Electric chemistry

We have discovered a smart, green way to choreograph the dance of atoms. **Gege Li** investigates

IT ISN'T long after waking each day that we meet the handiwork of chemists. The flavourings in toothpaste, scents in shower gel, polyester in clothes – all have been created through the breaking and making of chemical bonds. The same goes for nearly all the materials on which the modern world relies.

It isn't easy work. Take remdesivir, the antiviral drug that could help us treat covid-19. To make it, chemists begin with a small molecule called alanine and add a further 64 atoms to it over the course of 25 separate chemical reactions. Whew.

Making such molecular marvels isn't just taxing, it can also be a grubby affair. Synthetic chemists spend most of their time amid pastes, powders and bubbling solutions: it is a messy and often smelly craft.

But perhaps there is a way to make it simpler and cleaner. More and more chemists are experimenting with a new tool of subtle power: the electric field. Not only does it promise to help us control the jiggling of atoms more precisely, but in a world where green credentials are important, it could also make chemical synthesis a lot less damaging to the environment. If this works, chemistry will be transformed.

To see why this new tool is so promising, we need to consider the thing that matters most in any reaction – the flow of electrons. We think of electrons as negatively charged particles that swirl between the positively charged atomic nuclei in a molecule, gluing the atoms together. The job of the synthetic chemist is to cajole this electron glue into flowing from one place to another, and so rearrange and extend the atomic scaffolding to form exciting new substances. To aid this, chemists often pay attention to the polarity of the molecules involved, the overall distribution of positive and negative charge within them. Understand and manipulate this, and you can guide where the glue goes.

Reactions come in many flavours, but often have just a few components. Typically, there is a chemical dissolved in a liquid together with one or more other substances that will join to or change the starting material in some fashion. Then, crucially, there is often a catalyst. These additives make a reaction go faster without being used up themselves in the process. Without them, chemistry can be so sluggish as to be impracticable.

Wonderful as catalysts are, they make life difficult in the lab. They must be made or purified from raw materials, which takes time and often requires energy-intensive processes that belch out carbon dioxide. When the reaction is finished, they must be carefully separated from the product. You must isolate and recycle valuable catalyst and, anyway, you don't want any of it contaminating whatever you have made. All of this is messy, painstaking work.

> **“Heating a reaction can speed it up, but it is a bit of a sledgehammer”**

If we could avoid having to rely on this kind of catalyst, it would be a huge advantage. There are a few old tricks chemists can use to attempt to do this. Heating a reaction usually speeds it up, but as tools go, this is a bit of a sledgehammer that can create undesirable side reactions. Particular wavelengths of light can also kick-start reactions, but only a select few.

Sason Shaik at the Hebrew University of Jerusalem in Israel has been wondering for decades if there might not be a much better trick. As a student in the 1970s, he came across a reaction that used a high concentration of salt as a very effective catalyst. Salts in solution conduct electricity and it struck Shaik that perhaps it was the electric field that was doing the business.

That makes some sense in principle. An electric field is effectively a space in which the electric charge goes from positive at one end to negative at the other. If you could apply an electric field to a molecule, then you might conceivably persuade its electron glue to flow more readily. Flip the orientation of the field and maybe the electrons would flow the other way. Shaik thought that applying an external electric field might speed up a chemical reaction and enable you to decide exactly what it produces. “These are the effects that every chemist would like to control,” he says.

Shaik first tried the idea using computer simulations – and it seemed to work. In 2009, he looked at a stalwart of chemical synthesis, the Diels-Alder reaction, in which two strings of carbon atoms form a ring. He showed that electric fields could quicken the reaction and affect the form of ring produced.

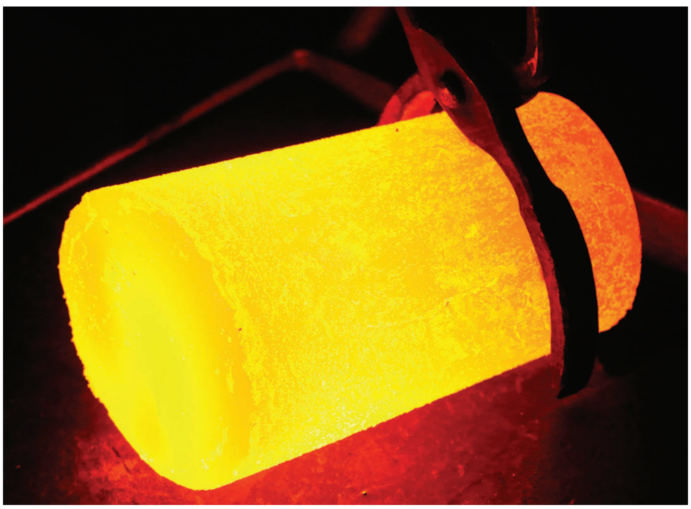
Despite this success, it seemed like little more than a theoretical nicety. In Shaik’s simulations, the alignment between electric field and molecule was crucial to success. In the chaotic reality of a round-bottomed flask, molecules in solution are tumbling around at all angles, meaning that any external electric field would only line up with a fraction of them at any time. For years, it seemed Shaik’s dream catalyst was just that.

