Q&A

SUSTAINABLE TECHNOLOGY

Green chemistry

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Modern life depends on the petrochemical industry — most drugs, paints and plastics derive from oil. But current processes for making chemical products are not sustainable in terms of resources and environmental impact. Green chemistry aims to tackle this problem, and real progress is being made.

Why is chemical manufacture becoming unsustainable?

There are two main reasons. The first is that most chemical products — from perfumes to plastics to pharmaceuticals — are based on carbon, which currently is supplied by Earth's finite petroleum feedstocks. Alternative carbon sources do exist — for example, coal was the basic feedstock for chemical production before oil, and could be used again. But readily accessible coal is also in limited supply, and the conversion of coal into fine chemicals requires catalysts based on metals that are themselves becoming scarce. The second, equally pressing issue is waste. In general, industrial chemical processes generate large amounts of waste, the safe disposal of which imposes an increasing burden on the environment.

Can't these problems be dealt with using existing technology?

Unfortunately not. The chemical industry has made great improvements in the efficiency of its processes, but finite natural resources will inevitably limit our ability to manufacture chemical products for the increasing global population. Unless there is radical innovation, the industry will eventually struggle even to supply existing consumers. The challenge of green chemistry for both academics and industrialists is to devise sustainable strategies that meet the demand for chemical products from an ever-increasing population.

What aspects of manufacturing does green chemistry address?

All of them. Working through the arc of an industrial process, the first challenge is to identify renewable feedstocks. The current front-runners are non-food plants, in which case chemists must find effective ways of converting the whole plant into useful products. Next, the reactions involved in making chemical products must be devised to minimize environmental impact. For example, many traditional catalysts are based on metals, which can be toxic or scarce; nonmetallic catalysts must therefore be developed, perhaps based on organic compounds (organocatalysts) or on enzymes that have been modified to perform useful reactions. Engineering is also crucial — industrial processes and reactors must be designed to maximize efficiency and reduce waste. Improved analytical techniques are necessary to monitor the fate of potentially harmful chemicals in reactions and in the environment. And finally, the impact of chemicals on the environment can be reduced by finding replacements with reduced toxicity and increased biodegradability compared with existing mass-produced compounds.

How can you tell if a chemical process is green?

This question puzzled chemists for some time. A standard set of 12 principles has emerged that can be used to assess any process (Fig. 1). These address several issues, including the amount of waste produced; the number of sequential chemical steps (the fewer the better); the use of catalysts (which is to be encouraged, because catalysts are needed only in small amounts and reduce the quantities of reagents used); and the toxicity of the products. It isn't expected that new chemical processes should always satisfy all 12 principles, but the checklist does provide a rough idea of whether one process is greener than another.

Is it possible to quantify how green a process is?

Several methods have been proposed, but the easiest thing to measure is the amount of waste generated. From the balanced chemical equation for a process, the theoretical quantity of waste can be calculated per unit mass of starting material, assuming that the yield of product is 100%. But in reality, most reactions give lower yields, and the actual amount of waste is higher than the theoretical value. To address this issue, processes are assessed using their 'E-factor' — the ratio of the mass of waste to that of the product. All processes should aim for the lowest possible E-factor; for truly green processes, the E-factor should be zero.

So which manufacturing processes are currently the worst, according to their E-factors?
E-factors often throw up surprises. Large-scale manufacturing processes for bulk chemicals are generally perceived as being bad for the environment, compared with the relatively small-scale operations of the pharmaceutical sector. But E-factors for bulk chemical manufacturing are typically much less than 5 — even though the volumes produced are so high that the amount of waste is very large. By contrast, E-factors in the pharmaceutical industry can be greater than 100; for example, when the antidepressant sertraline was launched, 250,000 litres of solvent were needed for each 1,000 kilograms of product. Applying the principles of green chemistry reduced solvent usage tenfold.

