

Forbidden chemistry

Extended version of an article published in *New Scientist*, 21 January 2012

The award of the 2011 Nobel prize for chemistry to Dan Shechtman for discovering quasicrystals allowed reporters to relish tales of experts being proved wrong. For his heretical suggestion that the packing of atoms in crystals can have a kind of fivefold (quasi)symmetry, Shechtman was ridiculed and ostracized and almost lost his job. The eminent chemist Linus Pauling derided him as a “quasi-scientist”.

Pauling of all people should have known that sometimes it is worth risking being bold and wrong, as he was himself with the structure of DNA in the 1950s. As it turned out, Shechtman was bold and right: quasicrystals do exist, and they earn their ‘impossible’ fivefold symmetry at the cost of not being fully ordered: not truly crystalline in the traditional sense. But while everyone enjoys seeing experts with egg on their faces, there’s a much more illuminating way to think about apparent violations of what is ‘possible’ in chemistry.

Here are some other examples of chemical processes that seemed to break the rules – reactions that ‘shouldn’t’ happen. They demonstrate why chemistry is such a vibrant, exciting science: because it operates on the borders of predictability and certainty. The laws of physics have an air of finality: they don’t tolerate exceptions. No one except cranks expects the conservation of energy to be violated. In biology, in contrast, ‘laws’ seem destined to have exceptions: even the heresy of inheritance of acquired characteristics is permitted by epigenetics. Chemistry sits in the middle ground between the rigidity of physics and the permissiveness of biology. Its basis in physics sets some limits and constraints, but the messy diversity of the elements can often transcend or undermine them.

That’s why chemists often rely on intuition to decide what should or shouldn’t be possible. When his postdoc student Xiao-Dong Wen told Nobel laureate Roald Hoffmann that his computer calculations found graphane – puckered sheets of carbon hexagons with hydrogens attached, with a C:H ratio of 1:1 – was more stable than familiar old benzene, Hoffmann insisted that the calculations were wrong. The superior stability of benzene, he said, “is sacrosanct - it’s hard to argue with it”. But eventually Hoffmann realized that his intuition was wrong: graphane *is* more stable, though no one has yet succeeded in proving definitively that it can be made.

You could say that chemistry flirts with its own law-breaking inclinations. Chemists often speak of reactions that are ‘forbidden’. For example, symmetry-forbidden reactions are ones that break the rules formulated by Hoffmann in his Nobel-winning work with organic chemist Robert Woodward in 1965 – rules governed by the mathematical symmetry properties of electron orbitals as they are rearranged or recombined by light or heat. Similarly, reactions that fail to conserve the total amount of ‘spin’, a quantum-mechanical property of electrons, are said to be spin-forbidden. And yet neither of these types of ‘forbidden’ reaction is impossible – they merely happen at slower rates. Hoffmann says that

he (at Woodward's insistence) even asserted in their 1965 paper that there were no exceptions to their rules, knowing that this would spur others into finding them.

So this gallery of 'reactions they said couldn't happen' is not a litany of chemists' conservatism and prejudice (although – let's be honest – that sometimes played a part). It is a reflection of how chemistry itself exists in an unstable state, needing an intuition of right and wrong but having constantly to readjust that to the lessons of experience. That's what makes it exciting – it's not the case that *anything might happen*, but nevertheless big surprises certainly can. That's why, however peculiar the claim, the right response in chemistry, perhaps more than any other branch of science, is not "that's impossible", but "prove it".

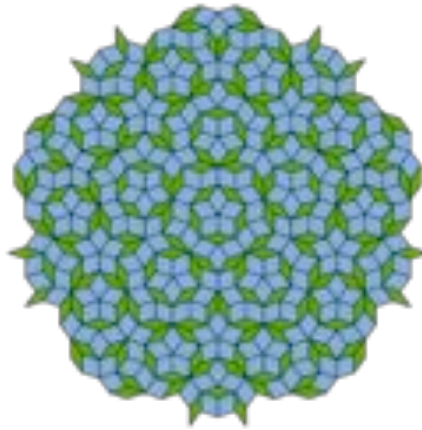
Crazy tiling

In the early 1980s, Daniel Shechtman was bombarding metal alloys with electrons at the then National Bureau of Standards (NBS) in Gaithersburg, Maryland. Through mathematical analysis of the interference patterns formed as the beams reflected from different layers of the crystals, it was possible to determine exactly how the atoms were packed.

