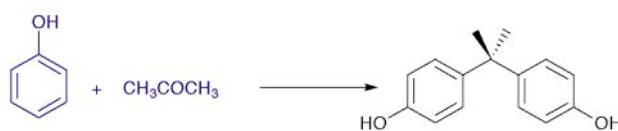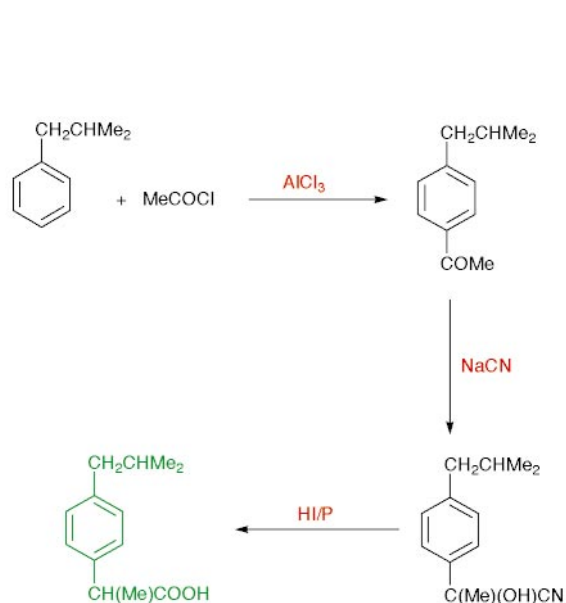| Element	Fate	Atom utilisation
Carbon	Product(s)	Up to 100%
Hydrogen	Product and waste	Up to 33%
Oxygen	Product and waste	Up to 13%
Manganese	Waste	0%
Sulfur	Waste	0%
Iron	Waste	0%
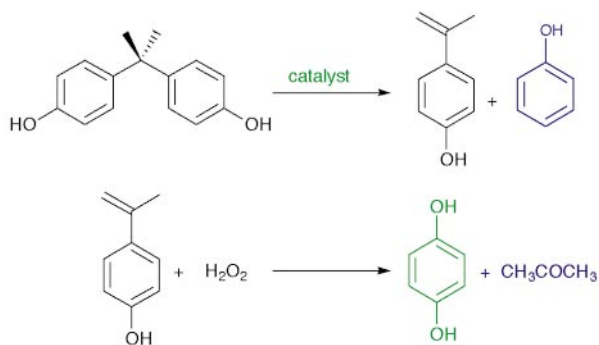
Fig. 4 The new Upjohn route to hydroquinone.

Fig. 5 The traditional manufacturing route to 4-isobutylacetophenone.

lyst waste in this step is an important development in the pursuit and application of green chemistry. In the overall process 6 stoichiometric steps with <40% atom utilisation have been replaced by 3 catalytic steps with *ca.* 80% atom utilisation.

Important generic areas of chemistry

To help illustrate the many challenges ahead and the opportunities for new greener chemistry, two very broadly based generic areas of chemistry can be at least superficially examined in terms of their scope, the environmental unacceptability and poor atom economics of typical processes, and the goals and possible approaches of green chemistry. The emphasis will be on batch-type processes involving liquid phase reactions as practiced by fine, speciality chemical and chemical intermediate manufacturers around the world.

Acid catalysed reactions

Acid catalysis is the most widely used type of catalysis with applications in all sectors of the chemical, pharmaceutical and allied industries, although the largest scale use is in the petrochemical industries where the processes are largely quite efficient and the use of solid acids is well established.[5]

