重庆大学药学院成立 10 周年系列报告
第三十八期

天然产物全合成与创新药物研究重庆市重点实验室学术报告

第三百九十四讲

报告题目： **Enantioselective catalytic strategies for the synthesis of bicyclo[2.1.1]hexanes as phenyl bioisosteres**

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主 持 人： 熊阳 教授

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地　　点： 药学院学术报告厅

报告人简介：

2022-present: Postdoctoral Researcher, Autonomous University of Madrid, Spain
2020-2022: Postdoctoral Researcher, Technical University of Munich, Germany
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2015-2020: PhD in Organic Chemistry, Autonomous University of Madrid, Spain
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Current research interests
enantioselective catalysis；photocatalysis；synthesis of bioisosteres.

Awards
Spanish Royal Society of Chemistry (RSEQ) Prize for Young Postdoctoral

Researchers, 2025;
Marie Skłodowska-Curie Postdoctoral Fellowship (European Commission), 2024;
Technical University of Munich Foundation Postdoctoral Fellowship, 2021;
Award for the Best PhD Thesis from the Autonomous University of Madrid, 2021.

报告简介：

Bicyclo[2.1.1]hexanes are bridged bicyclic scaffolds with well-defined exit vectors that are becoming increasingly popular building blocks in medicinal chemistry since they represent saturated bioisosteres of disubstituted phenyl rings. In this context, the development of enantioselective strategies that enable the obtainment of phenyl bioisosteres with control of the tridimensionality is highly desirable since enantiomers often display a completely different behavior in biological systems. Herein we disclose the development of unprecedented enantioselective catalytic strategies to obtain differently disubstituted bicyclo[2.1.1]hexanes. These enantioenriched sp3-hybridized skeletons are appropriate mimics of ortho- and meta-substituted phenyl rings, representing versatile building blocks for the construction of a variety of drug analogues. Retention of the biological activity of the bicyclo[2.1.1]hexane-containing analogues in the specific proteins targeted by the original drugs has been confirmed. Moreover, their cytotoxicity in a panel of cancer cell lines was evaluated, observing markedly differential effects for the two enantiomers and, in some cases, a substantial improvement over the corresponding sp2-based drugs. This showcased that the control of the absolute configuration has an impact on the biological properties of the bioisostere-containing drug analogues, opening new avenues for lead optimization in drug discovery.