made from natural gas) via the Haber-Bosch process. This process is so large that it stands in a class all on its own: worldwide production of ammonia in 2021 was a mind-boggling 235 million tons. Today, the ammonia process alone accounts for >2% of the world's energy consumption (roughly the same amount of energy consumed by Mexico in a year).

Man-made nitrogen is essential for making fertilisers, nylons, explosives and many other chemicals. Many of these products are made using nitric acid, HNO_3, of which 70 million tons were produced in 2021. This impacts the environment, as the nitrogen atoms eventually end up in the bio ecosystem, and the amounts are too large for nature to deal with. The result is increased amounts of nitrogen oxides (which are potent greenhouse gases) in the atmosphere, and higher concentrations of nitrate and ammonium ions in terrestrial and aquatic systems. These ions are basically 'food additives' for the ecosystem, and they create a celebration of growth, causing eutrophication and decreasing biodiversity. All these disturb the natural nitrogen cycle. Just like with carbon, we need to rethink our impact on the nitrogen cycle, and just like with carbon, this need opens opportunities for start-ups and new businesses [34].

1.3.5.4 The Importance of Biodegradable Products

One way to reduce our ecological footprint is by making products that can be readily decomposed under natural conditions. Ideally, this decomposition should not have an adverse effect on the environment. This is a very big challenge, for two reasons: First, consumers strongly prefer new-looking and long-lasting products, so the decomposition should happen only when the product reaches its end-of-life. Second, even when the product decomposes only at the disposal, there is no guarantee that its remains will not affect the environment. Additional nitrogen or phosphorous in the soil, for example, can enrich it and promote the growth of different plants and microorganisms, changing the ecosystem. Often, these changes are observed only after many years, but the knowledge that this can happen creates barriers for approval of product use.

Nevertheless, biodegradable products, and especially biodegradable plastics, are extremely important for dealing with our enormous waste problem. In 1950, each person on Earth used on average 1.7 kg of plastic. Today the figure is >150 kg. The total production of plastics in 2019 was 370 million tons per annum, and biodegradable plastics formed less than 2% of this [35]. Figure 1.14 shows the material flow analysis for plastics in 2019. Recycling accounted for only 23 million tons, while landfill and mismanaged waste together accounted for 165 million tons. That's a lot of plastic that ends up in the environment. Unfortunately, landfills and mismanaged waste are the major causes of microplastics in the environment. Between 15% and 40% of mismanaged plastics enter the oceans from coastal cities [36]. Most of the microplastics that form in these conditions (soil and coastlines) are difficult to quantify [37]. Estimates of microplastics released in the soil in Europe are comparable to those reported for the oceans in the same region.

There is clearly a case for switching to biobased and biodegradable plastics. But this switching will take decades, if it happens at all. The reason is that the current processes for making durable plastics from fossil-based carbon are mature and highly optimised. Replacing them incurs a short-term risk that currently offsets any future gain. Regulations for separation and recycling of traditional plastics can help this transition, because they turn plastic waste from an externality (i.e. somebody else's problem) to something with a defined cost and therefore value.

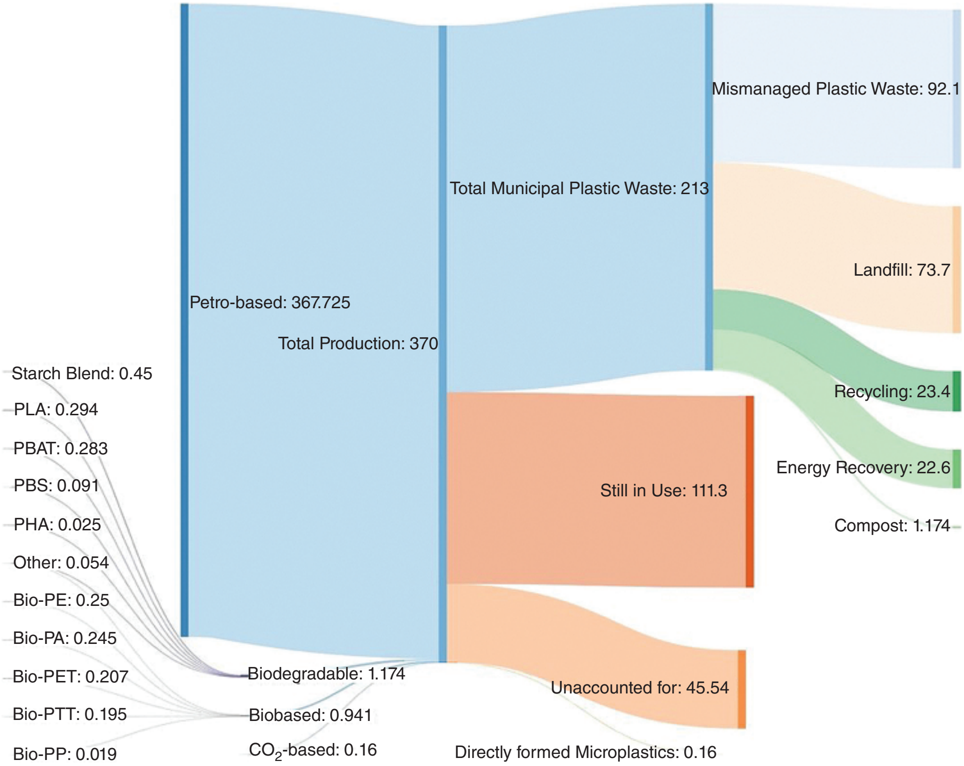

Figure 1.14 Sankey diagram showing the material flow analysis (MFA) for fossil-carbon-based, biodegradable, biobased, and CO_2-based plastics in 2019. All values are in millions of tons. *Source*: [35] / John Wiley & Sons.

