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Chemical Rope Trick at Molecular Level - Mechanism Research Helps when "Trial & Error" Fails

In most industrial chemical reactions, catalysts combine with the starting materials and accompany them through intermediate stages to the product. In chemistry, this pathway is known as the reaction mechanism, and it is a kind of black box: nobody knows what is happening at the molecular level at first. If the reaction result in the laboratory falls short of expectations, chemists first resort to trial and error. Put simply, they modify the reaction until it works. Sometimes, however, it is worth taking a closer look at the reaction mechanism, as Dr. Nora Jannsen at the Leibniz Institute for Catalysis in Rostock shows using a model reaction.

She recently published her findings, which she obtained as part of her doctorate, in JACS, the renowned Journal of the American Chemical Society.

The model reaction sounds unspectacular and, above all, strange to the layman's ear, explains Dr. Jannsen: "Benzotriazole, usually a corrosion inhibitor, is converted into a new substance with an allene (the emphasis here is on the second syllable) using a rhodium catalyst." This is then called allylbenzotriazole and can be used in a variety of syntheses. The reaction was developed by a research group led by Prof. Breit at the University of Freiburg.

Fig. 1: Symbolic image, reaction vessels in the laboratory. (LIKAT/Gohlke)

Functional Group Set Precisely

The colleagues in Freiburg succeeded in precisely linking a "functional group" to a very specific position in benzotrialzole. This is where a nitrogen-hydrogen bond (N-H) is located, as Dr. Jannsen explains.

"Functional groups" are important as molecular segments because they are responsible for the specific, e.g. pharmaceutical, effect. "The Freiburg team wanted to place such a group in benzotriazole exactly where the N-H bond is, and the N-H bond has to give way for this," Dr. Jannsen continues. The colleagues managed to do this. "But they didn't understand on what basis they had achieved this."

That is unfortunate. Because only with an understanding of the molecular events can the reaction be specifically applied and optimized in the future. This was the aim of Nora Jannsen's dissertation, which she successfully defended in Rostock in 2023.

Idea: Catalyst Breaks Bond

So how does such a reaction work? The start and end are known. What is also known about this reaction is that every single atom from the starting materials is later found in the product; chemists call this an "atom-economic" reaction. This means that in the course of the reaction, the hydrogen from the N-H bond must pass from the benzotriazole to the second starting material, the allene.

Dr. Jannsen: "The Freiburg scientists thought that the catalyst breaks the nitrogen-hydrogen bond, i.e. a so-called oxidative addition of the benzotriazole takes place. Rhodium catalysts are known for this type of reaction." Nora Jannsen tested the idea by first reacting the rhodium catalyst with only one starting material, benzotriazole. She isolated samples from this reaction for nuclear magnetic resonance spectroscopy (NMR) and X-ray crystal structure analysis. The result: "The N-H bond is not broken at all. The benzotriazole remains completely intact, it only attaches itself to the catalyst."

Result: Simple Coordination

The chemist then discovered that the second starting substance, allen, also binds to the catalyst. And this is where the following happens: "The two starting materials come into direct contact with each other, and the benzotriazole transfers the hydrogen atom, also known as the proton, to the allene. The catalyst merely holds the starting materials in place, but does not intervene directly in this step." Dr. Jannsen then substantiated this proposal in detail using quantum mechanics, i.e. by theoretically modeling the reaction pathway.

Nora Jannsen was surprised that the catalyst manages the whole thing so simply. For laypeople, it may sound a bit like a chemical rope trick. In technical terms, such a process is well known and is called protonation.

This process had an advantage. Dr. Jannsen: "Interestingly, the reaction conditions for protonation can be significantly improved by adding another proton source." For example, she succeeded in reducing the reaction temperature from 80 degrees Celsius to room temperature by adding a type of co-catalyst.

A Lot Does Not Always Help a Lot

Nora Jannsen also discovered that the benzotriazole can also block the catalyst under certain circumstances. This is the case when this starting substance occupies the catalyst twice, so that its reaction partner, the allen, cannot find a free space on the catalyst. This paralyzes the catalytic activity and leads to the catalyst being "consumed". "It probably helps here to simply add the starting material to the reaction successively so that the catalyst comes into less contact with it."

Nora Jannsen no longer had the time to experimentally substantiate this suggestion for the further work of her colleagues in Freiburg. She is now working as a postdoc at the University of Oxford.

Fig.: 2: Dr. Nora Jannsen completed her doctorate at the Leibniz Institute for Catalysis, LIKAT, in Rostock in the research department of Prof. Dr. Torsten Beweries. The research group "Mechanisms of Homogeneous Catalysis", which is part of his department "Modern Concepts of Molecular Catalysis", was previously headed by Prof. Dr. Detlef Heller.

Nora Jannsen is currently working as a postdoctoral researcher in Charlotte Williams' group at the University of Oxford.

(picture: private)

Publication

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