Among the alloys Shechtman studied, a blend of aluminium and manganese produced a beautiful pattern of sharp diffraction spots, which had always been found to be an indicator of crystalline order. But the crystal symmetry suggested by the pattern didn't make sense. It was fivefold, like that of a pentagon. One of the basic rules of crystallography is that atoms can't be packed into a regular, repeating arrangement with fivefold symmetry, just as pentagons can't tile a floor in a periodic way that leaves no gaps.

Pauling wasn't the only fierce critic of Shechtman's claims. When he persisted with them, his boss at NBS asked him to leave the group. And a paper he submitted in the summer of 1984 was rejected immediately. Only when he found some colleagues to back him up did he get the results published at the end of that year.

Yet the answer to the riddle they posed had been found already. In the 1970s the mathematician Roger Penrose had discovered that two rhombus-shaped tiles could be used to cover a flat plane without gaps and without the pattern ever repeating. In 1981, the crystallographer Alan Mackay found that if an atom were placed at every vertex of such a Penrose tiling, it would produce a diffraction pattern with fivefold symmetry, even though the tiling itself was not perfectly periodic. Shechtman's alloy was analogous to a three-dimensional Penrose tiling. It was not a perfect crystal, because the atomic arrangement never repeated exactly; it was a quasicrystal.



A Penrose tiling fills a plane without gaps and without the pattern ever repeating. It has fivefold quasi-symmetry.

Since then, many other quasicrystalline alloys have been discovered. They, or structures very much like them in polymers and assemblies of soap-like molecules called micelles. It has even been suggested that water, when confined in very narrow slits, can freeze into quasicrystalline ice.

You can't have it both ways

For poor Boris Belousov, vindication came too late. When he was awarded the prestigious Lenin prize by the Soviet government in 1980 for his pioneering work on oscillating chemical reactions, he had already been dead for ten years.

Still, at least Belousov lived long enough to see the scorn heaped on his initial work turn to grudging acceptance by many chemists. When he discovered oscillating chemical reactions in the 1950s, he was deemed to have violated one of the most cherished principles of science: the second law of thermodynamics.

This states that all change in the universe must be accompanied by an increase in entropy – crudely speaking, it must leave things less ordered than they were to begin with. Even processes that seem to create order, such as the freezing of water to ice, in fact promote a broader disorder – here by releasing latent heat into the surroundings. This principle is what prohibits many perpetual motion machines (others violate the first law – the conservation of energy – instead).

Violations of the second law are thus something that only cranks propose. But Belousov was no crank. He was a respectable Russian biochemist interested in the mechanisms of metabolism, and specifically in glycolysis: how enzymes break down sugars. To study this process, Belousov devised a cocktail of chemical ingredients that should act like a simplified analogue of glycolysis. He shook them up and watched as the reaction proceeded, turning from clear to yellow.

Then it did something astonishing: it went clear again. Then yellow. Then clear. It began to oscillate repeatedly between these two coloured states. The problem is that entropy can't possibly increase in *both* directions. So what's up?

Belousov wasn't actually the first to see an oscillating reaction. In 1921 American chemist William Bray reported oscillations in the reaction of hydrogen peroxide and iodate ions. But no one believed him either, even though the ecologist Alfred Lotka had shown in 1910 how oscillations could arise in a simple, hypothetical reaction. As for Belousov, he couldn't get his findings published anywhere, and in the end he appended them to a paper in a Soviet conference proceedings on a different topic: a Pyrrhic victory, since they then remained almost totally obscure.

