ALS SCIENCE HIGHLIGHT

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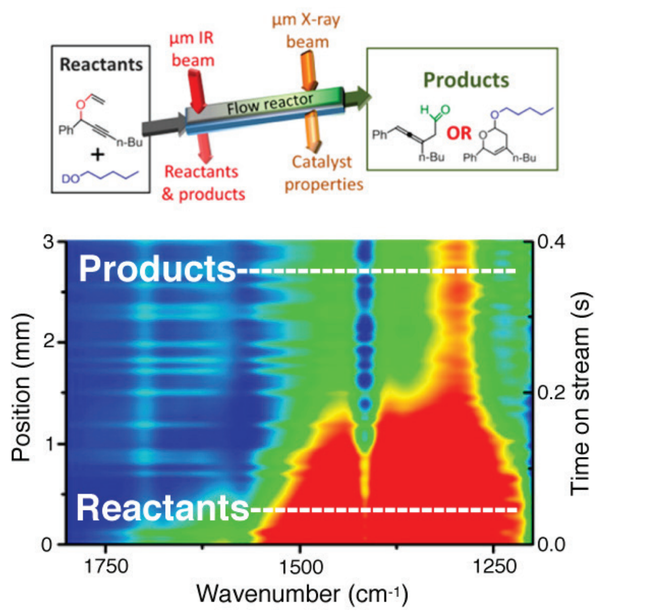
Infrared Mapping Helps Optimize Catalytic Reactions

A pathway to more effective and efficient synthesis of pharmaceuticals and other flow-reactor chemical products has been opened by a study in which, for the first time, the catalytic reactivity inside a microreactor was mapped in high resolution from start to finish. The formation of different chemical products during the reactions was analyzed in situ using infrared microspectroscopy, while the state of the catalyst along the flow reactor was determined using x-ray absorption spectroscopy. The results not only provide a better understanding of the chemistry behind the catalytic reactions, they also reveal opportunities for optimization, resulting in better catalytic performances.

Catalysts—substances that speed up the rates of chemical reactions without themselves being chemically changed—are used to initiate virtually every manufacturing process that involves chemistry. For this study, the researchers used a catalyst of gold nanoclusters to produce dihydropyran, an organic compound whose formation involves multiple reactant steps. Each of the reactants and products shows a distinguishable infrared signature, allowing their evolution into the final product to be precisely monitored with infrared spectroscopy.



Top: Schematic of multistep organic catalysis in a flow microreactor. Reactants flow through a 0.7-mm channel in a 2-cm-long reactor, with catalyst nanoclusters evenly dispersed along its length. Reactants and products were tracked through the reactor using infrared light. Catalyst activity was analyzed using x-rays. Bottom: Example of an infrared microspectroscopy scan that tracks the chemical processes through the microreactor.

Although other (non-synchrotron) spectroscopic tools have the ability to tune into such chemical signatures, they usually do not have sufficient spatial or spectral resolution for detailed analysis of the reactions taking place in catalytic microreactors. Synchrotron-based infrared microspectroscopy at the ALS, with a diffraction-limited infrared beam diameter of less than 10 μm, can overcome this hurdle. And while previous studies used synchrotron microspectroscopy to characterize simple gas-phase catalytic reactions, in this work the researchers obtained detailed mechanistic information about multistep, multiphase catalytic processes within a flow reactor under reaction conditions.

With this new method, researchers can effectively watch an entire catalytic movie, from reactants to product formation, instead of only snapshots of the catalytic process. Previously, in most cases, chemists had to extrapolate information on the reaction process based on analysis of the final product. With

Publication about this research: E. Gross, X.-Z. Shu, S. Alayoglu, H.A. Bechtel, M.C. Martin, F.D. Toste, and G.A. Somorjai, "In Situ IR and X-ray High Spatial-Resolution Microspectroscopy Measurements of Multistep Organic Transformation in Flow Microreactor Catalyzed by Au Nanoclusters," *J. Am. Chem. Soc.* **136,** 3624 (2014).

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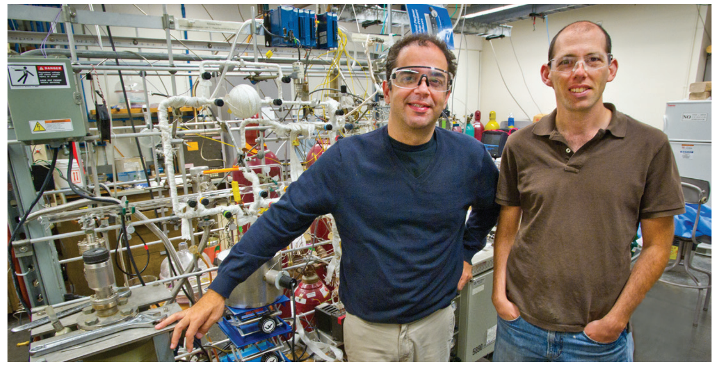
Go With the Flow

There are two basic modes for synthesizing complex organic chemicals through catalytic reactions: batch, in which a final chemical product is produced over a series of separate stages in large vessels, and flow, in which chemical reactions run in a continuously flowing stream through a channel about a millimeter in diameter (microreactors). With the implementation of microreactors, the pharmaceutical industry aims to make the switch from batch mode to flow mode, as flow reactors provide a highly recyclable, scalable, and efficient setup that enhances the sustainability and performance of catalysts.

