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Open Access ChemistryOPEN Cover Profile

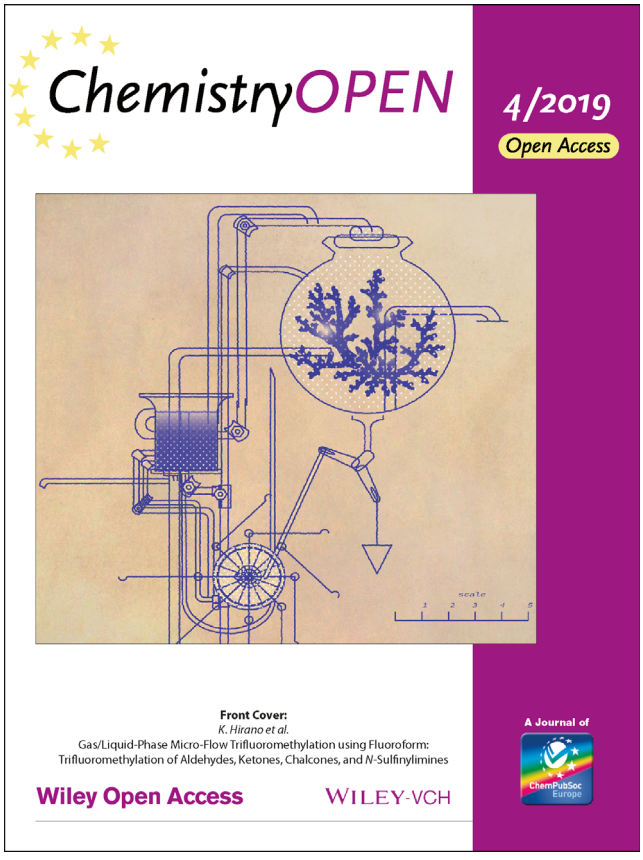
Gas/Liquid-Phase Micro-Flow Trifluoromethylation using Fluoroform: Trifluoromethylation of Aldehydes, Ketones, Chalcones, and *N*-Sulfinylimines

Group Photo

Invited for this month's cover picture is the group of Norio Shibata at the Nagoya Institute of Technology (Japan). The cover picture shows an image related to the perpetual motion machine of the second kind in the eighteenth century, and "alchemy". Our biggest challenge on the path to the results presented in this paper was the creation of alchemy using fluorine chemistry. Read the full text of their Communication at 10.1002/open.201800286.

How would you describe to the layperson the most significant result of this study?

Fluoroform flows: Fluoroform, a chemical structure of HCF_3, is a hydrofluorocarbon (HFC) also known as HFC-23. It is a potent greenhouse gas. One ton of HFC-23 is equivalent to 11,700 tons of carbon dioxide based on Global Warming Potential (GWP). Therefore, the release of HFC-23 into the atmosphere is strictly prohibited. Even though HFC-23 does not exist naturally, an enormous amount of HFC-23 is continuously present in the world. This is because HFC-23 is an industrial by-product of the manufacture of synthetic fluoropolymers, such as all-season material Teflon®, which has numerous applications. Despite its attractive chemical structure, the taming of HFC-23 as a source of the trifluoromethyl (CF_3) unit for organic synthesis, is highly challenging, due to its inevitable decomposition to difluorocarbene (CF_2:) and fluoride (F^-). The decomposition of HFC-23 into inorganic metal fluorides (MF) and carbon dioxide by thermal or plasma methods is the industrial waste treatment process of HFC-23. Several research groups, including ours, have struggled to make a breakthrough in this area in recent decades. Through continuous efforts, several attractive synthetic methods for trifluoromethylation of organic compounds using HFC-23 have been disclosed, thus the taming of HFC-23 for organic synthesis is surely going to become a reality. However, due to the huge amount of HFC-23 routinely produced as an unavoidable byproduct in industrial processes, conventional organic synthesis in the laboratory batch system is far from an ideal solution for dealing with HFC-23. To ad-



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dress this challenge, we suggest one solution, which is the flow transformation of HFC-23 into organic compounds. Flow chemistry is a powerful technology used at a large scale that involves large quantities of both starting materials and products. In a flow chemical reaction, both starting materials and reagents are continuously mixed by pumping both, allowing products to be transformed into a flowing stream, like a river. Thus, flow technology should be ideal for the continuous treatment of a large quantity of HFC-23. Our micro-flow continuous process is expected to contribute to the consumption of a large quantity of HFC-23 and to enable the transformation of HFC-23 into attractive fluoro-organic compounds. Fluoro-organic compounds are fabulous materials used in a wide range of fields, in particular, pharmaceuticals and agrochemicals. In other words, we would be able to turn industrial waste into drugs. Thus, our result affects not only environmental issues involving the Kyoto Protocol and the recent Kigali Amendment to the Montreal Protocol, but also has the potential to greatly improve the health of people around the world if this technology is effectively implemented.

Who contributed to the idea behind the cover?

"Kyokyu to Kawaki": This painting is the work of Miss Mami Shibata, Japanese art painter. The title of this work is "Kyokyu to Kawaki" (Supply and Dryness). She was inspired to draw this cover from the perpetual motion machine of the second kind in the eighteenth century. She has already presented a series of works of perpetual motion machines at a couple of exhibitions and also in other scientific journal cover pictures including Chemical Science,[1] Organic Chemistry Frontiers,[2] and Chemical Communications.[3] Thus, the present painting is the fourth work of a series of chemistry journal covers. The picture illustrates that something liquid is continuously altered at the beginning of life's starting materials, which conjures an image of alchemy and life science.

What was the biggest challenge (on the way to the results presented in this paper)?

Chemists turn waste to drugs: As mentioned above, our technology has the potential to transform industrial waste of HFC-23 into pharmaceuticals and agrochemicals. To a certain extent, our technology could be considered a form of alchemy since material that is toxic to the environment can be transformed into drugs for human use. Considerable efforts are being made to ensure that this "alchemy" is realized.

[1] N. Shibata et al., Front cover, *Chem. Sci.* **2018**, *9*, 4921, DOI:10.1039/C8SC90115E.
[2] N. Shibata et al., Front Cover*Org. Chem. Front.* **2018**, *5*, 709-710, DOI: 10.1039/C8QO90016G.
[3] N. Shibata et al., Inside front cover,*Chem. Commun.* **2017**, *53*, 12716, DOI: 10.1039/C7CC90464A.

COVER PROFILE

"A gas/liquid-phase micro-flow nucleophilic trifluoromethylation of carbonyl compounds using gaseous fluoroform is developed. This method also allows the first micro-flow transformation of N-sulfinylimines into trifluoromethyl amines with excellent diastereoselectivity. To demonstrate the synthetic utility of this micro-flow synthesis, the formal micro-flow synthesis of Efavirenz is described…" Find out more about the story behind the front cover research at 10.1002/open.201800286.

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