Can't waste be completely eliminated from chemical processes?
Some waste is unavoidable, because energy is required to break the bonds in the starting materials of a reaction. If the energy input is not balanced by the energy generated from bonds forming in the product (which is often the case), then extra bonds must be created, usually in a by-product. Some by-products can be used as feedstocks for further reactions — for example, nitrous oxide (N_2O) generated in the production of nylon can be used as an oxidant to convert benzene into phenol, a bulk chemical with many applications. But many by-products are insufficiently reactive or too diluted to be recycled economically. In that case, the most sensible treatment for organic waste is careful incineration, so that at least its energy content can be exploited. But often, by-products do not form the bulk of the waste — solvents do.

So, are solvents high on the green-chemistry agenda?
They are a top priority. Many solvents are flammable or toxic, and most are volatile organic compounds that contribute to atmospheric pollution. Solvents are necessary for most reactions because they aid mixing, transfer heat and sometimes control the reactivity of reagents. But the largest quantities of solvents are used in the isolation, separation and purification of materials. If reactions could be optimized to prevent the formation of by-products, then purification processes would be eliminated (or at least minimized), greatly reducing the amounts of solvents required for the overall process. Finding environmentally benign solvents would be even better.

What are the alternatives to traditional solvents?
Some reactions don't need any solvent, although the lack of a medium for heat transfer can make it difficult to stop certain reactions from potentially disastrous over-heating. But the most useful alternatives to traditional solvents are supercritical CO_2 (where the gas is compressed until it is nearly as dense as a liquid), ionic liquids (organic salts that are liquid at room temperature) and water.

Why not just replace all organic solvents with water?
One problem is that most organic compounds are insoluble in water. Despite this, a surprising number of organic reactions can be carried out in water; for example, propene (a hydrocarbon gas) can be reacted catalytically with carbon monoxide and hydrogen to make butanal — a reactive compound used as a starting material for a wide range of products. But often the main difficulty with aqueous systems is recovering products from them; evaporating large amounts of water is energy-intensive. One also has to keep the big picture in mind — claims that reactions are green because they are performed in tiny volumes of water are misleading if the purification process requires much greater quantities of organic solvents. It's like arguing that air travel is environmentally friendly because the passengers walk from the terminal to the plane.

What is so good about supercritical CO_2? Wouldn't its widespread use contribute to climate change?
The solubility of materials in supercritical CO_2 can be varied merely by changing the pressure of the gas. This opens up separation and purification methods that are not possible with conventional solvents. For example, a modest pressure of CO_2 can cause some compounds dissolved in water to separate out without the need for distillation, which could greatly simplify industrial-scale processes. Supercritical CO_2 is also revolutionizing the chromatographic purification of many active pharmaceutical ingredients, because the high rates of diffusion of compounds in CO_2 make the separation more effective than with conventional solvents. Furthermore, supercritical CO_2 is non-toxic — it has been used for many years to decaffeinate coffee. It wouldn't contribute to climate change, because the CO_2 used is a by-product from other processes. The downside is that compressing CO_2 to a supercritical form is energy-intensive.

Why are ionic liquids hailed as green solvents?
The great advantage of ionic liquids is that they undergo very little evaporation and so are not lost to the atmosphere. The biggest issue is their potential toxicity. Only a few have been tested so far and, as might be expected, some are as toxic as conventional solvents whereas others are relatively innocuous. But as with water, one must be cautious about labelling a reaction as 'green' just because it uses an ionic liquid as the solvent. Combinations of ionic liquids with other green solvents could be especially useful — for example, supercritical CO_2 has been used to pass reactants through an ionic liquid that contains a dissolved catalyst and to extract the products in a continuous process. Catalysts are often very expensive, and trapping them in the ionic liquid prevents them from being lost.