However, the synthesis of pharmaceutical drugs is a multiphase, complex process that needs to be carefully monitored. Until now, there has been no capability to follow the multistep production process of pharmaceutical drugs in flow reactors without perturbing the flow reaction. In this work, Gross et al. show that using infrared microspectroscopy to monitor the evolution of reactants into a desired product could be an invaluable tool for optimizing pharmaceutical-related synthetic processes that take place in flow reactors.



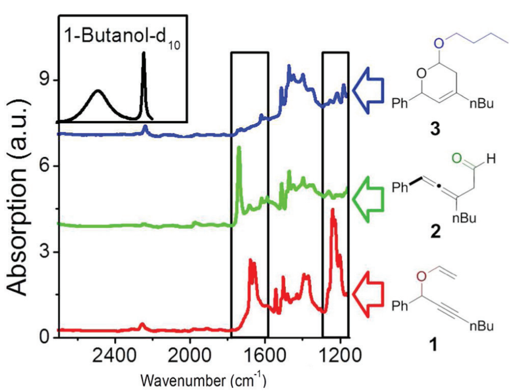
Dean Toste and Elad Gross. (Photo by Roy Kaltschmidt)

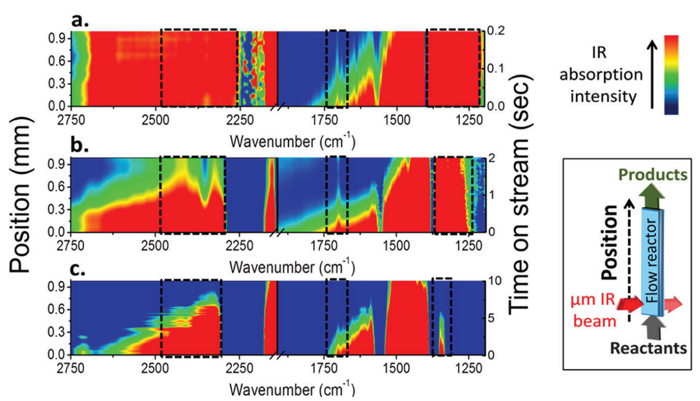
this novel infrared mapping technique, they don't have to guess what happened in the first scene based on what they saw in the final scene; instead they can now directly watch a high-resolution movie of the entire process.

At ALS Beamline 1.4, the researchers collected infrared absorption spectra along the length of the flow reactor with 15-µm spatial resolution and 4-cm^{-1} spectral resolution. Analysis of this data yielded information about the kinetic evolution of the reaction—answering questions about the various stages of the multistep process, which steps were rate-determining in each stage, and what reactant flow rate maximized production of the desired product.

In following the reactions step by step, the researchers also discovered that the catalytic reaction they were observing was completed within the first 5% of the flow reactor's volume, which meant that the remaining 95% of the reactor, though packed with catalyst, did not contribute to the catalytic process. X-ray absorption spectroscopy at the gold L_3 edge was performed at Beamline 10.3.2, revealing that the catalytically active Au(III) species gradually decreased due to catalyst recuction to Au(0). Based on this result, the researchers were able to minimize the volume of the flow reactor and the amount of catalyst by an order of magnitude without deteriorating the catalytic reactivity.

While the infrared microspectroscopy technique employed in this study allowed one-dimensional mapping of a catalytic reaction along the path of the flow reactor, the actual flow reactor is three dimensional. The team is now exploring techniques that would permit two- and three-dimensional mapping of catalytic reactions. Multidimensional imaging will give the ability to know where exactly inside the volume of the flow reactor the catalytic reaction takes place. This will provide advanced tools for better understanding and optimization of the catalytic reaction.





Left: Infrared signatures of the reactant, vinyl ether 1 (red), the intermediate product, allenic aldehyde 2 (green), and the final product, acetal 3 (blue). The high-energy regime of a second reactant, butanol-d_{10} (black) is shown in the inset. The black rectangles mark the areas in which the spectra can be easily distinguished from each other. Right: Infrared absorption scans along the flow reactor for flow rates of (a) 10, (b) 1, and (c) 0.2 mL/h. Markers were added to direct the eye toward the changes in the spectra at different flow rates.