Yet moving from traditional plastics to eco-friendly ones is a tricky challenge. The very definitions of 'biobased' and 'biodegradable' are unclear. Adjectives such as 'green', 'circular' or indeed 'eco-friendly' are even vaguer. Producers, consumers and policy-makers are faced with a plethora of choices and approaches, where relevant information is hard to come by. But one thing is certain: There is a large market out there for biobased and biodegradable plastics, if these can be made economically viable. I will discuss the subject of product-market combinations in more detail in Chapter 2, but even now, we can see that biodegradability, which is an end-of-life characteristic, is not trivial. When we throw something away, biodegradability is an advantage as the waste goes back into the ecosystem and is eventually recycled by nature into new raw material. But as long as the product is functioning, we don't want it to degrade.

Biodegradable products are suitable in some cases, especially when collection, recycling and reuse are difficult. Otherwise, keeping the material performance parameters can be essential for efficient recycling and reuse. Polyethylene can stay in the environment for hundreds of years, but this also means that if you can collect it and clean it, you can reprocess and reuse it again and again. In this way, the carbon atoms that form the polymer backbone remain 'stored' there instead of being released as CO_2. Even from a societal viewpoint, biodegradability is a two-edged sword, as it can also encourage single-use and wastage.

Ultimately, it all depends on the application. Biodegradable plastic packaging and film make sense, but Lego bricks, for example, are made from a copolymer called acrylonitrile butadiene styrene (ABS) for a reason: They last for decades and are valued for their durability and long-term performance. Chapters 8 and 9 tell the respective stories of the companies Avantium and Plantics, whose main value proposition centres on biobased and/or biodegradable products.

1.3.6 Replacing Stoichiometric Reagents with Catalytic Cycles (Principle IX)

Although I have left this one to the end, catalysis is one of the most important principles of green chemistry [38]. In fact, catalysis is the key to sustainability [39]. Catalysis also creates many business opportunities. Finding the right catalyst can disrupt large markets and sometimes even create whole new markets. One such example is the discovery of the zeolite ZSM-5, which enabled the selective formation of terephthalic acid and with it the

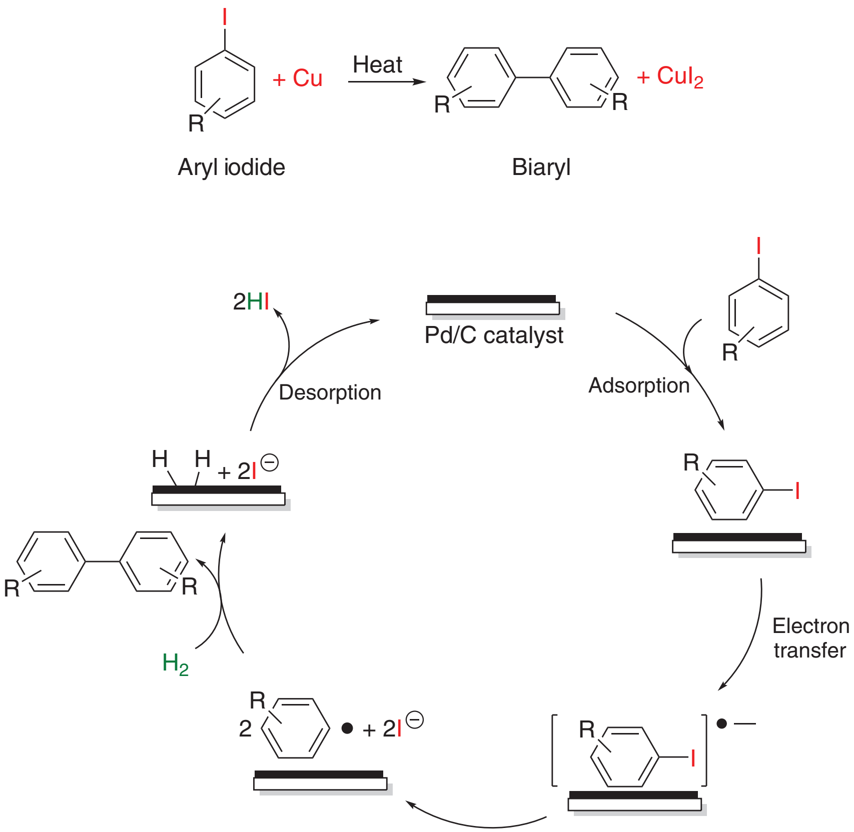

Figure 1.15 The Ullmann coupling of aryl iodides uses stoichiometric amounts of copper metal (top). Yet the copper is only used as a reducing agent (a source of electrons). The alternative Pd-catalysed cycle takes the electrons from a much lighter (and cheaper!) *source*: hydrogen gas (bottom), generating less waste. Switching from iodoaryls to bromo- and ultimately chloroaryls will further reduce both the price and weight of the waste part in the reagent. However, it also requires a catalyst that can activate the aromatic C—Cl bond, which is more stable than the C—I bond.

cheap production of high-grade polyethylene terephthalate (PET). Patented by the Mobil Oil Company in 1975, ZSM-5 revolutionised the plastics industry, so much that the product, PET, has become in itself a global pollution problem.

