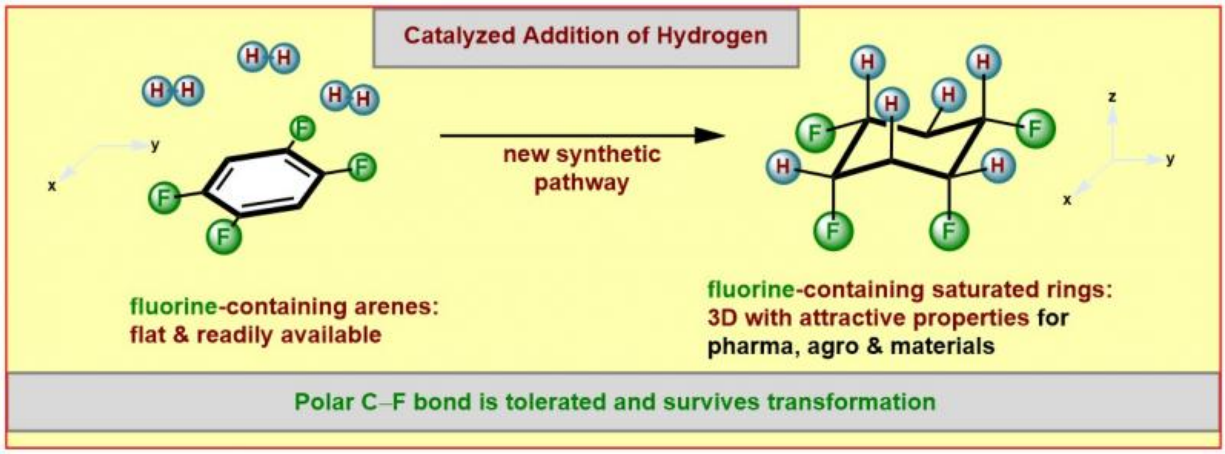
# A new method for the formation of fluorinated molecular rings

August 11 2017




llustration of the new synthetic method. Credit: WWU/Frank Glorius

Dyes, pharmaceuticals, and functional materials are generally based on innovative molecules made by chemists. For their production, several chemical reactions are available, but there are limitations. For example, fluorinated compounds, molecules that contain at least one fluorine atom, are often difficult to prepare. This is unfortunate, since they exhibit interesting chemical properties and are of great importance for the development of active ingredients. Thus, researchers seek new techniques to produce these compounds.

Chemists from the Westfälische Wilhems-Universität (WWU) have

developed a new and practical synthetic method for the formation of such fluorinated three-dimensional "saturated" (meaning only single-bond containing) molecular ring structures. The study has just been published online in the journal *Science*.

"I feel that our results are a breakthrough. It can have great importance for the efficient production of new molecules and, consequently, new drugs, crop protection agents and functional materials," says Frank Glorius.

His new synthetic method starts from flat, aromatic ring structures built up from carbon and bearing fluorine atoms. These starting materials include inexpensive, commercially available compounds and those that can be readily made.

Facilitated by a catalyst, the chemists added hydrogen atoms ("hydrogenation") selectively to one face of the ring system. Chemists and biochemists define catalysts as enzymes or molecules that can speed up or enable certain reactions. A selective addition allows the control of the properties of the resulting products, for example, the solubility, the aggregate state or the polarity. A molecule is considered to be polar if charges are separated to result in more negative and more positive molecular fragments. The products produced in this study contain the more negatively charged fluorine atoms on one face and the more positively charged hydrogen atoms on the other face of the ring.

Many fluorinated aromatic starting materials were successfully converted into the desired products by the group. Glorius says, "The attached fluorine atoms reduce the reactivity of the already not very reactive aromatic starting materials in the catalytic hydrogenation even further. This is especially true for substrates containing multiple fluorine atoms. Even more pronounced is the sensitivity of the carbon-fluorine bond against hydrogenation, generally leading to the loss of the fluorine

atom."

Many studies of the past reported this latter problem. Remarkably, the new synthetic method allows fluorine atoms to tolerate the catalytic hydrogenation. "We have identified a catalyst system that is powerful enough to overcome the aromatic stabilization. Yet it is mild enough to preserve the carbon-fluorine bonds." As a catalyst, the scientists used a combination of the noble metal rhodium and an especially electron-rich carbene ligand (a special metal-binding molecule) that greatly influences the properties of the catalyst.

First author Mario Wiesenfeldt says, "The new method provides surprisingly simple access to a fascinating structural motif: cyclic, saturated and selectively fluorinated on one face. Many of the products are characterized by a high level of polarity."

The compound "all-cis-1,2,3,4,5,6-hexafluorocyclohexane," in which the saturated six-membered carbon-cycle contains the maximum number of six fluorine atoms on the same face of the ring, represents one of the most polar organic molecules known to date. In 2015, this remarkable compound was first prepared and reported by Prof. David O'Hagan from the University of St. Andrews in Scotland. However, his team required a 12-step synthetic sequence for its formation. The new method allows the formation of this and many related compounds in a convenient single step, thus allowing the formation of larger amounts.

"Hydrogenation is an attractive and often very clean method of synthesis," says Frank Glorius. "An especially prominent example is the formation of ammonia through the Haber-Bosch process, the hydrogenation of nitrogen, consuming more than 1 percent of the world's annual energy supply. It is of fundamental importance for the nutrition of mankind, since it serves as a basis for the production of nitrogen fertilizer, among others."

**More information:** Mario P. Wiesenfeldt et al. Hydrogenation of fluoroarenes: Direct access to all- cis -(multi)fluorinated cycloalkanes, *Science* (2017). DOI: 10.1126/science.aao0270