Traditionally most liquid phase organic reactions have been catalysed by strong Brønsted acids such as H_2SO_4 and HF and by soluble Lewis acids such as $AlCl_3$ and BF_3. Their chemistry is extremely diverse with just a few examples shown in Fig. 6.
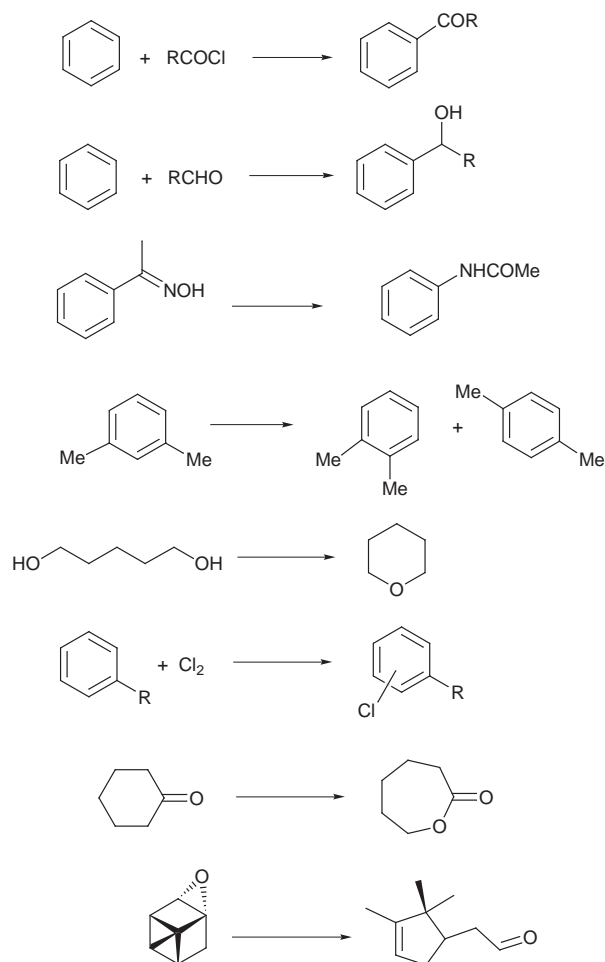

Fig. 6 Some examples of acid-catalysed organic reactions carried out in industry.

These acids have many important advantages—they are cheap, readily available and very active. Unfortunately, they also suffer from some serious disadvantages, which are becoming increasingly prominent in these environmentally conscious days—they are difficult to separate from the organic products and their use leads to large volumes of hazardous waste. In the petrochemical

industry, where acid catalysis is vital to many of the business areas, solid acids including zeolites have become established in the large-scale vapour phase processes. Continuous processes operating in contained plants can involve solid catalysts running for greater than a year before being removed and replaced. The efficiency of such processes is very high and the relative quantities of waste can be impressively low. Solid acids are only beginning to impact non-petrochemical process chemistry.[6]

Friedel–Crafts acylations (including benzoylations and sulfonylations) are real and alarming examples of very widely used acid-catalysed reactions which are based on 100 year old chemistry and are extremely wasteful. The reaction of an acid chloride with an aromatic substrate requires a greater than stoichiometric quantity of aluminium chloride as the 'catalyst' (>2 mole equivalents in sulfonylations). Every molecule of the ketone product forms a complex with one molecule of the catalyst, effectively removing it from the reaction. The organic product is released by using a water quench with the resulting emission of about 3 equivalents of HCl which need to be scrubbed from the off gases leading to the production of 3 equivalents of salt waste. Once the organic product has been recovered, aluminous water remains, which must be disposed of. The overall process generates considerably more waste than product (Fig. 7).
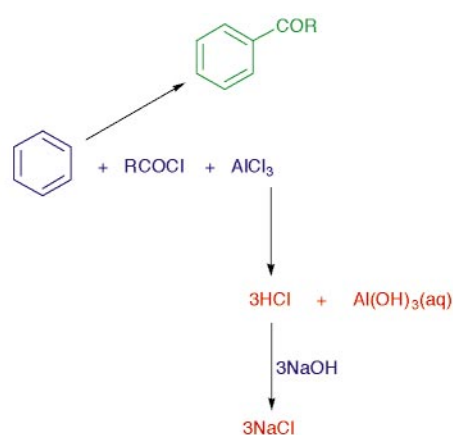
Substrates and reagents......... 1000 arbitrary weight units

Products................................... 120 arbitrary weight units

Waste.....................................880 arbitrary weight units

(based on R=Me and weight units calculated from relative molar masses)

Fig. 7 Friedel–Crafts acylation showing a typical starting materials/products/waste balance.