But not quite. In the 1960s another Soviet chemist, Anatoly Zhabotinsky, modified Belousov's reaction mixture so that it switched between red and blue. That was pretty hard for others to ignore. The Belousov-Zhabotinsky (BZ) reaction became recognized as one of a whole class of oscillating reactions, and after it was transmitted to the West in a meeting of Soviet and Western scientists in Prague in 1967, these processes were gradually explained.

They don't violate the second law after all, for the simple reason that the oscillations don't last forever. Left to their own devices, they eventually die away and the reaction settles down to an unchanging state. They exist only while the reaction approaches its equilibrium state, and are thus an out-of-equilibrium phenomenon. Since thermodynamics speaks only about equilibrium states and not what happens en route to them, it is not threatened by oscillating reactions.

The oscillations are the result of self-amplifying feedback. As the reaction proceeds, one of the intermediate products (call it A) is autocatalytic: it speeds up the rate of its own production. This makes the reaction accelerate until the reagents are exhausted. But there is a second autocatalytic process that consumes A and produces another product, B, which kicks in when the first process runs out of steam. This too quickly exhausts itself, and the system reverts to the first process. It repeatedly flips back and forth between the two reactions, over-reaching itself first in one direction and then in the other. Lotka showed that the same thing can happen in populations of predators and their prey, which can get caught in alternating cycles of boom and bust.

If the BZ reaction is constantly fed fresh reagents, while the final products are removed, the oscillations can be sustained indefinitely: it remains out of equilibrium. Such oscillations are now known to happen in many chemical processes, including some industrially important reactions on metal catalysts and even in real glycolysis and other biochemical processes. If it takes place in an unstirred mixture, the BZ oscillations can spread from initiating spots as chemical waves, giving rise to complex patterns. Related patterns are the probable cause of many animal pigmentation markings. BZ chemical waves are analogues of the waves of electrical excitation that pass through heart tissue and induce regular heartbeats; if they are disturbed, the waves break up and the result can be a heart attack.



Patterns formed by chemical waves in the Belousov-Zhabotinsky reaction. Photo: Stephen Morris, University of Toronto.

These waves might also form the basis of a novel form of computation. Andrew Adamatsky at the University of the West of England in Bristol is using their interactions to create logic gates, which he believes can be miniaturized to make a genuine “wet” chemical computer. He and collaborators in Germany and Poland have launched a project called NeuNeu to make chemical circuits that will crudely mimic the behaviour of neurons, including a capacity for self-repair.

The quantum escape clause

It's very cold in space. So cold that molecules encountering one another in the frigid molecular clouds that pepper the interstellar void should generally lack enough energy to react. In general, reactions proceed via the formation of high-energy intermediate molecules which then reconfigure into lower-energy products. Energy (usually thermal) is needed to get the reactants to get over this barrier, but in space there is next to none.

In the 1970s a Soviet chemist named Vitali Goldanski challenged that dogma. He showed that, with a bit of help from high-energy radiation such as gamma-rays or electron beams, some chemicals could react even when chilled by liquid helium to just four degrees above absolute zero – just a little higher than the coldest parts of space. For example, under these conditions Goldanski found that formaldehyde, a fairly common component of molecular clouds, could link up into polymer chains several hundred molecules long. At that temperature, conventional chemical kinetic theory suggested that the reaction should be so slow as to be virtually frozen.

Why was it possible? Goldanski argued that the reactions were getting help from quantum effects. It is well known that particles governed by quantum rules can get across energy barriers even if they don't appear to have enough energy to do so. Instead of going over the top, they can pass through the barrier, a process

known as tunnelling. It's possible because of the smeared-out nature of quantum objects: they aren't simply *here* or *there*, but have positions described by a probability distribution. A quantum particle on one side of a barrier has a small probability of suddenly and spontaneously turning up on the other side.

Goldanski saw the signature of quantum tunnelling in his ultracold experiments in the lab: the rate of formaldehyde polymerization didn't steadily increase with temperature, as conventional kinetic theory predicts, but stayed much the same as the temperature rose.

