Chemists develop new approach to inserting single carbon atoms into rings

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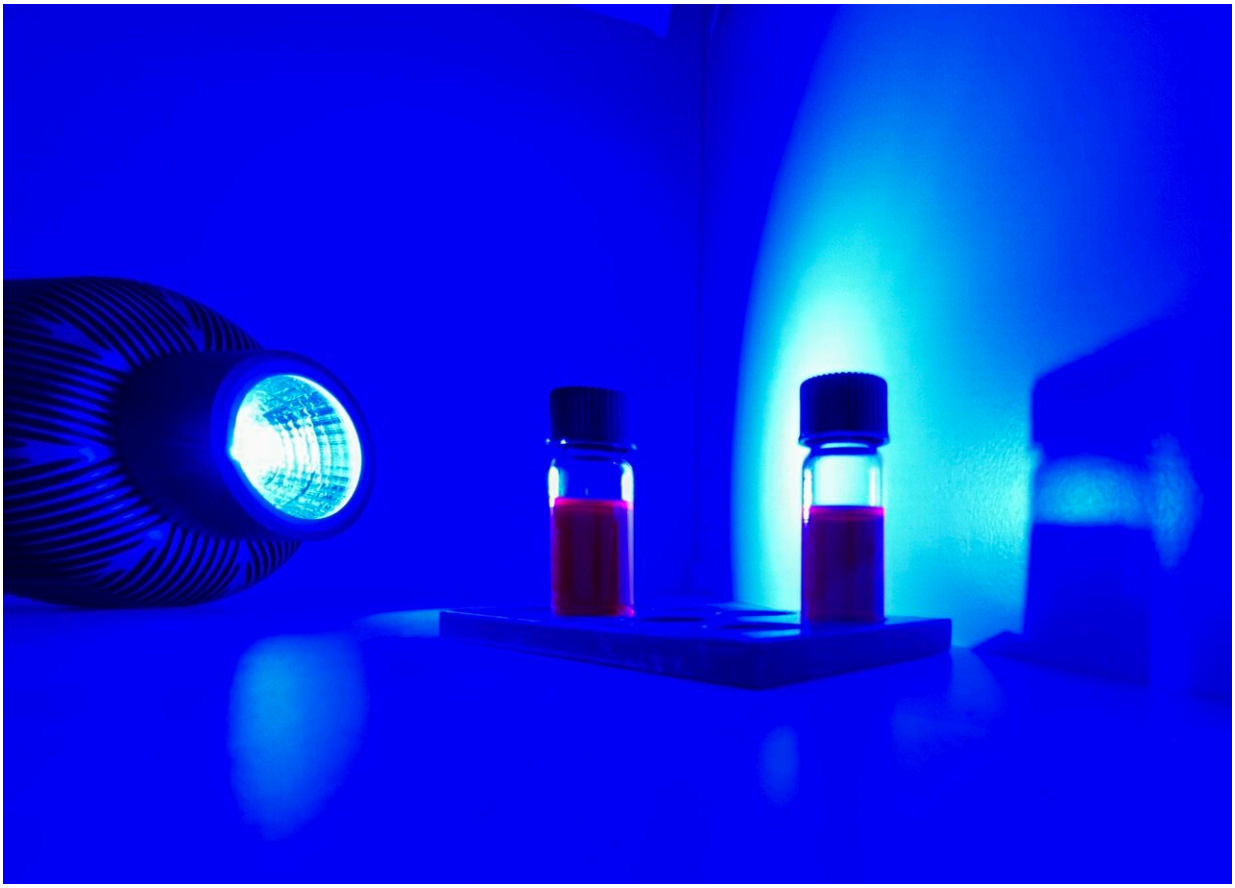

The experimental setup—the research team used visible light for photocatalysis. Credit: Uni MS, Fu-Peng Wu

Molecules with a central ring system play an important role in the search

for active ingredients for new pharmaceutical products—and it is important that the rings should have the correct size if the desired product is to be manufactured as efficiently as possible.

For this purpose, an international team of chemists led by Prof. Frank Glorius (University of Münster) and Prof. Osvaldo Gutierrez (Texas A&M University, U.S.) have developed a precise and efficient tool using "single atom skeletal editing." Their new approach consists in inserting a single carbon atom into the carbon skeleton of cyclic compounds, enabling the ring size to be adjusted from five- to six-membered rings. The method is published in the journal *Nature Catalysis*.

The results of the study, say the researchers, open up the way for the design and modification of complex molecular structures. Not only research but also industrial applications in pharmaceutical syntheses and in materials science could all benefit from the results.

Skeletal editing is a method used by chemists to replace atoms within a ring system. "In earlier approaches," says Dr. Fu-Peng Wu from the University of Münster, "the focus was on the insertion of nitrogen atoms. By contrast, inserting a single carbon atom into an all-carbon ring is an enormous challenge. The carbon reagent needs to be compatible with various functional groups which determine the chemical properties of the molecule. In addition, the compound should be stable, easy to handle and susceptible to uncomplicated activation." In recent decades, only a small number of such reagents have been developed.

The group led by Glorius employed so-called photoredox catalysis, using light energy to drive the reaction. Using special reactive carbon fragments (radical carbynes), the researchers inserted single carbon atoms with various functional groups into indene. Indene is a starting material frequently used in the production of organic compounds, as is the product naphthalene.

Gutierrez and his group carried out mechanistic computations in order to detect the underlying reaction mechanism in the radical chain. As postdoc Dr. Remy Lalisse says, "Our calculations seem to suggest that the reaction takes place via an initial addition of a diazomethyl radical to indene."

More information: Fu-Peng Wu et al, Ring expansion of indene by photoredox-enabled functionalized carbon-atom insertion, *Nature Catalysis* (2024). DOI: 10.1038/s41929-023-01089-x

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