Many other industrial processes are catalysed by AlCl$_3$. These include alkylations and the production of resins *via* cationic polymerisation. While these reactions do not require the use of stoichiometric quantities of the Lewis acid, none of the catalyst is recovered and all such processes show the same atom accounts (Table 2).

The green chemistry goal for such reactions should be to remove all elements from the accounts other than those involved in the organic chemistry and, of course, to push the organic chemistry towards 100% selectivity to the desired product.

A number of new, more environmentally friendly acids for liquid phase organic reactions, notably solid acids (which are generally easier and less energy and resource consuming to recover than soluble acids), have been discussed and are beginning to

Table 2 Atom accounts in a typical AlCl$_3$-catalysed Friedel–Crafts acylation

Element	Fate	Atom utilisation
Carbon	Products and by-products	Up to 100%
Hydrogen	Products, by-products and waste (from quench)	<<100%
Aluminium	Aluminous water/aluminium salts	0%
Chlorine	Waste water (from quench) and salt (from HCl scrubbing)	0%
Oxygen	Waste water	Down to 0%

find their way into industrial usage. These include zeolites,[7] clays and other mixed metal oxides, inorganic–organic composite materials, functionalised polymers and supported reagents[8,9] as well as lanthanide triflates.[10] Other interesting 'green' solutions to the problem include the use of ionic liquids.[11]

Bromination chemistry is a relatively small area of organic chemistry but one with many useful applications (including photographic chemicals, pharmaceutical and agrochemical intermediates) and an international speciality chemical industry based on it. The chemistry is largely based on the use of elemental bromine and the problems associated with the use of traditional acid catalysts are compounded by the low atom utilisation of the bromine. The most important bromination reactions include aromatic bromination, bromodehydroxylation and the α-bromination of carboxylic acids (Fig. 8).
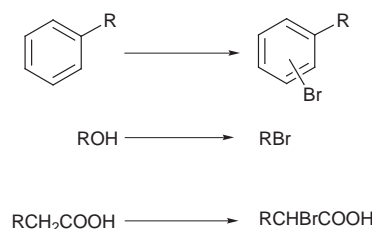
Fig. 8 Important bromination processes.

Aromatic bromination reactions are typically catalysed by Lewis acids such as FeCl$_3$ and AlCl$_3$ which present the familiar environmental problems of separation difficulties usually leading to HCl emissions and the production of large volumes of aqueous and salt waste. In the case of the aliphatic brominations phosphorus and sulfur reagents are commonly used. The α-bromination of carboxylic acids is carried out using red phosphorus, in some cases in near stoichiometric quantities. The phosphorus ends up as a cake of phosphates and other phosphorus species containing bromine and organic contaminants. It can only be disposed of after treatment. Additionally, all of the above reactions usefully employ no more than 50% of the bromine with an equivalent amount being converted to HBr which needs to be scrubbed from the off gases and removed as NaBr. The atom accountability in such reactions again tells a story of inefficiency and waste (Table 3).

In reactions using stoichiometric levels of phosphorus and with a substrate molecular weight of 100, even 100% efficient organic chemistry only gives 40% of the final mass as product, with 60% being waste. At a more likely level of 80% efficient organic chemistry, the figures change to 31% product and 69% waste.

A clean synthesis approach to bromination reactions should be able to greatly improve their environmental performance and atom efficiency. It is now known for example, that aromatic

Table 3 Atom accounts in a typical phosphorus-catalysed α-bromination

Atom	Fate	Atom utilisation
Carbon	Products (including side products)	Up to 100%
Hydrogen	Products plus HBr	<100%
Bromine	Products plus HBr	Up to 50%
Phosphorus	Phosphorus residues	0%
Sodium	Salt	0%

brominations, at least for other than strongly deactivated substrates, can be effectively catalysed by solid acids (including supported mild Lewis acids that are easily recovered and can be reused many times).[12] It should also prove possible to replace the phosphorus in aliphatic brominations. Furthermore, it should be possible to devise economical methods for oxidatively regenerating the bromide side-product to bromine ideally using oxygen, which will lead to water only as a side product. The effect of these improvements on the atom accounts would be dramatic (Table 4).

