Cyclic molecules are everywhere, and everything around us stems from the way they are assembled: not just taste, colour and smell but also (for example) pharmaceutical drugs. Nature by itself forms molecular rings of different sizes and chains of rings of varying lengths that scientists are able to reproduce artificially. Chemists from the University of Geneva (UNIGE) have now devised a new technique for creating these chains of molecular rings that do not use standard chemical interactions but contact with large molecular surfaces that are electron-poor and do not exist in nature. Unlike with standard procedures, this new technique works by autocatalysis – the rarest, but also the most ambitious, type of transformation that exists in chemistry. The results of this research, published in the journal Angewandte Chemie, open up new prospects for molecular cyclization and also provide the first part of the answer to an old contradiction in classical chemistry.
is the empty space it provides for molecules to assemble”, says Miguel Paraja, a researcher in UNIGE’s Department of Organic Chemistry. On contact with this new, spacious and electron-deficient surface, the molecules formed cycles of different sizes (4 to 8 atoms) and various sequences. “But the big news was the way the transformations occurred!” adds the Geneva-based chemist.

All these cyclizations took place autocatalytically. “With a conventional catalyst, the cyclizations are fast at the start, and then – since there is less and less substrate – they increasingly slow down, explains Xiaoyu Hao, a researcher in the same laboratory. But with autocatalysis, it’s the very opposite that happens!” Indeed, the molecular transformations accelerate on a massive scale. “Although this autocatalysis is a very rare transformation phenomenon in chemistry, it is also the most astonishing, says professor Matile. “It’s based on mutual aid between molecules: the first molecules transformed help the next to transform, which isn’t the case during normal catalysis, which decelerates rather than accelerates.”

The first step in answering an old contradiction of classical chemistry

This discovery helps answer one of the oldest contradictions in classical chemistry. “There is a very well-known chain of molecular rings, called a brevetoxin, which is found in the red tide and which has the effect of killing fish”, explains professor Matile. It was discovered by a towering figure in organic chemistry, Koji Nakanishi, who put forward an explanation for the possible construction of this extraordinary chain formed from eleven consecutive molecular rings in a single reaction. But this hypothesis did not agree with Jack Baldwin, a famous chemist who produced the rules explaining the formation of cycles that are now accepted as the basis of classical chemistry. The “Nakanishi hypothesis” violates these rules for every of the eleven rings. “Our rings can be formed according to Baldwin’s rules if we want them to, reports Paraja. More importantly, we can also break the Baldwin rules on demand with our new catalysts and create those forbidden rings that Koji Nakanishi dreamed of.” “The key to success, explains Hao, is the large empty space offered by our new catalysts.”

Professor Matile continues that: “With the discovery of autocatalysis in forming cyclic molecules, our anion-π contacts have helped us understand the most subtle way to transform the molecules that exists in chemistry. And this will help us create new chains of molecular rings.” The chemists will be able to influence and direct the nature of the transformation of the next substrate, creating new materials, one of the main objectives also of the NCCR Molecular Systems Engineering. “Most solutions to scientific problems, be they about food, medicine or environment, involve molecules and new contacts that can be created among them”, says the Geneva-based chemist.