Goldanski believed that his quantum-assisted reactions in space might have helped the molecular building blocks of life to have assembled there from simple ingredients such as hydrogen cyanide, ammonia and water. He even thought they could help to explain why biological molecules such as amino acids have a preferred 'handedness'. Most amino acids have so-called chiral carbon atoms, to which four different chemical groups are attached, permitting two mirror-image variants. In living organisms these amino acids are always of the right-handed variety, a long-standing and still unexplained mystery. Goldanski argued that his ultracold reactions could favour one enantiomer over the other, since the tunnelling rates might be highly sensitive to tiny biasing influences such as the polarization of radiation inducing them.

Chemical reactions assisted by quantum tunnelling are now well established – not just in space, but in the living cell. Some enzymes are more efficient catalysts than one would expect classically, because they involve the movement of hydrogen ions – lone protons, which are light enough to experience significant quantum tunnelling.

This counter-intuitive phenomenon can also subvert conventional expectations about what the products of a reaction will be. That was demonstrated very recently by Wesley Allen of the University of Georgia and his coworkers. They trapped a highly reactive free-radical molecule called methylhydroxycarbene, which has unpaired electrons that predispose it to react fast, in an inert matrix of solid argon at 11 degrees Kelvin. This molecule can in theory rearrange its atoms to form vinyl alcohol or acetaldehyde. In practice, however, it shouldn't have enough energy to get over the barrier to these reactions under these ultracold conditions. But the carbene was transformed nonetheless – because of tunnelling.

"Tunnelling is not specifically a low-temperature phenomenon", Allen explains. "It occurs at all temperatures. But at low temperatures the thermal activation shuts off, so tunnelling is all that is left."

What's more, although the formation of vinyl alcohol has a lower energy barrier, Allen and colleagues found that most of the carbene was transformed instead to acetaldehyde. That defied kinetic theory, which says that the lower the energy barrier to the formation of a product, the faster it will be produced and so the more it dominates the resulting mixture. The researchers figured that although

the barrier to formation of acetaldehyde may have been higher, it was also narrower, which meant that it was easier to tunnel through.

Tunnelling through such high barriers as these “was quite a shock to most chemists”, says Allen. He says the result shows that “tunnelling is a broader aspect of chemical kinetics that has been understood in the past”.

Not so noble

Dmitri Mendeleev’s first periodic table in 1869 didn’t just have some gaps for yet-undiscovered elements. It had a whole *column* missing: a whole family of chemical elements whose existence no one suspected. The lightest of them – helium – was discovered that very same year, and the others began to turn up in the 1890s, starting with argon. The reason they took so long to surface, even though they are abundant (helium is the second most abundant element in the universe) is that they don’t do anything: they are inert, “noble”, not reacting with other elements.

That supposed unreactivity was tested with every extreme chemists could devise. Just after the noble gas argon was discovered in 1894, the French chemist Henri Moissan mixed it with fluorine, the viciously reactive element that he had isolated in 1886, and sent sparks through the mixture. Result: nothing. By 1924, the Austrian chemist Friedrich Paneth pronounced the consensus: “the unreactivity of the noble gas elements belongs to the surest of all experimental results.” Theories of chemical bonding seemed to explain why that was: the noble gases had filled shells of electrons, and therefore no capacity for adding more by sharing electrons in chemical bonds.

Linus Pauling, the chief architect of those theories, didn’t give up. In the 1930s he blagged a rare sample of the noble gas xenon and persuaded his colleague Don Yost at Caltech to try to get it to react with fluorine. After more cooking and sparking, Yost had succeeded only in corroding the walls of his supposedly inert quartz flasks.

