

Synthesis of medium-sized ring structured compounds





Figure shows the reaction scheme of chemical compounds with nine- and tenmembered ring formation. Chiraphos and SIPHOX are two commercially available compounds. Credit: National University of Singapore

NUS chemists have discovered new reaction pathways to synthesise medium-sized heterocyclic compounds for the development of therapeutic drug molecules.

Compounds containing medium-sized (8 to 12 membered) rings are not commonly used in the development of pharmaceutical drug <u>compounds</u> despite their significance in many bioactive natural products. This is associated with the lack of efficient methods to create these compounds using synthetic chemical means. Cycloaddition (combining two or more molecules to form cyclic organic compounds) is a chemical technique which is usually used for constructing compounds with <u>ring structures</u> from readily available building blocks. There are well-established



methods for the synthesis of five-, six- and more recently sevenmembered ring compounds using this technique. However, the synthesis of heterocycles larger than eight-membered rings remains challenging.

A <u>research team</u> led by Prof Zhao Yu, from the Department of Chemistry, NUS has developed a series of palladium-catalysed reactions which can form nine- and ten-membered heterocycles through [5 + 4]and [6 + 4] cycloadditions. In these cycloaddition reactions, one compound provides a 4-atom unit, while the other cross partners provide either a 5- or 6-atom unit to prepare the nine- or ten-membered rings. These new <u>reaction</u> pathways make use of commercially available starting compounds and can produce heterocycles which are of a single type of stereoisomer. Stereoisomers are <u>chemical compounds</u> that have the same molecular formula and atom bonding sequence but differ in the orientation of their atoms in the three-dimensional space.

Prof Zhao said, "These structures represent new compounds with potential biological activities. There are many bioactive natural products that possess specific medium-sized rings, but their synthesis has been very difficult. We can now access this type of compounds with ease."

"We are continuing to explore the development of other medium-sized ring structured compounds and the biological screening of these classes of compounds as potential anti-cancer therapeutics," added Prof Zhao.

More information: Ya-Nong Wang et al. Pd-Catalyzed Enantioselective [6+4] Cycloaddition of Vinyl Oxetanes with Azadienes to Access Ten-Membered Heterocycles, *Angewandte Chemie International Edition* (2017). DOI: 10.1002/anie.201711648

Li-Cheng Yang et al. Construction of Nine-Membered Heterocycles through Palladium-Catalyzed Formal [5+4] Cycloaddition, *Angewandte Chemie International Edition* (2017). DOI: 10.1002/anie.201611474



Zi-Qiang Rong et al. Nine-Membered Benzofuran-Fused Heterocycles: Enantioselective Synthesis by Pd-Catalysis and Rearrangement via Transannular Bond Formation, *Journal of the American Chemical Society* (2017). DOI: 10.1021/jacs.7b09161

Provided by National University of Singapore

Citation: Synthesis of medium-sized ring structured compounds (2018, December 19) retrieved 27 April 2024 from <u>https://phys.org/news/2018-12-synthesis-medium-sized-compounds.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.