However, there is one way to get molecules to lie still: stick them to a surface. In 2016, that is how Michelle Coote at the Australian National University in Canberra managed to test Shaik’s Diels-Alder modelling for real. Working with Nadim Darwish, now at Curtin University in Perth, Australia, Coote and her team fixed a molecule of one substance to a metal surface, and a molecule of a substance they wanted it to react with to the tip of a special type of microscope. In this way, the two molecules were brought together in a controlled fashion in the presence of an electric field. When the field’s voltage was increased, the molecules snapped together more quickly. “It was totally consistent with what you’d expect if an electrical field was catalysing this reaction,” says Coote.

This proved to be a watershed moment. “It really broke the ice,” says Shaik. “Many chemists started seeing that these ideas derived from theory were not just a daydream, but something that creative chemists could do in the lab.” One of them is Ayan Datta at the Indian Association for the Cultivation of Science in Kolkata, who has begun exploring whether a wider range of reactions can be catalysed by electric fields. He recently simulated their effects on a reaction that is widely used in all sorts of synthetic chemistry. Applying the field lowered the energy needed to get the reaction going so much that it would happen at least twice as fast.

Still, none of this optimism gets around the impracticality of the method. In Coote’s work, the microscope tip worked on one molecule at a time. If we wanted to make a single gram of a typical-sized drug molecule in this way, we would have to work our way through 10^{21} molecules, which, at a rate of one per second, would take more than a trillion years. We need a better way of making these fields spark into action.

Several years ago, Matthew Kanan at



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Expensive metals like palladium are often used as catalysts

ANNA IVANOVA/ALAMY

Electric catalysis could make industrial processes greener

Stanford University in California created a small device in which a solution of chemicals flows continuously along a thin channel that passes through an electric field between two electrodes. He reported that this boosted the rate of reaction and that flipping the polarity of the field changed the product of that reaction. This suggested a much better method than Coote's use of a microscope. But Kanan hasn't pursued the idea and says there are still "substantial technical challenges".

Coote hasn't given up. Over the past few years, she has been exploring another way to harness electric fields in grand style – this time using a phenomenon most of us have experienced: static electricity. As you will know if you have ever rubbed a balloon against fabric and then held it to your hair, static electricity builds up when certain materials rub together and electrons are transferred from one to the other, creating an electric field.

Coote and her colleague Simone Ciampi, also at Curtin University, have been experimenting with this hair-raising stuff for a while. They take thin sheets of plastic, up to 1 metre across, and charge them by rubbing them together for a few seconds. They then put the sheets on a system of rollers that dips them through half-litre containers of reacting solution. In unpublished experiments, the pair have shown that these charged surfaces can catalyse reactions that involve the transfer of an electron from one molecule to another.

It is early days, but Ciampi says the method could "undoubtedly" be scaled up to industrial-sized reactors. It could also be made easier and more effective, perhaps by using not sheets, but rods, with one end of each dipped in the solution, the other rubbed to charge it up continuously. Another idea is to drip solutions onto the plastic sheets so they spread out and get more sustained contact with the static electric field.

All this suggests the problem with getting individual tumbling molecules to align with the electric field isn't the showstopper we once thought, according to Ciampi. This is because, first, some of the molecules will be randomly aligned with the field anyway, and the larger the statically charged surface and the longer you leave it, the more molecules that will apply to. Second, we are starting to find that, as the molecules approach the charged surface, they tend to align themselves with it anyway.

If electric catalysis does become a mainstream tool in chemistry, its green credentials will be most welcome. That is certainly why Datta is primarily interested. Regular catalysts are often metals – expensive and sometimes poisonous – that have to be carefully removed from reaction mixtures and ultimately disposed of. With an electric field, none of that is needed. "The good thing is you can just switch the field off," says Datta. "It's a much more clean and green way to do reactions."

Shaik is also hoping electric fields could provide solutions to truly knotty chemical problems, such as how to break down certain types of plastic for recycling. "Right now, it's a mess, there are no good methods," he says.

For her part, Coote is optimistic about the future role of electric fields in chemistry. Because all molecules have some degree of electric polarity, "catalysing reactions with electric fields is something that could be done for anything", she says. It may be several years before we get to that point, but in the meantime, electric fields might just make the work of the chemist a little less messy. ■

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