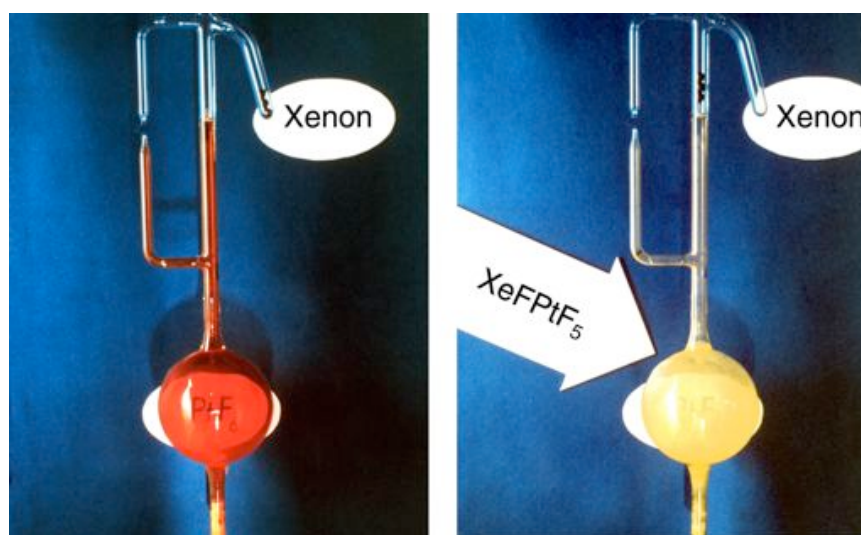
Against this intransigent background, it was either a brave or foolish soul who would still try to make compounds from noble gases. But the first person to do so, British chemist Neil Bartlett at the University of British Columbia in Vancouver, was not setting out to be an iconoclast. He was just following some wonderfully plain reasoning.

In 1961 Bartlett discovered that the compound platinum hexafluoride (PtF_6), first made three years earlier by US chemists, was an eye-wateringly powerful oxidant. Oxidation – the removal of electrons from a chemical element or compound – is so named because its prototypical form is the reaction with oxygen gas, a substance almost unparalleled in its ability to grab electrons. But Bartlett found that PtF_6 can out-oxidize oxygen itself.

In early 1962 Bartlett was preparing a standard undergraduate lecture on inorganic chemistry and happened to glance at a textbook graph of ‘ionization

potentials' of substances: how much energy is needed to remove an electron from them. He noticed that it takes almost exactly the same energy to ionize – that is, to oxidize – oxygen molecules as xenon atoms. He realised that if PtF_6 can do it to oxygen, it should do it to xenon too.

So he tried the experiment, simply mixing red gaseous PtF_6 and colourless xenon. Straight away, the glass was covered with a yellow material, which Bartlett found to have the formula XePtF_6 : the first noble-gas compound.



Xenon and platinum hexafluoride (red, left) react spontaneously to form yellow XePtF_6 (right), the first xenon compound to be discovered.

Since then, many other compounds of both xenon and krypton, another noble gas, have been made. Some are explosively unstable: Bartlett nearly lost an eye studying xenon dioxide. Heavy, radioactive radon forms compounds too, although it wasn't until 2000 that the first compound of argon was reported by a group in Finland. Even now, the noble gases continue to produce surprises. Roald Hoffmann admits to being shocked when, in that same year, a compound of xenon and gold was reported by chemists in Berlin – for gold is supposed to be a noble, unreactive metal too. You can persuade elements to do almost anything, it seems.

Improper bonds

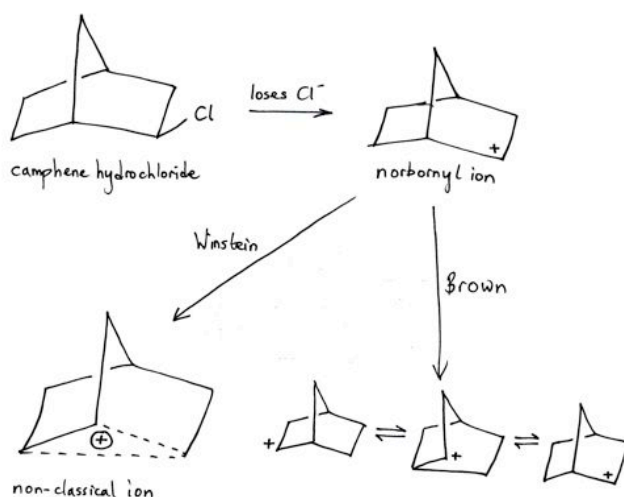
Covalent chemical bonds form when two atoms share a pair of electrons, which act as a glue that binds the union. At least, that's what we learn at school. But chemists have come to accept that there are plenty of other ways to form bonds.

