

A smart use of high-pressure carbon dioxide may make a special class of eco-friendly solvents known as ionic liquids much more attractive to the fine chemical industry. Researcher Dr. Maaïke Kroon has demonstrated that, on paper at least, the savings can be astronomical.

DAP HARTMANN

Carbon dioxide switching puts ionic liquid on the map

The ideal solution

Molten salt

The first ionic liquid was discovered in 1914 by a Latvian chemical engineer, Paul Walden. This was ethyl ammonium nitrate, which has a melting point of 12 degrees Celsius. Walden called it a 'molten salt'; the term 'ionic liquid' wasn't coined till much later. Ionic liquids were initially used as electrolytes (in wet and dry batteries) and for electrolysis purposes. However, some useful applications remained undiscovered at the time, such as the production of metallic magnesium from magnesium chloride ($MgCl_2$). In 1833 Michael Faraday managed to make metallic magnesium through electrolysis of liquid magnesium chloride. The problem is that the melting point of $MgCl_2$ is 714 degrees Celsius. The electrolysis of $MgCl_2$ in water is not an option, because magnesium immediately reacts with the water to form magnesium hydroxide, $Mg(OH)_2$. In an ionic liquid, magnesium chloride dissolves at room temperature. Electrolysis can then be used to produce metallic magnesium. This saves a lot of energy and produces no harmful vapours. Nevertheless, magnesium is still being produced by melting magnesium chloride. Obviously, this takes place mostly in countries where electricity is very cheap, such as Scandinavia.

The pharmaceutical industry is suffering from a bad public image. It uses up large amounts of energy and produces more waste than any other type of industry. On average, each kilo of useful product produces between 25 and 100 kilos of waste, and requires from 50 to 200 megajoules of energy – enough to boil 150 to 600 litres of water. In fact, the production of drugs generates a thousand times as much waste as the petrochemical industry does, and it uses twenty times as much energy.

The main culprits are the vast quantities of solvents used by the fine chemical process industry. Most of the chemical reactions take place in organic solvents such as methanol and acetone. Separating the reaction product from the solvent uses up lots of energy and produces lots of waste.

It will hardly come as a surprise that researchers have been looking for years to find more eco-friendly alternatives. Ever since the nineteen-nineties, much of the research effort has been directed towards the so-called ionic liquids. These liquids could well turn out to be the green alternative to organic solvents. Ionic liquids are salts that are liquid at room temperature. They consist of large, asymmetrical ion carrying positive and negative charges that remain liquid because they do not easily form crystal lattices. This also gives them a great advantage over organic solvents: ionic liquids do not evaporate. As soon as a negative-charge ion (anion) escapes, the positive charge of the remaining liquid pulls it back in again. This means that no solvent is wasted and that the air does not get polluted.

Another major benefit is the versatility of ionic liquids as solvents. Chemicals normally dissolve only in a solvent whose molecular structure is closely related. For example, fats dissolve readily in alkanes (saturated hydrocarbons) because both are apolar, and cooking salt dissolves in water because both molecules have a positive and a negative pole, which makes them both polar. But what if you want to make a polar chemical react with an apolar chemical? This is where ionic liquids come

in useful. "Ionic liquids can dissolve both polar and apolar chemicals," says Maaïke Kroon. "They enable chemicals that wouldn't normally mix to be brought together in a single phase to allow them to mix at a molecular level and react with each other."

Art

The number of possible ionic liquids is practically unlimited, as any combination between a positively charged ion (cation) and an anion produces an ionic liquid. The art lies in finding combinations with the right properties. "By now some 250 ionic liquids have been researched in depth," Kroon explains. "We are trying to find the link between the structure of such a salt and its properties. It will enable us to design custom ionic liquids with properties that enable it to do exactly what's needed." The main properties involved are solubility and thermal and electrochemical stability. Kroon: "You're looking for an ionic liquid that is not volatile, flammable, or poisonous, and which breaks down naturally." To make an ionic liquid useful to the chemical industry, it is also essential to know which

This could be the green alternative to organic solvents

chemicals do and which don't dissolve in the ionic liquid. "I have developed theoretical models that will let me design an ionic liquid in which the reagents will dissolve whereas the reaction product will not. The product will simply come floating to the surface, where it can easily be separated." Naturally, the industry's interest in the use of ionic liquids as 'green solvents' has been increasing. But things can get even better. The disadvantage of the current processes with ionic liquids is that they

25 Years old and a Ph.D. with honours

At the tender age of 25 Maaïke Kroon boasts an impressive scientific record: ten scientific articles, thirteen conference papers, a patent, and of course, her Ph.D. which she gained with honours in two years.