Note that one cannot literally 'replace stoichiometric reagents with catalytic cycles'. Every chemical reaction uses stoichiometric reagents, including all catalytic reactions. What we actually mean is 'replace heavy and/or toxic (and usually expensive) stoichiometric reagents with catalytic cycles that can use lighter, eco-friendlier (and hopefully cheaper) reagents'.

For example, consider the reaction of two iodoaryls with copper metal to give the corresponding biaryl and copper(II) iodide (Figure 1.15, top). This type of aryl-aryl coupling is known as the **Ullmann reaction**. Discovered by the German chemist Fritz Ullmann over 100 years ago, this reaction is still used today, owing to its high selectivity. Yet we see that the copper is not part of the desired product but is just used as a reagent and discarded as waste. The reaction only uses two electrons from the copper (because we start with Cu^0 and end with Cu^{2+}). That's a lot of expensive waste for just two electrons. We can try and replace the copper with another reducing agent that would give the same two electrons. One option is using hydrogen gas and thus swapping our CuI_2 waste for 2 mol of hydrogen iodide (HI, see Figure 1.15, bottom). This is where catalysis can help, because this reaction does not run spontaneously with hydrogen, but does run in the presence of small amounts of a Pd/C (read: palladium on carbon) catalyst [40].

Can we improve this reaction even further? We reduced the waste associated with the two electrons to two protons, and we cannot go much lower than that. But how about the iodide ions? Iodide is not only expensive – it is heavy! This is important because chemicals react based on their stoichiometry, but they're bought and sold by their mass. The molar mass of iodide is 127 g/mol. This means that when you purchase a tonne of iodobenzene, you're buying 680 kg of 'iodo' and only 320 kg of 'benzene'. So you're paying a lot of money for something that is over 2/3 garbage! Definitely not the best deal. We can improve here by using chlorobenzene instead. This reduce the weight of the waste by a factor of 3.5, and chlorine compounds are cheaper and more readily available than iodine ones. The catch is that breaking the C—Cl bond is more difficult and therefore requires a better catalyst [41].

The Importance of Aryl-Aryl bonds

Joining two aromatic rings is an important chemical reaction, useful in many industrial chemical processes. This is because monoaromatics (benzene, toluene and xylenes) are readily available from crude oil reforming, whereas many fine chemicals, agrochemicals and pharmaceutical intermediates contain two connected rings or have a molecular size that is roughly that of two connected rings with some substituents. The reason for this is that many biological receptors are triggered by molecules that are roughly the size of two connected rings, and the chemical industry makes and sells products that target these receptors (think of flavours and fragrances, but also medicines, drugs and pesticides, some examples of which are shown in Figure 1.16).

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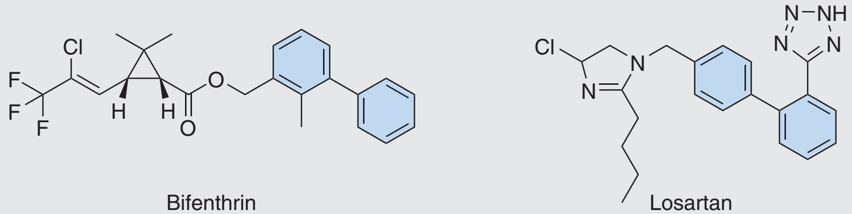
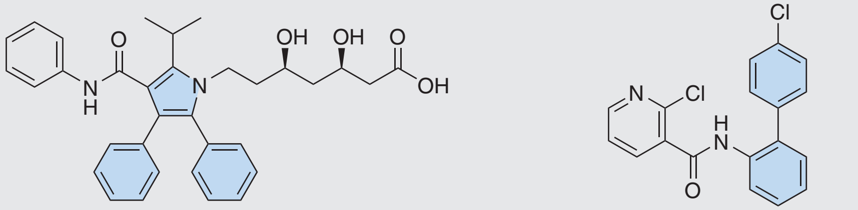


Bifenthrin
(pyrethroid insecticide)

Losartan
(hypertension and high blood
pressure treatment)



Atorvastatin
(cholesterol-lowering drug)

Boscalid
(broad-spectrum fungicide)

Figure 1.16 Examples of agrochemicals and pharmaceutical compounds that contain two connected aromatic or heterocyclic rings.

Literally, catalysis means the breaking down of stuff (from Ancient Greek: κατά = down, λυσις = loosening or dissolving). Today, we use the term catalysis to mean the speeding up of chemical reactions. For an outside observer, it seems that adding a catalyst 'makes the reaction go faster'. In fact, in most cases, the catalyst enables a different, faster reaction pathway. However, at this stage, we will use the following general definition:

A catalyst is something that makes a reaction go faster, without being consumed in the process.

In theory, each catalyst molecule or unit can participate in many consecutive cycles, so we need only a small amount of catalyst relative to the substrate. In practice, catalysts eventually deactivate and must be regenerated and/or replaced. The substrate:catalyst ratio reflects the catalyst's efficiency, which is measured as **turnover number** (TON) or **turnover frequency** (TOF).

