To make or to break: Novel reversible technique produces acyl fluoride using rare metal

April 9 2020

A new technique to produce value-added complex acyl fluorides from commercially available simple acyl fluoride. Credit: Tokyo University of Science

Acyl fluorides are organic compounds that contain a fluorine atom in their structure. These compounds have recently gained much attention in transition-metal catalysis due to their stability and selective reactivity. However, their commercial production remains a challenge. A group of researchers in Tokyo have found a way to generate complex acyl fluorides from widely available acyl fluorides through a reversible reaction, with the rare metal palladium at the core of this process.

In organic chemistry, metals have recently gained attention for their roles as catalysts of a variety of reactions where two different starting materials are joined together, generally known as cross-coupling reactions. Acyl fluorides are a special type of carbon compounds that contain fluorine in their structure. They are very important in various cross-coupling reactions due to their stability and reactivity, as evidenced by the increasing amount of research reporting their relevance.

Because of their central role in these reactions, synthesis of acyl fluorides is an important research topic explored by chemists worldwide. Scientists have already devised several techniques to synthesize acyl fluorides using metal catalysts, but using a simple acyl fluoride as a reagent for the synthesis of complex acyl fluorides has not been explored.

Junior Assoc Prof Yohei Ogiwara, Prof Norio Sakai, and Shintaro Hosaka, a group of scientists from the Tokyo University of Science, had previously identified a variety of techniques to transform acyl fluorides using palladium as a catalyst, including a technique involving the manipulation of the acyl C-F bond. As a result of detailed experiments, they found that palladium can help cleave the acyl C-F bond of acyl fluoride. What was more fascinating was that this reaction was reversible, meaning that the presence of palladium also catalyzed the formation of this bond.

These findings encouraged the scientists to now develop a novel strategy for the synthesis of acyl fluorides. "We envisioned reversibility of the acyl C−F bond cleavage/formation may be the answer to the conundrum of acyl fluoride synthesis," states Dr. Ogiwara, lead scientist of the study. In their recent report published in *Organometallics*, they detail the palladium/phosphine-catalyzed synthesis of a variety of acyl fluorides from a simple and commercially available acyl fluoride—called the benzoyl fluoride—as a fluoride source.

This novel method involves an 'acyl-exchange reaction,' whereby a reaction is induced between benzoyl fluoride and benzoic anhydride by palladium. Benzoic anhydride is a part of a larger subclass of compounds known as acid anhydrides, which are composed of two acyl groups bonded to the same oxygen atom. Therefore, this compound was a perfect supplier of acyl groups.

The researchers found that this reaction resulted in the production of adequate amounts of complex acyl fluorides as desired. By testing out various catalysts and substrates (the chemicals undergoing the reaction), they confirmed that benzoyl fluoride, benzoic anhydride, and palladium indeed provide the best results. However, the preferred complex acyl fluoride can be obtained by playing around with the substrates. This reaction is thus efficient and allows for the preparation of a variety of more complex acyl fluorides. "At its core," reports Prof Sakai, "this reaction proceeds through the cleavage and formation of the acyl C−F bond at the palladium center."

Using this method, Dr. Ogiwara and his team succeeded in obtaining 10 or more types of acyl fluoride from benzoyl fluoride, demonstrating the efficiency of this technique. An added bonus is that through this technique, acyl fluoride presents an attractive source of fluorine. "This study represents the first practical protocol to use commercially available acyl fluoride as a fluorination reagent for the catalytic generation of a variety of value-added acyl fluorides," reports Prof Sakai. The reversibility of the breaking and formation of the C-F bond is the highlight of this study, and it could potentially find many industrial applications.

More information: Yohei Ogiwara et al, Benzoyl Fluorides as Fluorination Reagents: Reconstruction of Acyl Fluorides via Reversible Acyl C–F Bond Cleavage/Formation in Palladium Catalysis, *Organometallics* (2020). DOI: 10.1021/acs.organomet.0c00028

Provided by Tokyo University of Science