Kroon began her study of chemical technology and bioprocess technology at TUD in September 1999. She gained her bachelor's (2002) and master's (2004) degrees with honours as well. She did laboratory research at Purac, did conceptual process design at Shell, and completed an internship at Toshiba (in Tokyo). She also attended an honours track in innovation management at the faculty of Technology, Policy, and Management. In December 2006 she gained her Ph.D. supervised by Dr. Cor Peters and Prof. Dr. Geert-Jan Witkamp, the latter of whom has referred to Kroon as "the brightest student I have ever met".

Her current place of residence is Barcelona, where she will spend a year delving into nanotechnology. Afterwards she will go to Delft, where she has been given a position as lecturer.

are slow, which is caused in particular by the fact that several production stages are involved, with some time-consuming intermediate stages (see illustration on pages 14-15).

Maaïke Kroon has discovered a way of speeding up the reaction process. During her promotion research she developed a method in which the reactions and separations take place in a single homogeneous solution. Since all the reactants are dissolved in a single phase, the reaction rate increases considerably. This makes the use of 'green solvents' a lot more attractive.

Supercritical

The key to the secret is carbon dioxide (CO_2), which, when added under high pressure to an ionic liquid, increases the solubility of certain chemicals. The CO_2 is in the so-called 'supercritical phase', a phase state in which there is no longer any difference between liquid and gas.

There is another advantage to using supercritical carbon dioxide. In the production process it can be used as a kind of switch between the various production stages. Once the reaction is completed, the pressure is lowered, and two phases are formed, the ionic liquid with the catalyst, and the supercritical CO_2 with the end product (see illustration, pages 14-15). Lowering the pressure even more will cause the CO_2 to evaporate, leaving only the product. The CO_2 can be repressurised, so it can be used again and again, as can the ionic liquid and the catalyst.

How big the consequences could be for the process industry became clear when in the course of her Ph.D. research Kroon investigated the effect of the new process on the production of Levodopa, a drug that is used to treat the symptoms of Parkinson's disease. The production of Levodopa currently involves ten process steps, all of which use energy and produce waste. In one of these steps, a reaction takes place between a solid and hydrogen, with methanol as the solvent. For each



kilo of (intermediate) product, the process step uses 17 megajoules of energy, producing 3 kilos of waste material (methanol and catalyst). Using ionic liquids, the same step would use less than a third of the energy, and produce no waste. Worldwide on a yearly basis, this would save 20,000 gigajoules of energy, 4800 tons of methanol, and 480 kilos of catalyst, Kroon calculated.

