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PRESS RELEASE

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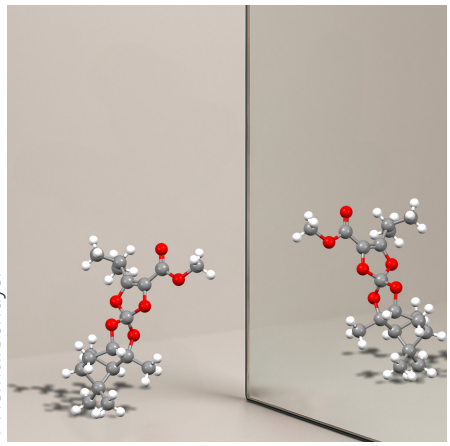
A new architecture at the heart of molecules

A team from UNIGE and the University of Pisa has designed surprisingly stable molecular assemblies, paving the way for new drug constructs and geometrically controlled materials.

Can you imagine a life-saving molecule whose "twin" is a deadly poison? As surprising as it may seem, this chemical reality is known as "chirality". Like a right hand and a left hand, two molecules can have the same composition, but a different shape and arrangement in space. And this difference can change everything. Understanding and controlling this phenomenon is crucial to drug design. A team from the University of Geneva (UNIGE), in collaboration with the University of Pisa, has developed a new family of remarkably stable chiral molecules. This work opens up new prospects for the design of geometry-controlled drugs. It is published in the *Journal of the American Chemical Society*.

A molecule, or any object, is said to be chiral if it cannot be superimposed on its mirror image by any combination of rotations, translations and geometric changes. This is similar to our two hands, which appear identical but cannot be superimposed, whether viewed from the back or the palm. This universal molecular asymmetry requires chemists to design chiral molecules capable of interacting precisely with living systems.



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Mirror molecules synthesized in this study, featuring an asymmetric carbon fully substituted by oxygen atoms, a novel configuration in molecular chirality. The carbon atoms are in grey, oxygen atoms in red, and hydrogen atoms in white.

High resolution pictures

Within a molecule, chirality often arises from the presence of one or more asymmetry centers, known as stereogenic centers. These are often made up of a central carbon atom, itself linked to four different groups or chains of atoms, usually carbon as well. The group led by Jérôme Lacour, Full Professor in the Department of Organic Chemistry, School of Chemistry and Biochemistry, UNIGE Faculty of Science, has created a new type of stereogenic center. This time, the central carbon atom is not surrounded by carbon chains, but only by oxygen and nitrogen atoms. A first in the field of chemistry.

"Molecules with this new type of stereogenic center had never been isolated in a stable form. Their synthesis and characterization mark a major conceptual and experimental breakthrough," explains Jérôme Lacour.

Outstanding stability

The stability of chiral molecules is a particularly important parameter. Mirror molecule pairs are structurally very close, and in many cases spontaneous switching from one to the other is possible, for example under the effect of temperature. As if a left hand were suddenly transformed into a right hand. In this way, we could switch from a drug to an inactive or even toxic molecule! The new molecular structures developed by the UNIGE team feature exceptional chiral stability, meaning that the switch from one molecule to its mirror sister is particularly unlikely.

Olivier Viudes, PhD student and first author of the study explains: “Using dynamic chromatography techniques and quantum chemistry calculations, we have shown that, for the first molecule developed, it would take 84,000 years at room temperature for half a sample to transform into its mirror molecule”. For a drug, such stability guarantees safe storage, without the need for specific conditions. For the second molecule, this time has been estimated at 227 days at 25°C.

The new stereogenic centers developed by the Geneva team should enable the design of stable, controlled, three-dimensional chiral molecules. These structures open up new possibilities for drug design and the creation of new materials. “These novel stereogenic centers offer a new way of organizing molecular space. They open up a whole new degree of freedom and imagination in chemical synthesis,” concludes Gennaro Pescitelli, professor at the University of Pisa and co-principal investigator of the article.

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