

DOI: 10.1002/open.201400003

Read the full text of the article at 10.1002/open.201300044

Diastereoselective Additive Trifluoromethylation/ Halogenation of Isoxazole Triflones: Synthesis of All-Carbon- Functionalized Trifluoromethyl Isoxazoline Triflones



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Invited for this month's cover is the group of Prof. Norio Shibata. The cover shows the Japanese painting "Tsuibamu" ("Pecking") by Mami Shibata: our novel isoxazoline triflones will support our life. For more details, see the Communication on p. 14 ff.

What aspects of this project do you find most exciting?

Three into one: Heterocycles have a very long history as common fragments of biologically active natural products as well as drugs on the market. On the other hand, fluorinated organic compounds have become key components in pharmaceuticals and agrochemicals over the last decades, despite unavailability of these compounds in nature. In this respect, heterocycles with fluorine or fluorinated functional groups on their skeletons have emerged as potential drug targets in medicinal chemistry. Researchers have been engaged in the development of new methodologies, in particular, for the construction of carbon–fluorine (C–F) bonds and carbon–trifluoromethyl (C–CF₃) units in heterocyclic frameworks. Recently, we became interested in trifluoromethanesulfonyl (triflyl, SO₂CF₃) groups as hydrophobic isosteres of nitro (NO₂) groups, and thus several new methods for the synthesis of triflyl heterocyclic compounds (heteroaryl triflones) were reported. In the present paper, we synthesized all-carbon-functionalized diaryl-isoxazoline derivatives, which contain several challenges. The C–F, C–CF₃, and C–SO₂CF₃ bonds are all together introduced in a single, small heterocyclic molecule. In addition, these heterocyclic frameworks contain two quaternary stereogenic carbon centers. Thus, the next challenge is an asymmetric synthesis.

What is in your opinion is an upcoming research theme likely to become one of the 'hot topics' in the near future?

We are interested in the pentafluoro-λ⁶-sulfanyl (SF₅) group as a new, potential functional group. The SF₅ moiety is considered to be a "super-trifluoromethyl group" and therefore is expected to be used for a variety of applications in pharmaceutical and agrochemical industries as well as materials sciences. How-

ever, synthetic methods for SF₅ compounds are not well investigated; currently, especially the synthesis of aliphatic SF₅ compounds are tough compared with those of aromatic ones. Our efforts toward the synthesis of SF₅ compounds will be reported in future.

Who contributed to the idea behind the cover?

When I asked my daughter Mami, who is studying Japanese-style painting at the Tama Art University, for a cover design of our isoxazoline triflones, she painted this for me. The fluorine-functionalized diaryl-isoxazolines are potential insecticides actively researched in several agrochemical companies, and show potent blocking of insect GABA receptors on a broad pest range. This year, the Japanese Government has announced to promote agriculture development, essential for global food security.