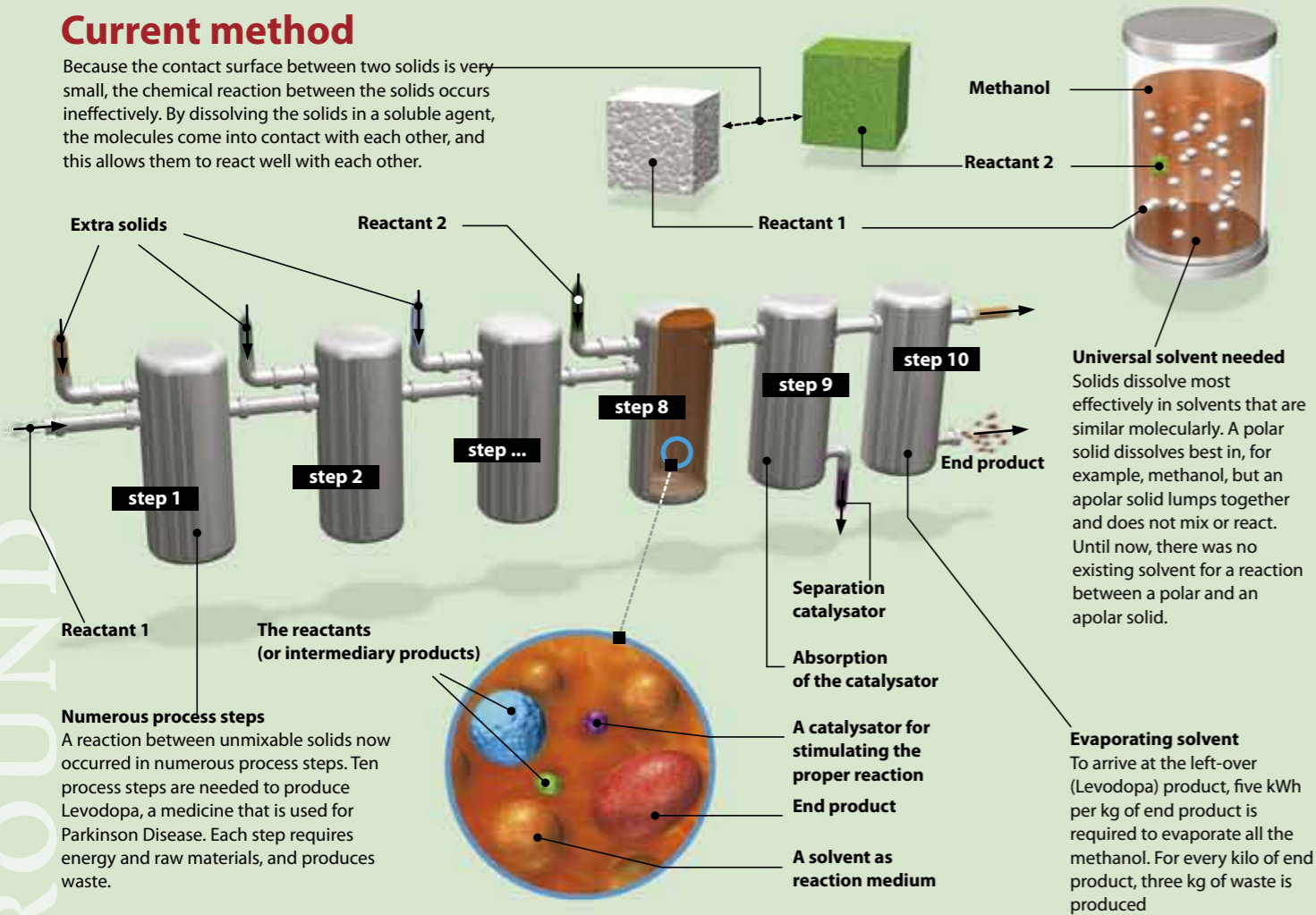
The process has already been patented. Kroon: "Of course, the new technology looks fine in a laboratory environment, but I want it to be used in the real world of the fine chemical industry."