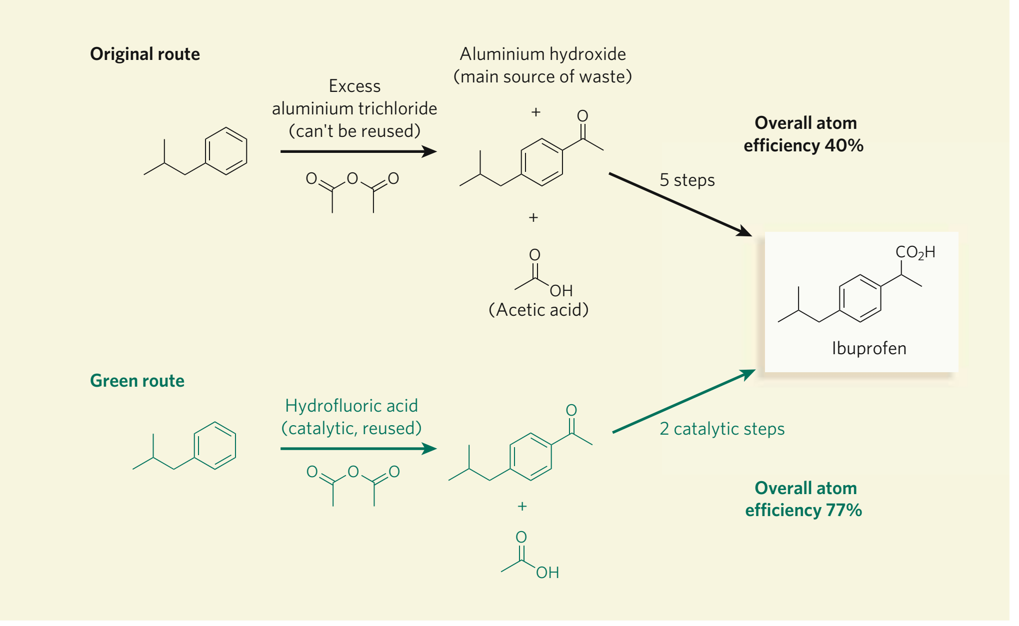
Prevent wastes
Renewable materials
Omit derivatization steps
Degradable chemical products
Use safe synthetic methods
Catalytic reagents
Temperature, pressure ambient
In-process monitoring
Very few auxiliary substances
E-factor, maximize feed in product
Low toxicity of chemical products
Yes, it is safe

Figure 1 | The principles of green chemistry. Green chemical processes adhere to 12 principles, shown here in a simplified version to form a mnemonic. Catalytic reagents reduce the amount of chemicals needed in a reaction; in-process monitoring allows harmful substances to be detected and eliminated; auxiliary substances are those that don't take part in the chemical reaction, such as solvents or separating agents; and the E-factor is the mass of waste generated in a process divided by the mass of product. (Figure taken from S. L. Y. Tang, R. L. Smith and M. Poliakoff *Green Chem.* 7, 761–762; 2005.)

Can any reactions be performed in green solvents that weren't possible in traditional solvents?
Green solvents have been a little disappointing in this respect, as few examples of such reactions have been described. But there are many cases in which known reactions can be carried out more efficiently, including some industrially useful ones. For example, reactions of organic compounds with hydrogen work well in supercritical CO_2, and certain alkylation reactions — in which hydrocarbon groups are attached to aromatic compounds — excel in ionic liquids. Both of these types of reaction are widely used in the manufacture of chemical products.

Doesn't chemical engineering have a role to play in green chemical processes?
Engineering chemical processes is just as vital as developing reactions. An exciting aspect of green chemistry is that it brings chemists and chemical engineers together. Green solvents open up new design options for reactors, and the need for quantitative data on reactions in these media is leading to renewed interest in physical organic chemistry. Chemistry and chemical engineering departments of universities are collaborating closely to address these needs.

