FACULTY OF SCIENCE
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DEAN
Professor Qiang ZHOU

Press release For immediate release

HKU Chemists Harness Light to Build 3D Molecular Structures for Drug Discovery

25 August 2026

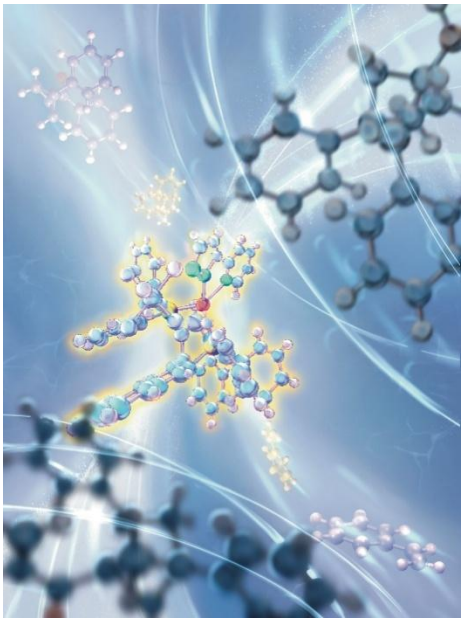

Image 1: Artistic illustration of a light-driven reaction for constructing three-dimensional BCH molecular structures. Image credit: Emily R.-C. Yang.

Researchers from the Department of Chemistry at The University of Hong Kong (HKU), led by Professor Jian HE and collaborators, have developed a new light-driven method for constructing three-dimensional molecular building blocks that could give medicinal chemists greater flexibility in designing new drug candidates. The approach broadens the range of starting materials that can be used while suppressing unwanted polymerisation, overcoming key limitations of existing synthetic methods. The findings have been published in *Nature Chemistry*.

Benzene rings are among the most common structural building blocks in medicines. They are chemically stable and provide a useful framework for positioning other functional groups within a drug molecule. However, their flat and relatively lipophilic nature can sometimes contribute to undesirable properties, such as poor water solubility or less favourable interactions with biological targets.

Medicinal chemists are therefore increasingly exploring three-dimensional alternatives that can replace benzene rings while performing a similar structural role in drug molecules. One promising class is bicyclo[2.1.1]hexanes, or BCHs. Their compact, three-dimensional shape offers researchers another way to fine-tune the shape and properties of drug molecules, potentially improving characteristics such as solubility, selectivity and metabolic stability.

One important route to BCHs involves combining bicyclo[1.1.0]butanes or BCBs with alkenes. BCBs are highly strained small-ring molecules that serve as useful starting materials for building more complex three-dimensional structures. However, synthesising structurally diverse BCHs has remained difficult. Existing methods may work

only with a limited range of starting materials and can also trigger unwanted polymerisation or suffer from catalyst instability.

Professor He's team and their collaborators have now developed a new class of copper(I) photosensitisers that use visible light to drive this reaction. After absorbing light, the copper complex transfers energy to one of the starting materials, enabling BCH structures to form in a more controlled manner.

The new strategy expands the range of starting materials that can be used and allows chemists to control where different chemical groups are positioned on the BCH scaffold. The team also demonstrated gram-scale synthesis and further modification of the resulting BCHs with a variety of functional groups, highlighting the method's potential usefulness in medicinal chemistry and drug development.

Professor Jian He expressed optimism about the potential impact of this discovery, stating, "The heteroleptic copper(I) photosensitisers developed by our team provide a new approach to the efficient and selective synthesis of BCHs. By modulating the triplet energy levels of copper complexes, we have effectively suppressed polymerisation side reactions and expanded the substrate scope to include electron-deficient alkenes, enynes, dienes, and even aliphatic alkenes. This opens new opportunities for sustainable chemical production and the development of more diverse drug candidates."

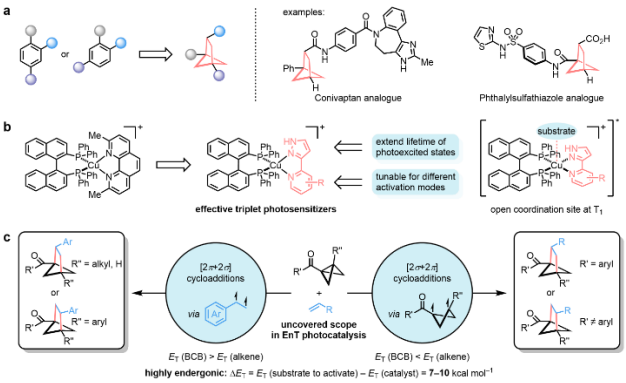

Image 2: Catalytic photosensitisation strategies for the synthesis of BCH bioisosteres via intermolecular cycloadditions. Image adapted from Tang et al., Nature Chemistry (2026).

For details of the research, please refer to the journal paper "*Modulating endergonic triplet photosensitization for cycloadditions between bicyclo[1.1.0]butanes and alkenes*".

About Professor Jian He: https://www.scifac.hku.hk/f/upload/9040/ProfessorJianHE.pdf

About the Research Team: PhD student Wing Yi TANG and Research Assistant Professor Dr Jun GUO from Professor HE's research group are the co-first authors. Other researchers, including Shaowei NIE, Jingyu YANG, Meng-Ying SUN, Yao ZHANG, Dongyi LIU, Zekun LI, and Professor Jun YANG from HKU, as well as collaborators from ShanghaiTech University, the University of Chinese Academy of Sciences, and Jinan University, contributed to this project.

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