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Current method

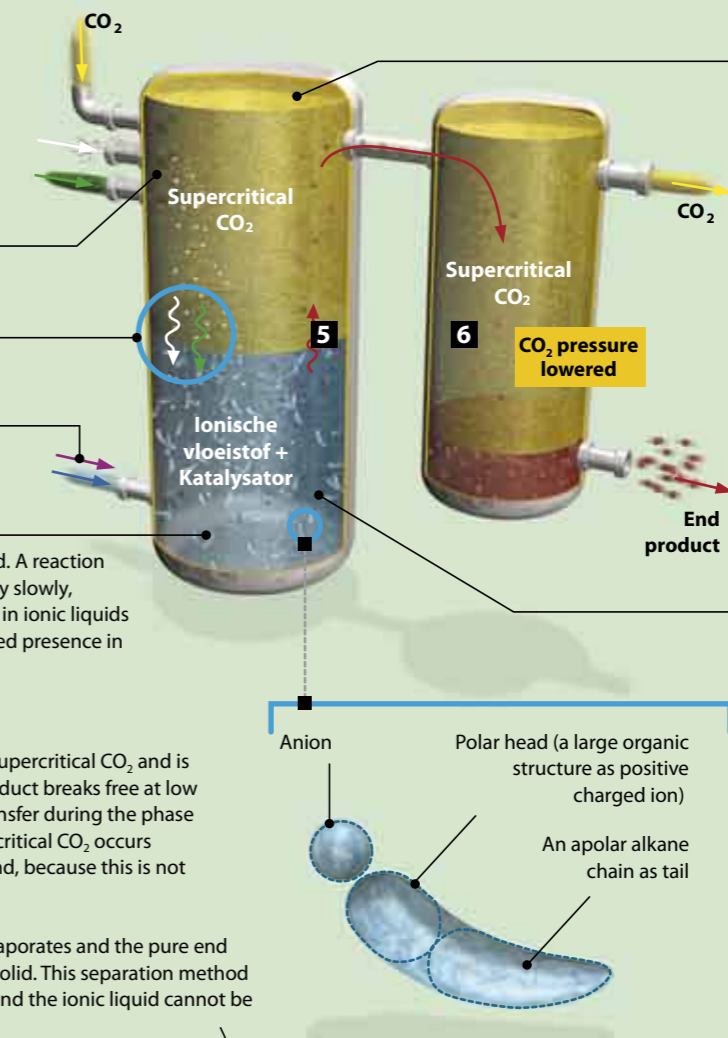
Because the contact surface between two solids is very small, the chemical reaction between the solids occurs ineffectively. By dissolving the solids in a soluble agent, the molecules come into contact with each other, and this allows them to react well with each other.



Two-phase process

The combination of ionic liquids and supercritical CO₂ is an existing method for a two-phase-reaction procedure.

- The reactants flow into the reactor chamber
- The reactants dissolve in the ionic liquid
- The catalyst is added and dissolves in the ionic liquid
- Ionic liquid-phase**
The reaction occurs in the ionic liquid. A reaction between a gas and a solid occurs very slowly, because a gas does not dissolve well in ionic liquids and therefore has an extremely limited presence in the ionic salt.
- Supercritical CO₂-phase**
The end product is dissolved in the supercritical CO₂ and is transported by the CO₂. The end product breaks free at low rates of speed, because the mass-transfer during the phase transition from ionic liquid to super-critical CO₂ occurs slowly. The catalyst remains behind, because this is not dissolved in the ionic liquid.
- By lowering the pressure, the CO₂ evaporates and the pure end product precipitates as a liquid or a solid. This separation method works well, because the catalyst and the ionic liquid cannot be dissolved in the supercritical CO₂.