Box 1 | Green ibuprofen



Ibuprofen is the main active ingredient in many over-the-counter painkillers. It was first prepared and patented in 1961. The original synthetic route involved six consecutive steps and had an overall atom efficiency of just 40% — of the mass of all the atoms going into the process, 60% ended up in waste products. This route was used to manufacture the drug until the patent expired in 1984. If ibuprofen were still made in this way, more than 20,000 tonnes of waste would be generated annually.

In the early 1990s, the BHC company (now part of BASF) redesigned the synthetic route using many of the principles of green chemistry. The power of its approach is demonstrated by comparing the first steps of the two routes (shown here). The same chemical transformation occurs, but it is achieved in very different ways. Originally, aluminium trichloride was required to promote the reaction. This generated aluminium hydroxide, which was filtered off as a cake of solid waste. To get a high-yielding reaction, the aluminium trichloride was needed in excess (in larger quantities than the theoretical amount suggested by the reaction equation), adding to the waste problem.

But in the green route, hydrofluoric acid is used to promote the reaction instead of aluminium trichloride. Because it is used as a catalyst, only a small amount of the acid is required; even better, it is recycled and used for making the next batch of product. In this way, a large amount of solid waste was eliminated from the process.

The green route then adopts a synthetic strategy that is quite different from the original process, so that only two more steps are required (compared with five more needed in the original process). Each step eliminated reduces the resources used and the waste generated. Both the remaining steps in the green route are catalytic — unlike those in the original synthesis — further reducing waste.

In this way, the overall atom efficiency of the green process was increased to an impressive 77%. In principle, the efficiency could be improved to more than 99% by recycling the by-product of the first reaction (acetic acid, which can be easily converted to acetic anhydride, a reagent for the first step). The green route thus produces more ibuprofen in less time and using less energy than the original process — which means cheaper products for the consumer with increased profits for the manufacturers. **M.P. & P.L.**

How has re-engineering processes changed things?
One obvious improvement is the switch from batch reactions to continuous processing — which is a bit like replacing baths with showers. For a given mass of chemicals, a continuous reactor can be much smaller than the corresponding batch reactor because smaller amounts of material are undergoing reaction at any given time. And higher reaction rates can be achieved without overheating, as product and reacted materials are being continuously removed. Continuous processing is not only safer, but can often give a higher-purity product. It also allows manufacturing to be more flexible — small batches of compounds can be prepared on demand, rather than having to be made in large amounts at a time, which then have to be stored until they're needed.

Can the chemical industry break free from petroleum as a basic feedstock?
The only renewable source of carbon is biomass derived from plants. But biomass has a different chemical composition from oil (it contains more oxygen), so new reactions will have to be developed to turn it efficiently into useful compounds. This issue will have to be addressed by the chemical industry, although biological approaches — such as using enzymes to convert biomass into chemicals — also show promise. Other obvious problems with biomass include the seasonal nature of crops, possible conflicts with food supplies and the variability of its composition — different processes may need to be devised to convert different kinds of biomass into chemicals.

How does industry view green chemistry?
Initially, there was little appreciation of the potential benefits. But industrialists have become more interested as it has become clear that green processes can be more profitable than traditional ones (Box 1). For example, enzymatic reactions have completely displaced conventional catalysis as a low-cost option in the manufacture of several generic pharmaceuticals. The globalization of the chemical industry means that it requires only a few committed individuals to trigger substantial changes. A relatively small group of industrial-process chemists has achieved a considerable reduction in the volume of toxic solvents used in pharmaceutical manufacture across the world, by producing a simple toolkit that identifies less harmful replacements.

What is the real intellectual challenge for the future?
Perhaps the greatest challenge facing green chemists is the eventual elimination of all environmentally harmful chemical products. In other words, when designing compounds for a particular application, how can we ensure from their conception that they have low toxicity and rapid biodegradability while retaining their desired effect? Chemists are still a long way from being able to predict the properties — both chemical and biological — of compounds on the back of an envelope. Reaching that point is a daunting task, but it will inspire the next generation of chemists. ■

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