Note that catalysis is a kinetic phenomenon – you can make your reaction go faster towards the thermodynamic equilibrium. But catalysis *cannot* change the thermodynamic equilibrium. This is important: you cannot use catalysis to circumvent the laws of thermodynamics. For example, CO_2 conversion is a 'hot topic' these days, but reacting CO_2 incurs a thermodynamic energy penalty, and no catalyst can avoid (or even lower) this penalty.

There are many types of catalysts (Figure 1.17). These range from simple ions like H^+ and OH^-, through Lewis acids, various metals, organometallic complexes, organic and inorganic polymers and all the way to enzymes. To simplify things, we divide catalysis into three categories: homogeneous catalysis, heterogeneous catalysis, and biocatalysis. Although the catalysts and the process conditions in each category can be very different, the principles of

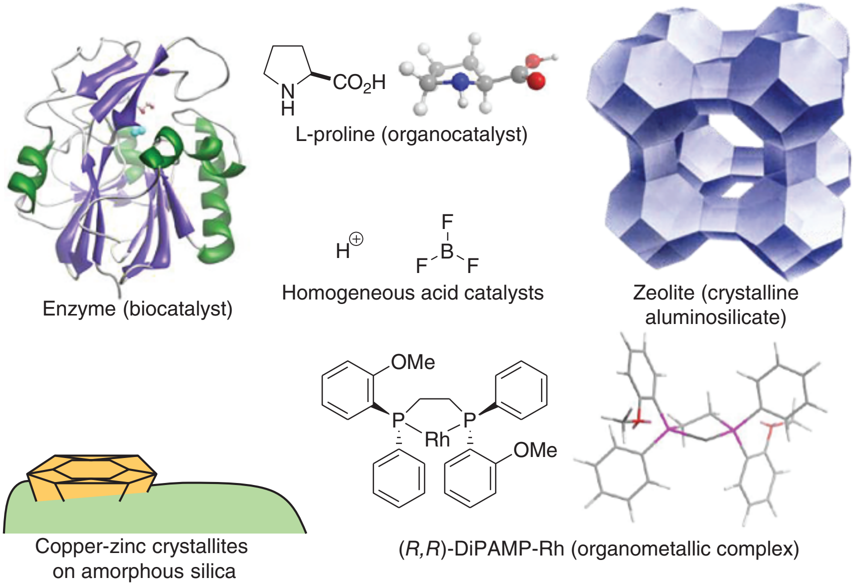


Figure 1.17 Catalysts come in many shapes and sizes – from a single proton all the way to millimetre-sized particles of solid materials. Yet they all share a common factor: they open a more effective chemical pathway from the reactants to the products.

catalysis are the same. Once you understand these principles, you can easily apply them in all three categories.

Most people are simply unaware of the role that catalysis plays, literally, in their lives. Practically all of the reactions in all living cells are catalytic ones. Our bodies burn fuel, for example (by reacting oxygen with sugar), yet they do so at the amazingly low temperature of 37°C, thanks to complex catalytic cycles. Our modern society is also highly dependent on catalysis: the manufacturing of petrochemicals, plastics, medicines, agrochemicals and modern materials all use catalytic processes.

The Different Types of Selectivity

The main advantage of using catalysis is that you can get the desired product faster, using less resources and generating less waste. A catalyst can open a selective route to the desired product. There are various kinds of product selectivity (compare the examples in Figure 1.18). Chemical selectivity, or **chemoselectivity**, denotes a situation where two different chemical reactions can occur, giving two different products. Similarly, **regioselectivity** is when the same chemical reaction at different regions of the molecule leads to different products. When a reaction gives two (or more) diastereomers, the selectivity to each one of those is called **diastereoselectivity**. In the special case when two products are mirror-image diastereomers, or enantiomers, we talk about **enantioselectivity**.

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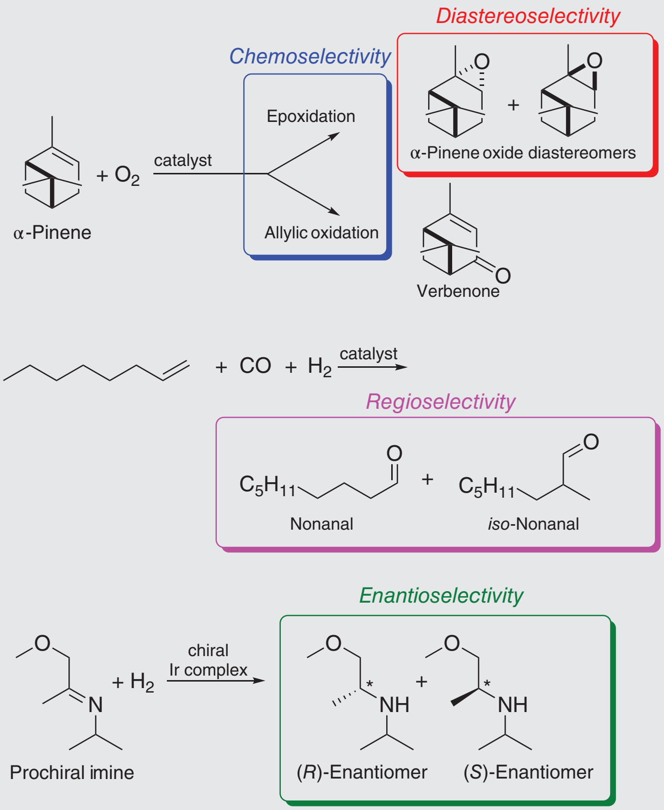

Figure 1.18 Examples of chemoselectivity and diastereoselectivity in the oxidation of α-pinene (top), regioselectivity in the hydroformylation of 1-octene (middle) and enantioselectivity in the hydrogenation of the prochiral isopropyl(2-methoxyisopropyl)imine (bottom). '*' indicates the asymmetric carbon atoms.