Table 4 Atom accounts in a clean bromination using a reusable catalyst and aerial regeneration of the bromide

Element	Fate	Atom utilisation
Carbon	Products (including side-products)	Up to 100%
Hydrogen	Products	Up to 100%
Bromine	Products	Up to 100%
Oxygen	Water/steam	0%

The effect on the mass efficiency is equally impressive with 100% efficient organic chemistry leading to 94% of the final mass as product and only 6% as waste. Even at 80% efficient organic chemistry, the figures are 75% product and only 25% waste respectively.

Partial oxidations

The partial oxidation of organic molecules (typically hydrocarbons) is a diverse and widely used area of chemistry with applications in almost all of the important fine and speciality chemicals industries including the manufacture of pharmaceuticals, agrochemicals and monomers (some of the most important transformations are shown in Fig. 9). Established manufacturing methods include those based on cobalt–acetic acid–bromide systems (*e.g.* for the side chain oxidation of alkylaromatics). While these are catalytic in cobalt the corrosive nature of the systems and the large reaction volumes are drawbacks. These coupled with the high temperatures and pressures that are often required give rise to problems for the operator and the plant, and improved catalytic reaction systems need to be developed.[1]

Peroxide reagents are useful in many partial oxidation reactions including epoxidations, Baeyer–Villiger reactions and hydroxylations. Peroxides can be hazardous however, and the more reactive organic peroxides such as percarboxylic acids do present serious difficulties to the operator especially in large-scale processes.

Stoichiometric metal oxidants such as chromium(VI) and manganese(VII) are perhaps the best known oxidising agents in chemistry. While they are commonly associated with volumetric analysis and bench scale reactions, their use on a large scale leads
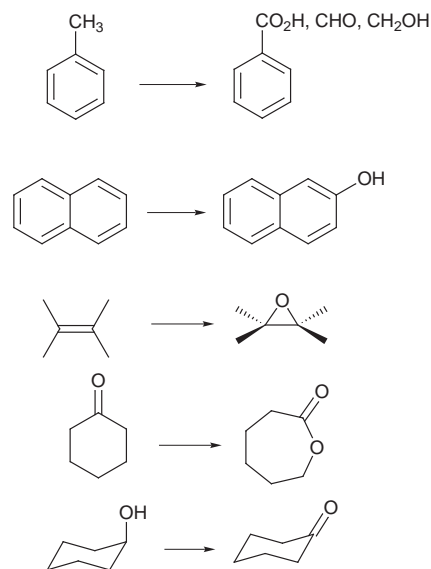
Fig. 9 Some important partial oxidation reactions.

