

RESEARCH NEWS STORY

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One Catalyst, Two Reactions: Toward More Efficient Chemical Synthesis

Researchers leverage the unique properties of cerium to perform multiple reaction steps in a single vessel

Most high-performance materials and pharmaceuticals require multiple chemical reaction steps during synthesis, each needing different conditions, reagents, and catalysts. In a recent study, researchers from Japan developed a new method—redox-adaptive autotandem catalysis—that enables two entirely different reactions to occur sequentially in a single container using an inexpensive cerium-based catalyst. This approach streamlines synthesis, reduces energy use and chemical waste, and offers a greener pathway for producing valuable compounds under mild conditions.

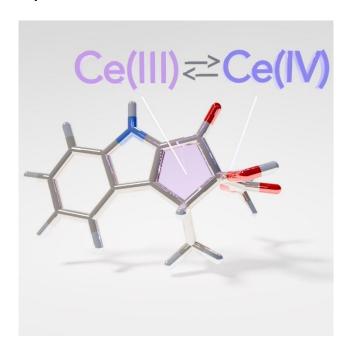


Image title: Synthesizing complex molecules in one step

Image caption: This new cerium-based catalyst interconverts between two oxidation states with distinct chemical properties, enabling two completely different reactions to occur in the same container.

Image credit: Dr. Shinji Harada from Chiba University, Japan

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Most of the drugs, plastics, and industrial materials widely used today are produced through chemical reactions. In general, most high-performance and sophisticated substances have

complex structures, and their assembly involves multiple chemical reaction steps carried out one after another. This creates significant overhead, as each step requires specific conditions, reagents, and catalysts, as well as considerable energy and labor.

Tandem reactions offer a promising solution to this issue. The core idea is to carry out multiple reactions in sequence within the same container without needing to isolate intermediate products or change catalysts. While repeating the same type of reaction is relatively straightforward, a major challenge has been developing a single catalyst that can facilitate completely different types of reactions.

Now, a research team led by Associate Professor Shinji Harada from the Graduate School of Pharmaceutical Sciences, Chiba University, Japan, has developed a groundbreaking solution to this problem. Their new method, known as "redox-adaptive auto-tandem catalysis," uses a single catalyst to enable two different chemical reactions in a single container. Their study, which was co-authored by Professor Tetsuhiro Nemoto and Ms. Nanami Tsuji from Chiba University, was <u>published online in the journal ACS Catalysis on August 3, 2025</u>.

The researchers achieved this by leveraging the unique catalytic properties of cerium, a widely used rare-earth element. By sheer accident, a member of the team left a reaction flask exposed to air when studying a reaction involving cerium. To their surprise, they found a new, completely unexpected product as a result of this exposure. This fortunate event caught the team's attention and ultimately led them to a key discovery useful for tandem reactions.

Unlike other rare-earth elements, cerium can easily interconvert between two oxidation states, adopting two configurations that promote different chemical transformations. Inspired by the unexpected results of their previous experiment, the researchers explored ways to leverage this property.

After screening and testing with various inexpensive cerium-based catalysts, they succeeded in linking two different reactions. The first reaction is a ring-forming step, which acts on the initial reactants to produce an intermediate compound with a five-membered ring structure. The second reaction is an oxidation reaction, which adds oxygen to the intermediate compound to produce the final compound. Each reaction is catalyzed by a different oxidation state of cerium, and the act of catalyzing either reaction "flips" cerium to the other oxidation state. In this way, as Dr. Harada puts it, "Cerium acts like a chameleon, dynamically changing its function to perform completely different types of reactions sequentially in a single vessel."

Using this method, the researchers synthesized various α -hydroxylated cyclopentenones, compounds valuable for pharmaceutical synthesis, in high yields under mild conditions. The fact that a single cerium catalyst can change roles autonomously without external intervention between two different reactions could help make chemical manufacturing much simpler and energy efficient. "Our findings may lead to lower costs and reduced chemical waste, contributing to greener and more sustainable synthetic processes," says Dr. Harada. Notably, this technique requires no hazardous reagents and can be performed with standard laboratory equipment without the need for special devices.

The team will focus on expanding their newfound redox-adaptive auto-tandem catalysis

method to a broader range of chemical reactions, especially those relevant in pharmaceuticals and functional material manufacturing. This would not only accelerate drug development and innovations in next-generation materials, but also contribute to creating new manufacturing technologies with a lower environmental impact.

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About Associate Professor Shinji Harada from Chiba University

Dr. Shinji Harada obtained his PhD from The University of Tokyo in 2007. He then joined Chiba University, where he currently serves as an Associate Professor at the Institute for Advanced Academic Research and the Graduate School of Pharmaceutical Sciences. His research focuses on synthetic organic chemistry, catalyst design, and rare-earth metals. He has published nearly 50 scientific papers on these topics. He is also a member of several learned societies, including The Pharmaceutical Society of Japan, The Rare Earth Society of Japan, The Chemical Society of Japan, and The Society of Synthetic Organic Chemistry, Japan.

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Reference:

Title of original paper: Redox-Adaptive Auto-Tandem Catalysis: Ce(III)/Ce(IV) Interconversion-Mediated Integration of Nazarov Cyclization and Oxidative Hydroxylation **Authors:** Shinji Harada^{1,2}, Nanami Tsuji¹, Sora Fukushima³, Juntaro Yamamoto¹, Shigeru Arai¹, and Tetsuhiro Nemoto¹

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