These same advantages also form the basis for new business opportunities in the context of sustainable chemistry and the circular economy. Catalysis can help us switch from fossil-based material and energy sources to renewable ones, and/or replace expensive, toxic or hazardous reagents with cheap and environmentally benign ones. Nature gives here amazing inspirations: Some strains of bacteria can bind nitrogen from the air at ambient temperatures and pressures, and all plants use photosynthesis to bind and react CO_2 to lignocellulosic biomass. This doesn't mean that this is the best way. Bacteria typically grow in dilute solutions, and industry needs large amounts of pure or highly concentrated chemicals. Similarly, growing trees takes years, while companies want to manufacture chemicals in minutes or hours. But nature does show us what is possible when the right catalyst is found.

1.4 Industrial Examples

1.4.1 The BHC Synthesis of Ibuprofen

In 1992, BASF opened a 35,000 tpa ibuprofen production plant in Bishop, Texas. This plant was the result of the elegant green chemistry route developed by the Boots Hoechst Celanese (BHC) consortium. The clean synthesis of ibuprofen is an excellent example of how combining catalysis and green chemistry can yield both commercial success and environmental benefits. Ibuprofen is a nonsteroidal, anti-inflammatory painkiller. It is a popular over-the-counter drug against headache, toothache and muscular pains. You may know it better as Ibux, Advil, Motrin or Nurophen.

Like many other drugs, ibuprofen is a rather simple chemical compound. It was first patented by Boots in 1962. The original production route consisted of six steps, starting from 2-methylpropylbenzene and acetic anhydride. Each of these steps involved additional reagents, many of which are absent from the final product molecule (Figure 1.19, left). The overall atom economy of the process was only 40%. This means that more than half of the materials that entered the process were thrown away as waste (in addition to large amounts of water and salt waste from separation steps). For example, note the addition of hydroxyl amine, NH_2OH, in step 4: This functional group is used to create the imine **7**, which is then converted to the cyano derivative **8** and finally oxidised to give the carboxylic acid product **9**. Effectively, what happens is that the hydroxyl amine is first added to the molecule and then removed and thrown away. This type of 'roundabout synthesis' is precisely what green chemistry aims to avoid.

Ibuprofen quickly became a popular painkiller, and Boots made good profits. But they knew that this would not last forever. Patents give limited protection to their owners, but they also expire after 20 years. When the patent rights on ibuprofen were about to expire, Boots knew that the market would soon be flooded with cheap generic alternatives. Moreover, thanks to strict regulatory procedures, the ibuprofen in the generic pills would be just as good as that in their own, and most customers would opt for the cheaper alternative. Think about it: when you purchase painkillers at the supermarket, do you choose the original brand name, or do you buy the cheaper supermarket brand, which is chemically just as good?

To keep their market share, Boots *had* to innovate. It was not a question of doing something for the environment, but simply a question of economics. Boots teamed with Hoechst Celanese and formed the BHC consortium, developing a new process for making ibuprofen [42]. The consortium started from the same raw materials but replaced the stoichiometric six-step process with a three-step catalytic one (Figure 1.19, right). The overall atom economy of this new process was 77%, with acetic acid as the only by-product. The consortium then also developed methods for recovering and recycling the acetic acid, increasing the atom utilization to 99%, and creating an essentially waste-free synthesis. Using anhydrous hydrogen fluoride (HF) as both catalyst and solvent offers important advantages in reaction selectivity and waste reduction, as the new route also eliminates the large volumes of aqueous salt waste associated with the old ibuprofen manufacturing process.

The BHC ibuprofen process is an innovative, efficient technology that has revolutionized bulk pharmaceutical manufacturing. The process provides an elegant solution to

