Homogeneous hydrogenolysis with molecular palladium

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The new tritiation reaction is practical and robust to execute and could have an immediate impact in the discovery and development of pharmaceuticals. Credit: Frank Vinken

Tritium 3H, a radioactive isotope of hydrogen, is commonly used in

medicinal chemistry as a label to follow the course of a drug in the human body. Chemists like to use the technique to evaluate drug candidates and their metabolism. A team led of researchers at the Max-Planck-Institut für Kohlenforschung in Mühlheim, Germany, has now found a new way to label complex small molecules with tritium. In a joint research project with the research and early development organization of the Swiss pharmaceutical company Roche, they investigated ways to incorporate tritium into pharmaceuticals and other similar molecules that are important derivatives for drug development.

The team took advantage of the special properties of arylthianthrenium salts that they developed two years ago. The thianthrene group can be introduced into pharmaceuticals selectively and at a late stage in a direct and predictable manner. The new approach does not require an inert atmosphere or dry conditions, making it practical to use.

"The unusual feature of this work is the reaction of arylpseudohalides with hydrogen, catalyzed for the first time by a homogeneous catalyst," explains Tobias Ritter from the Max Planck Institute for Coal Research. "Such reactions were previously unknown with conventional groups that can be introduced into pharmaceuticals. Normally, chemists use heterogeneous catalysts but those also often destroy other functional groups, which are frequently found in pharmaceuticals," the director annotates.

The study is published in *Nature*.

More information: Da Zhao et al, Tritiation of aryl thianthrenium salts with a molecular palladium catalyst, *Nature* (2021). DOI: 10.1038/s41586-021-04007-y

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