

## Scientists in Singapore open door to new medicines for drug discovery applications

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Deviated from the standard logic of synthesis by designing a new strategy

Researchers from the National University of Singapore (NUS) have pioneered a new catalytic transformation that converts epoxides into fluorinated oxetanes, a coveted but difficult-to-make class of drug molecules that escaped synthetic preparation for years. By unlocking a pathway to these valuable drug scaffolds, this discovery potentially opens the door to new medicines for drug discovery applications.

The researchers deviated from the standard logic of synthesis by designing a new strategy that inserts a difluorocarbene species selectively into the structure of readily available three-membered epoxides. This process is facilitated by an inexpensive copper catalyst, which stabilises the difluorocarbene generated from a commercially available organofluorine precursor. The resulting copper difluorocarbenoid complex coordinates with the epoxide and triggers site-selective ring cleavage and cyclisation, to yield the desired ?,?-difluoro-oxetane product via a metallacycle intermediate. Computational studies further provided insight into the new reactivity mode and its underlying mechanism. Additionally, lipophilicity and metabolic stability studies supported the potential of these fluorinated oxetanes as valuable drug scaffolds.

Studies are now ongoing to investigate the biological properties of these newly synthesised drug analogues and extend the methodology to other classes of heterocyclic drug-like compounds.