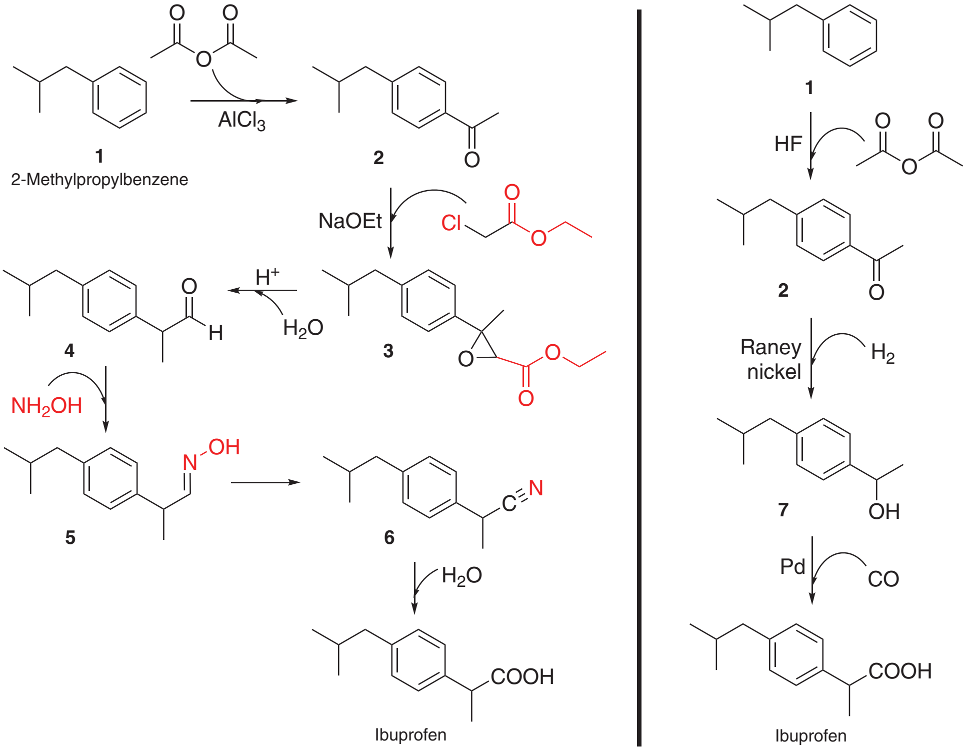

Figure 1.19 Synthesis of ibuprofen: The six-step Boots route (left; additional reagents highlighted in red) and the three-step BHC route (right).

a prevalent problem encountered in bulk pharmaceutical synthesis: It avoids the large quantities of solvents and waste (especially aqueous salt waste streams) associated with the traditional stoichiometric reagent use. The anhydrous HF catalyst is recovered and recycled with greater than 99.9% efficiency. No other solvent is needed in the process, simplifying product recovery and minimising emissions. The new ibuprofen process became a model for environmental excellence in chemical technology, and BHC received the Kirkpatrick Achievement Award for ‘outstanding advances in chemical engineering technology’ in 1993 and the U.S. Presidential Green Chemistry Award in 1997. It was also a commercial success: the BHC consortium sold the process to BASF for more than $100 million.

And a short postscript: In 2013, I was on the train going to the Amsterdam Science Park, and a British gentleman sitting across from me asked, ‘excuse me, but are you a chemist?’ (I was reading the *Journal of Organic Chemistry*, so he less clairvoyant than you might think). I pleaded guilty and we started talking. He was also a chemist, currently working for Philips. We exchanged business cards (this was before QR codes and WeChat), and I looked at his card and said – ‘You’re Graham Mott! You invented the BHC process – I teach about you in my class!’

As coincidence would have it, this was indeed the same man who used to head the R&D division at Hoechst. Graham was surprised (and pleased!) to learn that he was so famous and even agreed to come to our institute’s Christmas Event and tell the story. He gave us a rare view into what went on behind the scenes during the setting up of the consortium and the process development. For example, one of the biggest hurdles was convincing the management of Hoechst Celanese, a company then focused on producing large-scale bulk chemicals and materials, to enter the pharmaceuticals market and manufacture something as esoteric and small-scale as ibuprofen (bulk chemicals are produced in millions of tons, three orders of magnitude larger than medicines). But Boots needed Graham and his team because they wanted the know-how and facilities for using anhydrous HF, which was the key to the new process. Very few companies knew how to do this, and Hoechst was one of them. It all worked out well in the end, and the consortium made a handsome profit. But companies are often wary of entering new markets, especially in cases where there is a mismatch between market sizes.

1.4.2 The BP AVADA Ethyl Acetate Process

Ethyl acetate is a common solvent known since the mid-18th century. It has a fruity odour and is widely used in paints, pharmaceuticals and fragrances. A simple ester, the classic way of making it is by **Fischer esterification** of ethanol and acetic acid (Eq. (1.3)). This is an equilibrium reaction, which gives about 65% of the ester product at room temperature. The reaction can be accelerated by using an acid catalyst, and the equilibrium can be shifted to the right by removing the water by-product. Alternatively, ethyl acetate can also be prepared using the **Tishchenko reaction**, by reacting two equivalents of acetaldehyde in the presence of an alkoxide catalyst (Eq. 1.4).

$$CH_3CO_2H + CH_3CH_2OH \rightleftharpoons CH_3CO_2CH_2CH_3 + H_2O \tag{1.3}$$

$$2CH_3CHO \rightarrow CH_3CO_2CH_2CH_3 \tag{1.4}$$

Both of these reactions rely on liquid acid/base catalysts that result in large aqueous waste streams. For many years, this was not a problem. But in the 1990s, BP Chemicals, one of the large manufacturers of ethyl acetate, underwent restructuring. Business unit managers had to either come up with new technological solutions that would make their units more profitable or close down plants. BP's new AVADA process (AdVanced Acetates by Direct Addition), which went on stream in Hull in a 220 ktpa plant in June 2001, is an excellent example of how combining heterogeneous catalysis and process innovation can create economic value *and* environmental benefits [43]. The process (Figure 1.20) converts ethene and acetic acid directly to ethyl acetate, cutting out the intermediate esterification step and the need for ethanol. Instead of using a liquid Brønsted acid, it uses a solid heteropolyacid, which is supported on porous silica for additional stability. The process gives 99.98% pure ethyl acetate, in what is now the largest EtOAc plant worldwide. Moreover, the simpler design requires fewer operators and saves ~20% on energy costs compared to the conventional routes. In 2002, the AVADA process won the 2002 AstraZeneca Award for Excellence in Green Chemistry and Engineering.

