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Tutu for the catalyst: Hydrogenation of quinoline at room temperature succeeds by using manganese

They are indispensable in the production of pharmaceuticals: quinolines, cyclic carbon compounds whose characteristic ring structure contains a nitrogen atom. They are hydrogenated in catalytic processes - and thus converted into active pharmaceutical ingredients. The pharmaceutical industry usually uses expensive noble metal catalysts for this purpose. At the Leibniz Institute for Catalysis (LIKAT) in Rostock, this reaction has now been successfully carried out for the first time with the non-noble metal manganese - at room temperature and under normal pressure. The paper of PhD student Veronica Papa was published in NATURE CATALYSIS.

As a basic structure of medical active agents, quinolines are modified in a classical chemical reaction, the hydrogenation. Hydrogen atoms are added to double bonds, thus changing the structure of the starting material. So far, this only works with the help of noble metal catalysts. "However, these are expensive and only available in limited quantities," says Veronica Papa, lead author of the paper (DOI: 10.1038/s41929-019-0404-6).
LIKAT director Prof. Dr. Matthias Beller, Papa's doctoral supervisor and co-author, has therefore specialized in non-precious metals such as iron and manganese for years. Thus, the Leibniz Institute is in line with the current line of the EU Commission, which duns in a report published in 2018 the replacement of "critical raw materials" and the development of a recycling economy.

Cons: Reaction conditions and structure

After iron, manganese is the third most common chemical element in the earth's crust of all so-called transition metals. The fact that it has so far been neglected for such a classic reaction as hydrogenation is, as Veronica Papa explains, due to the drastic conditions that would require hydrogenation of quinoline: temperatures above 100 degrees Celsius and pressures of up to 50 bar.
And there is another hurdle: The metal atom in the catalyst - in this case manganese - is stabilized as an active center by a complex molecular corset, so-called ligands. The effort this involves for the pharmaceutical industry quickly outweighs the advantages of this cheap material.

Discovery by coincidence

As part of her PhD thesis Veronica Papa discovered rather by chance that this elaborate corset is not necessary at all. She discovered this within a control experiment when she added manganese salt, commercially available from the chemical catalogue, to the reaction solution without the complicated ligands. Papa: "Surprisingly, this reaction led to a good result."
This motivated her to optimize the conditions of this reaction in further experiments. In the meantime, the simple manganese salt manages the hydrogenation under mild conditions:

normal pressure (1 bar) and room temperature - a novelty for the experts. Veronica Papa was able to prove that the manganese catalyst in the reaction spares functional molecular groups in the starting substance. This means that it can be used for the entire substance class of quinolines, including their derivatives.

Dr. Kathrin Junge, research group leader of Veronica Papa and co-author, explains: "The producer does not need to develop the catalyst anew for each new active substance, but can get it off the shelf, cheaply, at any time".

Intermediates isolated

When something works in the laboratory in a surprising way, chemists want to know more about it. How can such a simple catalyst control a complex reaction? To answer this question, Veronica Papa has been researching the reaction mechanism of this hydrogenation. She discovered that the manganese catalyst changes its structure several times during the reaction and forms different intermediates.

For this discovery, she had to "stop" the reaction cycle, which runs continuously in a solution in a laboratory Schlenk vessel, again and again. She succeeded in doing this by allowing the intermediate stages to crystallize in the reaction vessel under defined conditions and "with a little luck", as she says. The crystals isolated in this way were measured at the Institute by means of X-ray crystal structure analysis and provide information on the structure of the catalyst at the molecular level.

Pas de trois with tutu

So far, three intermediates have been proven, which the manganese catalyst takes up during its work and life cycle. To get a 3 dimensional idea of the structure of their results, chemists usually present them in structural formulas, which often stimulates their imagination. Veronica Papa reminded the structural formulas of the manganese catalyst and its intermediate stages of spread ballet skirts. This gave her the idea of a pas de trois, which she used to illustrate her paper.

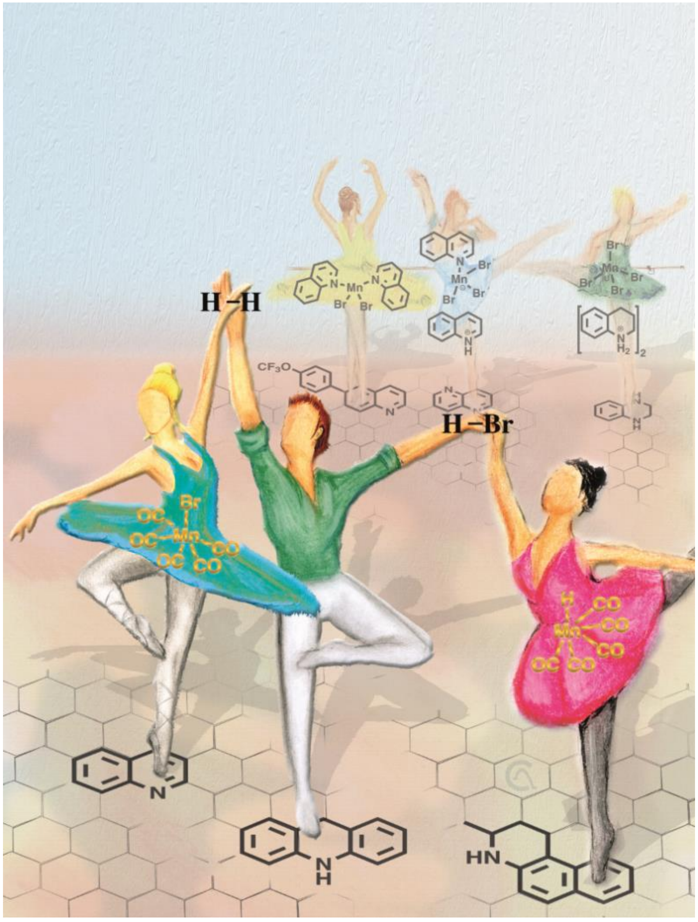

Fig. 1: Illustration of the Manganese Compounds as „Pas de trois“