New method

Discovering the homogenous phase

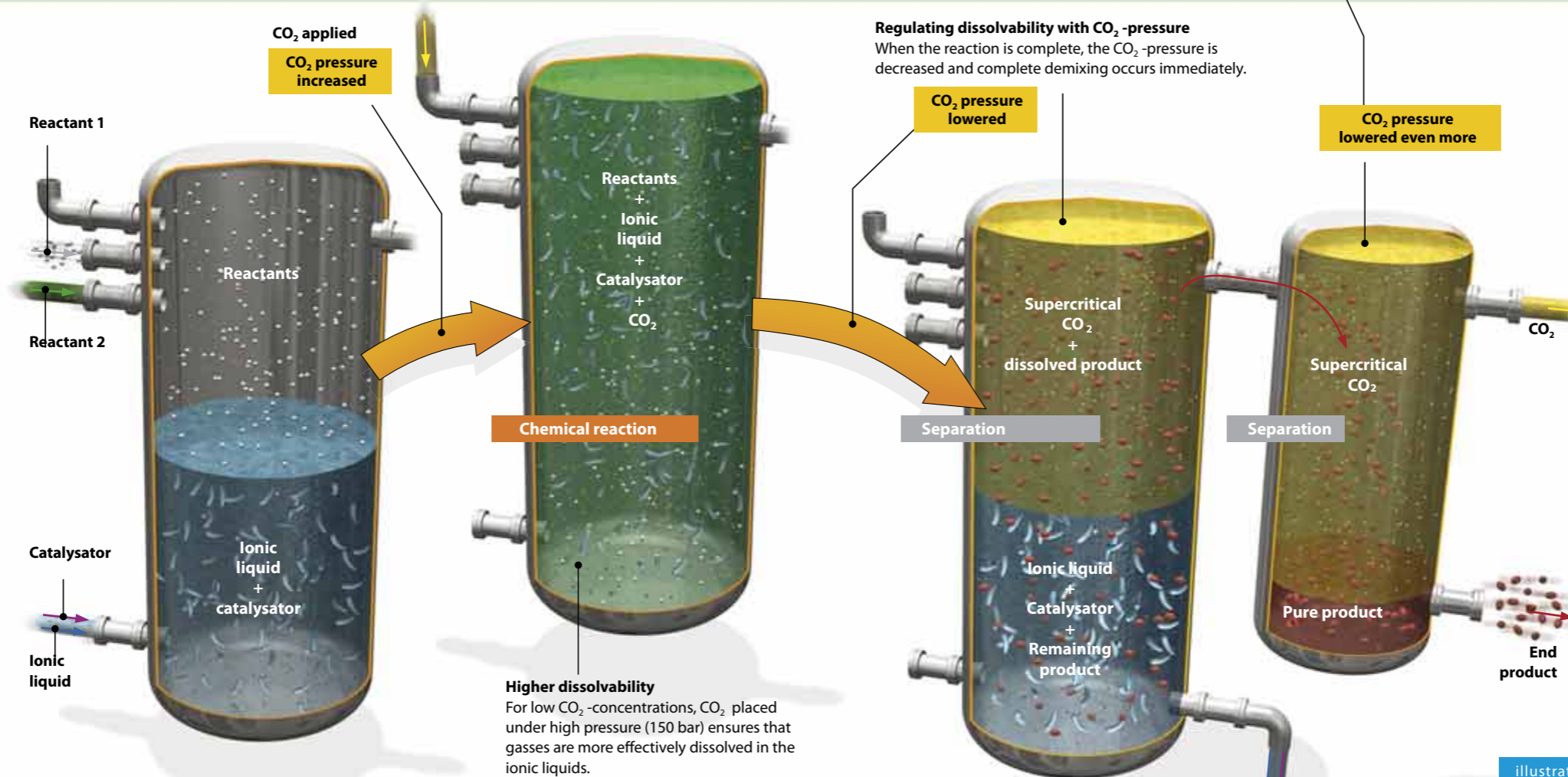
By increasing the CO₂-pressure in the reactor chamber, the two non-mixable phases (supercritical CO₂ and the ionic liquid with catalyst) lead to a homogenous phase, in which all solids are dissolved. The reaction occurs during this phase. When the pressure is then decreased, the end product separates.

Why not discovered earlier?

Although the CO₂-pressure is also increased during the two-phase process, a homogenous phase had never before been discovered. This was because of the (too) high CO₂-concentrations (for supporting the extraction of the product from the ionic salt). Instead of a homogenous phase, two unmixable liquids (liquid CO₂ and ionic liquid) emerged when the CO₂-pressure was increased.

ADVANTAGE 1 High reaction speed

Because all solids (the reactants, the catalyst, the end product and the ionic liquid) are dissolved in one homogenous phase, the reaction speed is greatly increased.



Regulating dissolvability with CO₂-pressure

When the reaction is complete, the CO₂-pressure is decreased and complete demixing occurs immediately.

ADVANTAGE 2 Immediate separation/demixing

At low CO₂-pressure, the homogenous phase immediately occurs in two-phases: the ionic liquid, with dissolved catalyst and any remaining products, and the supercritical CO₂, with dissolved products (and any reactants). The CO₂-pressure is an ideal parameter for switching between one phase for the reaction and two phases for the separation of the end product.

ADVANTAGE 3 No pollution and safe

Traditional organic solvents (often flammable, poisonous and non-biodegradable) evaporate easily and enter into the air. Ionic liquid do not evaporate at room temperature and therefore do not pollute the air.

ADVANTAGE 4 Energy-saving

The combination of reaction and separation in the same process step does not produce waste (fewer process steps are needed and no solvents evaporate) and uses much less energy. The CO₂ is once again compressed and is completely reusable. The catalyst is added and dissolves in the ionic liquid. The reactants flow into the reactor chamber. The reactants dissolve in the ionic liquid.

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