The AVADA process combines several green chemistry principles: It uses simple, non-toxic feedstocks, converting these directly to the desired product. It features 100% atom economy – all of the atoms in the reactants are incorporated in the product. Using a solid catalyst, the process is practically waste-free, avoiding waste stream problems. AVADA is an excellent example of sustainable chemistry. But it also illustrates another

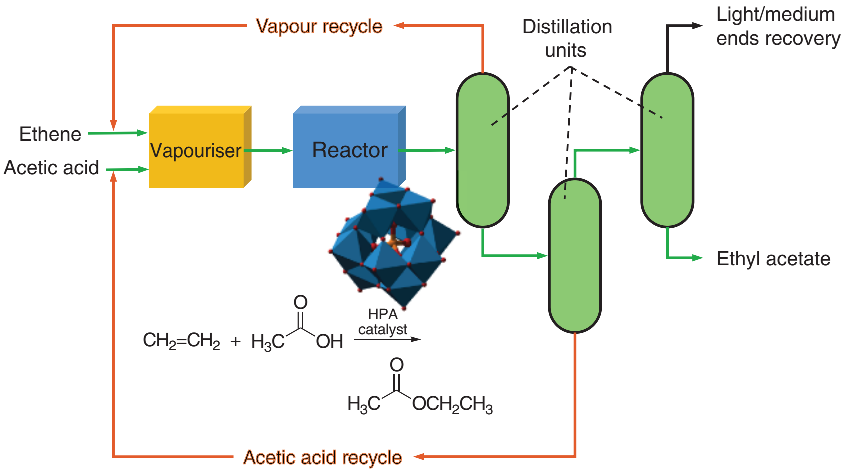

Figure 1.20 Chemical reactions and simplified process schematic for BP's AVADA ethyl acetate process. The exact structure of the catalyst is undisclosed; it is most probably a 'superacid' (a Keggin-type phosphotungstic heteropolyacid, shown in dark blue, with the general formula $H_3PW_nM_{12-n}O_{40}$, wherein M is tungsten or another metal). Such heteropolyacids are used in the laboratory both in solution and as solid salts [44]. Their industrial application is limited, however, due to rapid deactivation [45]. To solve this problem, BP impregnated the heteropolyacid in porous silica beads.

important point: BP developed it purely out of commercial considerations, demonstrating again how economic benefit drives green chemistry.

Exercises

Q1.1
a) Examine the 12 principles of Green Chemistry. Which three of these principles are, in your opinion, the most important ones? Explain your answer (100–150 words).
b) Explain the concepts of E-factor, atom economy, and environmental quotient Q. Discuss and compare these factors for the petrochemical industry and the pharmaceutical industry. Which industry is more sustainable? (100–150 words)
c) Hydroquinone is used in cosmetics as a skin-lightening agent. It can be made by reacting benzoquinone with metallic iron and water (Figure 1.21). Calculate the E-factor for this reaction and estimate its environmental quotient. What type of reaction is this? What is the iron used for in this reaction?

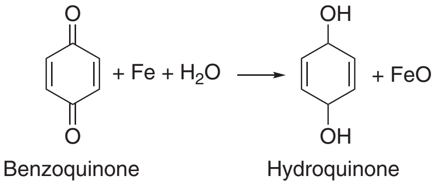

Figure 1.21 The reaction of benzoquinone with metallic iron and water to give hydroquinone.

Q1.2 Polyethylene terephthalate (PET) is the most common ‘plastic’. It has become so thanks to the invention of ZSM-5, a zeolite solid acid catalyst that enabled the selective synthesis of *p*-xylene, the precursor of terephthalic acid.

a) Write down the chemical equation for the acid-catalysed reaction for making xylenes from toluene and methanol.

b) Draw a schematic showing how ZSM-5 catalyses the selective reaction between toluene and methanol to give over 99.99% of *p*-xylene.

c) Explain why this high selectivity is important for the production of PET, and how it contributes to the economic efficiency and sustainability of the process (100–150 words).

Q1.3 In 2008, when the price of crude oil peaked at $110 per barrel, governments and companies looked towards biomass as an alternative source for gasoline and diesel. The transesterification of oils and fats (triglycerides) to fatty acid methyl esters (FAME) was thought to be the answer.

a) List two advantages and two disadvantages of using FAME as biodiesel.

b) Examine the reaction profiles for the acid-catalysed esterification of dodecanoic acid with 2-ethylhexanol shown in Figure 1.22. What is the advantage of using a solid acid as the catalyst in this reaction? What are the disadvantages?

c) Today, governments and companies focus on biofuels made from lignocellulosic material. What caused the shift away from fatty acids towards cellulose and hemicellulose?