Take the hydrogen bond – the interaction of electron 'lone pairs' on one atom such as oxygen or nitrogen with a hydrogen atom on another molecular group with a slight positive charge. This interaction is now acknowledged as the key to water's unusual properties and the glue that sticks DNA's double helix together. But the formation of a second bond by hydrogen, supposedly a one-bond atom, was initially derided in the 1920s as a fictitious kind of chemical "bigamy".

That, however, was nothing compared to the controversy that surrounded the notion, first put forward in the 1940s, that some organic molecules, such as 'carbocations' in which carbon atoms are positively charged, could form short-lived structures over the course of a reaction in which a pair of electrons was dispersed over three rather than two atoms. This arrangement was considered so extraordinary that it became known as non-classical bonding.

The idea was invoked to explain some reactions involving the swapping of dangling groups attached to molecules with bridged carbon rings. In the first step of the reaction, the 'leaving group' falls off to create an intermediate carbocation. By rights, the replacement dangling group, with an overall negative charge, should have attached at the same place, at the positively charged atom. But it didn't: the "reactive centre" of the carbocation seemed able to shift.

Some chemists, especially Saul Winstein at the University of California at Los Angeles, argued that the intermediate carbocation is bridged by a non-classical bond that bridged three carbon atoms in a triangular ring, with its positive charge smeared between them, giving the replacement group more than one place to dock. This bonding structure would temporarily, and rather heretically, give one of the carbon atoms five instead of the usual four bonding partners.



Such an unusual kind of bonding offended the sensibilities of other chemists, most of all Herbert Brown, who was awarded a Nobel prize in 1979 for his work on boron compounds. In 1961 he opened the "non-classical ion" war with a paper dismissing proposals for these structures as lacking "the same care and same sound experimental basis as that which is customary in other areas of experimental organic chemistry". The ensuing arguments raged for two decades in what Brown called a "holy war". "By the time the controversy sputtered to a halt in the early 1980s", says philosopher of chemistry William Goodwin of Rowan University in New Jersey, "a tremendous amount of intellectual energy, resources, and invective had been invested in resolving an issue that was crucial neither to progress in physical organic chemistry generally nor to the subfield of carbocation chemistry." Both sides accused the rival theory of being 'soft' – able to fit any result, and therefore not truly scientific.

Brown and his followers didn't object in principle to the idea of electrons being smeared over more than two atomic nuclei – that happened in benzene, after all. But they considered the nonclassical ion an unnecessary and faddish imposition for an effect that could be explained by less drastic, more traditional means. The argument was really about how to interpret the experiments that bore on the matter, and it shows that, particularly in chemistry, it could and still can be very hard to apply a kind of Popperian falsification to distinguish between rival theories. Goodwin thinks that the non-classical ion dispute was provoked and sustained by ambiguities built into the way organic chemists try to understand and describe the mechanisms of their reactions. "Organic chemists have sacrificed unambiguous explanation for something much more useful – a theory that helps them make plausible, but fallible, assessments of the chemical behavior of novel, complex compounds", he says. As a result, chemistry is naturally prone to arguments that get resolved only when one side or the other runs out of energy – or dies.

The non-classical ion argument raged for two decades, until eventually most chemists except Brown accepted that these ions were real. Ironically, in the course of the debate both Winstein and Brown implied to a young Hungarian emigré chemist, George Olah, that his claim to have isolated a relatively long-lived carbocation – a development that ultimately helped resolve the issue – was unwise. This was another 'reaction that couldn't happen', they advised – the ions were too unstable. But Olah was right, and his work on carbocations earned him a Nobel prize in 1994.