OIST | Innovation

Versatile and selective fluoroalkylation catalyst

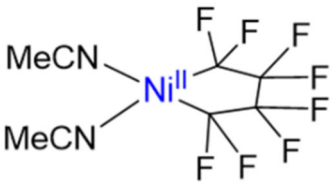
Summary

Fluorination of heterocycles is a widely used strategy to selectively modify chemical intermediates and proteins, including drug compounds and intermediates. Current fluoroalkylation catalysts often include expensive metals/ligands and are limited by costly reagents, effectively restricting the reaction to trifluoromethylation. Inexpensive Ni-based protocols have the significant disadvantage of requiring a tailored nickel catalyst to transfer different fluorinated groups.

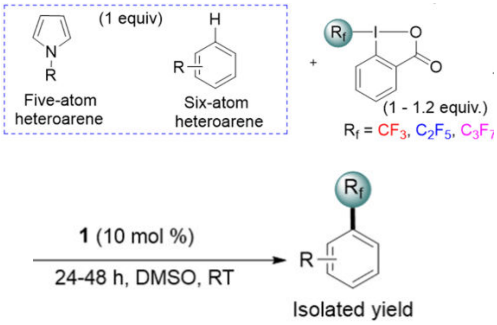
A team of OIST researchers led by Dr. Eugene Khaskin have developed a novel platform to functionalize heteroarenes with any perfluoroalkyl group using a single catalyst. The catalyst is highly stable and the fluorination reaction can be conducted in a variety of solvents under mild conditions. This novel approach opens the door to virtually unlimited fluoroalkylation options, to achieve optimum chemical and biological properties.

Technology

This simple Ni^{II} catalyst features a cyclometalated fluorocarbon cycle which allows access to high valent Ni^{III}/Ni^{IV} species in the presence of an external fluoroalkyl substrate, e.g. from a Togni reagent. The fluorocarbon cycle is not cleaved from the metal and only the desired fluoroalkyl substrate leaves as a $\cdot C_nF_{2n+1}$ radical, making this a universal catalyst for any fluoroalkyl group. The reaction can be performed at room temperature in any wet, Lewis-base solvents. The fluoroalkylation is selective to the 1-position with respect to the heteroatom, yielding a single product. This catalyst can also be used to fluorinate peptides and proteins selectively at heteroarene-containing amino acids.



Nickel catalyst **1** can be used to transfer virtually any fluoroalkyl group



Five- and six-atom heteroarenes can be readily functionalized under mild reaction conditions

Applications

- Fluoroalkylation
- Protein functionalization
- Drug and functional compound development

Advantages

- A single catalyst to screen different fluoroalkyl functional groups
- Inexpensive
- Mild reaction conditions

Category
Chemistry & Materials Science

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Intellectual Property
Patent Pending

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