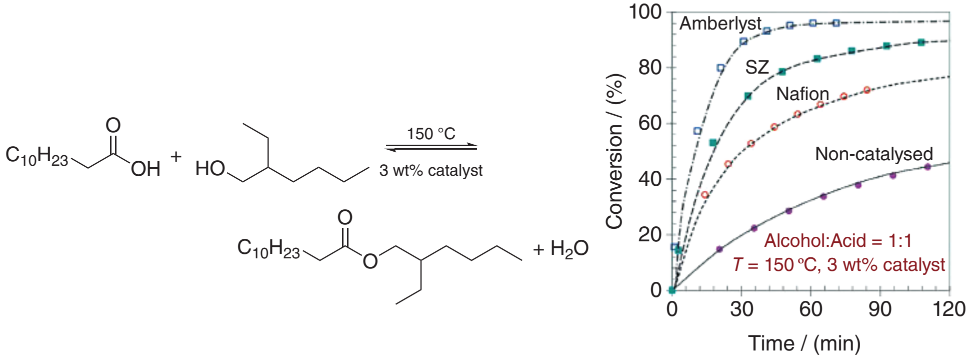

Figure 1.22 Time-resolved reaction profiles for the esterification of dodecanoic acid with 2-ethylhexanol in the presence of different solid acid catalysts. *Source*: [46] / John Wiley & Sons.

Q1.4 Anthropogenic emissions of CO_2 are related to global warming and climate change. In the past decade, annual CO_2 emissions averaged at over 35 Gton per year! There are three main solutions to this problem: burn less fossil carbon, capture the CO_2 and store it somewhere (CCS) or capture the CO_2 and make something from it (CCU).

a) Compare these three options and explain which one is the most suitable in your opinion and why (150–200 words).

b) What are the main challenges for the CCU route? Can you address these challenges using sustainable chemistry? Support your answer with quantitative arguments (150–200 words).

Q1.5 Converting CO_2 emissions back to chemical products is said to be the solution to CO_2 emissions and global warming.

a) Do you think this is true? Explain your answer (100–150 words).

b) Draw a catalytic cycle for converting CO_2 and hydrogen to methanol in the presence of a copper catalyst. Assuming a methanol yield of 100%, calculate the E-factor for this reaction and estimate its environmental quotient Q.

c) There are other greenhouse gases than CO_2. List two of them and suggest how you can convert them into useful products, and which markets you would address.

Q1.6 The Suzuki reaction is a method for coupling organoboronic acids to organohalides. It is typically catalysed by small amounts of homogeneous organometallic Pd complexes and requires water and 1.5–2 equivalents of base. An example is shown in Figure 1.23.

a) Balance the reaction equation and calculate for this example the E-factor and the Atom Economy and estimate the value of the environmental quotient.

b) Suggest two methods for reducing the amount of waste generated by this reaction and explain the pros and cons of each method.

c) Company **A** uses the Suzuki reaction for synthesising a drug for fighting a rare disease. Company **B** uses the reaction for synthesising a pesticide against a bug that attacks bananas. Explain the considerations of each company when choosing their reagents and process in this reaction.

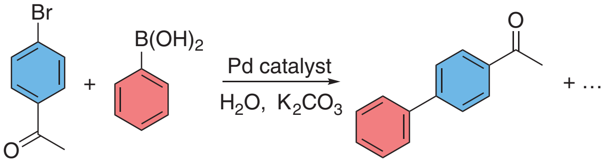

Figure 1.23 The Suzuki cross-coupling of 4-bromoacetophenone with phenylboronic acid.

Q1.7 The hydro-dehalogenation of chlorobenzene with zinc powder and water (Figure 1.24, top) is a method for removing Cl atoms from organics. This reaction gives >99% yield.

a) Balance the reaction equation, calculate its E-factor and Atom Economy, and estimate the value of the environmental quotient.

b) Another version of this reaction uses hydrogen gas as the reducing agent, in the presence of 1 mol% Pt/Al_2O_3 catalyst (Figure 1.24, bottom). This reaction gives 100% conversion, but only 80% yield. Balance the reaction equation and calculate its E-factor and Atom Economy, and estimate the value of the environmental quotient.

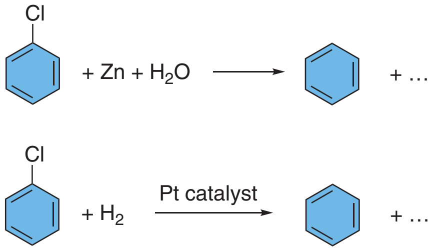

Figure 1.24 Hydro-dehalogenation of chlorobenzene with zinc and water (top) and the Pt-catalysed variant with hydrogen gas (bottom).

c) Compare the two reaction alternatives and explain which one you would use for making a drug on a 500 kg scale and which one you would use for making a pesticide a 10,000-ton scale.

Q1.8 Phenol, C_6H_5OH, is an important bulk chemical, with a worldwide production of 11 million tons in 2024. Today, it is produced almost exclusively via the partial oxidation of cumene (isopropylbenzene, see Eq. (1.1)). This process is used on a multi-million-ton scale per year, yet there are several alternatives. One is the oxidation of toluene, developed by Dow Chemical (Eq. (1.2)).

$$C_6H_5CH(CH_3)_2 + O_2 \rightarrow C_6H_5OH + (CH_3)_2CO \tag{1.5}$$

$$C_6H_5CH_3 + 2O_2 \rightarrow C_6H_5OH + CO_2 + H_2O \tag{1.6}$$

a) Calculate the E-factor and estimate the size of the environmental quotient for both processes.

b) List two advantages and two disadvantages for each process, explaining which process you favour. If you favour the Dow process, how do you explain the fact that over 95% of phenol production worldwide goes via the cumene route?

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