to large volumes of toxic metal waste.[1,13] Rather surprisingly, such reagents continue to be used in some industrial processes such as the conversion of secondary alcohol functions to ketones. In a typical reaction, the feedstocks are a source of chromium(VI), acid and an organic solvent as well as the organic substrate (Fig. 10). The wasteful nature of such processes is evident when the work-up of the final reaction mixture is considered (Fig. 11). Typically, the mixture will undergo a water quench to
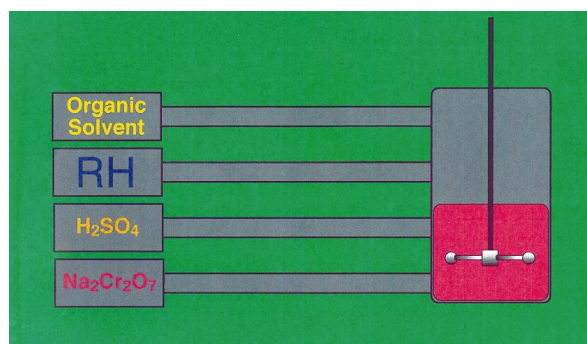
Fig. 10 The feedstocks for a typical partial oxidation process based on stoichiometric chromium(VI).
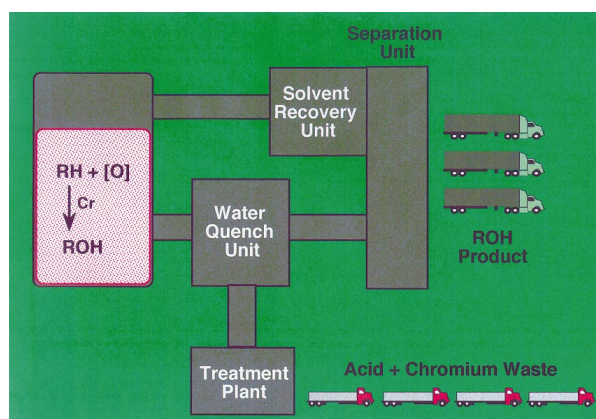
Fig. 11 The work-up and product recovery from a process based on stoichiometric chromium(VI).

liberate the product and considerably larger quantities of acid and chromium waste. The combination of toxic metal, acid and organic residues represents a particularly difficult form of waste, which must be treated before disposal. Even with 100% efficient solvent recovery, these processes will generate considerably larger volumes of waste than product. The high added value of partially oxidised products may continue to make the chemistry economically viable but it cannot be considered environmentally acceptable.

A simple exercise in atom accountability in the partial oxidation of an organic substrate with a stoichiometric chromium reagent system can also be used to highlight the problems (Table 5).

Table 5   Atom accounts in a typical organic partial oxidation using a stoichiometric chromium reagent system

Element	Fate	Atom utilisation
Carbon	Product(s)	Up to 100%
Hydrogen	Product(s) and waste acid	<<100%
Chromium	Chromium salts	0%
Sodium	Waste salts	0%
Sulfur	Waste acid	0%
Oxygen	Product(s) and waste salts	<<100%

Of the input atoms in the case of a simple hydrocarbon oxidation, only carbon, hydrogen and oxygen are required in the final product. Chromium, sodium and sulfur are used yet do not appear in the final product.

In the ideal synthesis, the only atoms that leave a process should leave in the form of useful product (Table 6). The most

Table 6   Atom accounts for a partial organic oxidation using air/oxygen and a catalyst (excludes any catalyst waste)

Element	Fate	Atom utilisation
Carbon	Product(s)	Up to 100%
Hydrogen	Product(s) (may include water)	Up to 100%
Oxygen	Product(s) (may include water)	Up to 100%

environmentally acceptable source of oxygen is air, directly leading to only nitrogen as waste (of course, oxygen itself or oxygen-enriched air can also be used in the actual process). For most organic oxidations using air, a catalyst will be required to enable the reaction to occur at moderate temperatures and pressures (even with a catalyst many important partial oxidations currently require very forcing conditions suggesting the need for improved catalysis). Thus, in the ideal partial oxidation process, only the organic substrate, air and (a small amount of) catalyst should be introduced into the reactor (Fig. 12). If the catalyst can be retained in the reactor in some way (and subsequently reused either *via* a continuous mode of operation, or *via* fresh charge of substrate), then the work up of the reaction mixture should only involve product recovery and unreacted substrate recycling (Fig. 13). In some partial oxidations (*e.g.* the side chain oxidation of alkylaromatics), water will also be produced in the reaction but water is just about the most environmentally acceptable side product, at least when pure, and can be used as a source of
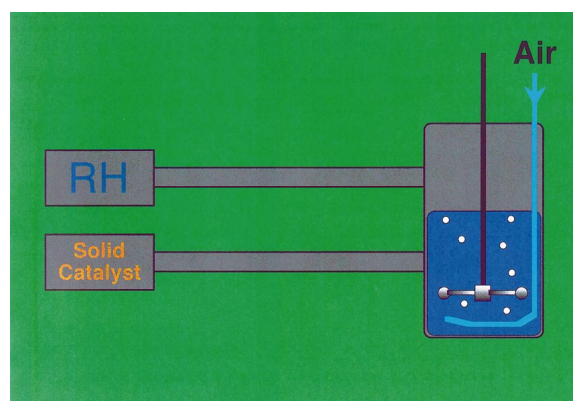

Fig. 12   Feedstocks for an ideal partial oxidation using air and a catalyst.
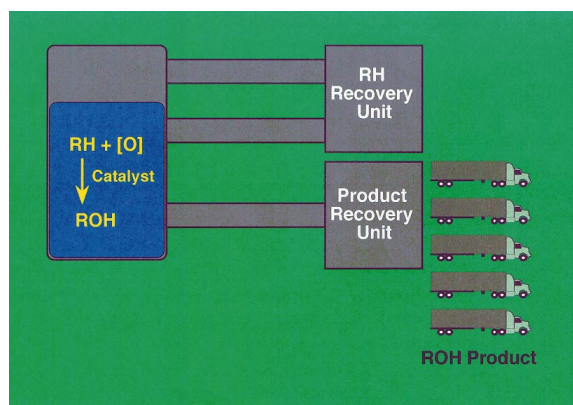

Fig. 13   The work-up and product recovery from an ideal catalytic partial oxidation process using air.

energy if vented off as steam. This, of course, ignores any organic side products which commonly occur in many partial oxidations but these are also prevalent in the older and more wasteful processes, indeed the use of some newer forms of catalysis (*e.g.* those based on shape selective microporous solids) can improve reaction selectivity.[14]

To keep such an ideal process as simple, efficient and clean as possible, an active and selective catalyst is required. Furthermore, to avoid any potentially difficult catalyst separation stages, it should remain in a separate phase from the organics (and, of course, not leach any of its component parts into the organic phase). In the case of a simple stirred reactor, a particulate solid catalyst could be used although the ultimate separation of such a material from a liquid (decantation, filtration, *etc.*) may not be a trivial exercise. For continuous flow reactions, catalyst pellets may be more appropriate. Fortunately, useful progress is being made in the discovery and application of solid catalysts for partial oxidation reactions. These include mixed metal oxides such as the titanium silicate 'TS1' (*e.g.* for the hydroxylation of small aromatic compounds) and supported reagent type catalysts (*e.g.* for alkene epoxidations).[9,14,15]

Concluding remarks

The drive towards clean technology in the chemical industry and the emergence of green chemistry related issues in chemical research and education are unlikely to be short term 'fashions'. In the future, the synthetic chemist will need to be as concerned about atom efficiency as the synthetic route and the process chemist will need to be as concerned about the waste produced as

the product to be made. It is already becoming evident that the more successful chemical manufacturing companies of the future will be those that can exploit the economic, legislative and public image advantages that a clean technology approach to chemical manufacturing can provide. Also, the more successful chemistry researchers and educationalists will be those that can appreciate the value of green chemistry in innovation, application and teaching (as well as recognising the important role that green chemistry can play in enhancing the attractiveness of chemistry as a discipline).

While many exciting new greener chemical processes are being developed it is clear that a far greater number of challenges lie ahead. In two of the largest generic areas of chemistry, acid catalysis and partial oxidations, there are countless processes operated by almost every type of chemical manufacturing company, producing products of incalculable value yet also producing almost immeasurable volumes of hazardous waste. New greener chemistry is needed. One of more important development areas in this context will be the more widespread use of heterogeneous catalysis in liquid phase organic reactions. The enormous range of reactions and the rapidly growing number of new catalysts will require the use of rapid screening methods and the use of innovative engineering to fully exploit the new chemistry. Synthetic chemists must be more prepared to work with catalyst chemists who must in turn work more closely with chemical and process engineers. For every challenge offered by the green chemistry revolution there is also an exciting opportunity.

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