研究含硼化合物新合成法 潘伯申師生論文登國際期刊

學習新視界

【記者麥嘉儀淡水校園報導】化學系副教授潘伯申與實驗團隊學生兩篇論文，成功刊登國際期刊，其中一篇：「Robust Synthesis of Tetra-Boronate Esters Analogues and the Corresponding Boronic Acids Derivatives.可靠的四重硼酯以及相對應的硼酸之合成方法」，更登上《European Journal of Organic Chemistry》期刊封面。另一篇論文：「Protection-Free Strategy for the Synthesis of Boro-Depsipeptides in Aqueous Media under Microwave-Assisted Conditions 起始物不需要保護且以水為溶劑的含硼化合物微波合成方法」，則發表在《Molecules》期刊。

潘伯申及第一作者化學系校友邱碩蓓表示，此兩篇論文的實驗皆在本校完成，未來可應用於癌症藥物開發及其他，研究成員還包括蕭景瀚、陳品睿、艾冠霖、潘冠霖等化學系畢業系友，和國家衛生研究院副研究員陳仁焜及榮總醫師陳一瑋一起合作完成，第2篇化學系教授王伯昌亦參與。其中歐洲的期刊影響因子為3.261（2021），Molecules影響因子為4.412（2021）。

第一篇論文被European Journal of Organic Chemistry接受並採用為期刊封面，可見受到重視，是由潘伯申夫人設計成微波爐，旋鈕包含不同條件選項，傳達的意念是：「只要利用所開發的微波合成條件，就能簡單合成不同結構的含硼化合物。」潘伯申特別表示感謝，她在沒有化學背景訓練之下，能確切傳達設計出簡單明瞭的封面。

潘伯申指出，含硼化合物應用層面很廣，舉凡半導體材料、玻璃、防火材料，甚至小分子藥物，皆可由硼元素扮演重要角色。含硼化合物具有獨特性及功能，卻受限於合成相當不容易，且絕大多數含硼化合物採用傳統的合成策略，不但曠日費時，且極耗人力投入，最終導致生產及開發成本高昂而中斷。

為降低其合成難度，潘伯申與實驗室團隊積極投入研發，實驗結果顯示，新合成策略具有操作簡單、 反應時間短及合成效率高等優點。對於想開發含硼藥物的公司而言，可大幅降低研發成本，目前已申請專利，潘伯申希望「未來可有效協助藥物開發，特別是乳癌治療上。」

邱碩蓓開心地表示，論文能登上期刊封面很感動，表示能力和努力被認可，讓她在研究這條路上更有信心。她說：「這篇論文的產出其實是意外中的產物。將四硼酯化合物透過溫和的反應條件，變成四硼酸化合物。實驗過程中，嘗試了許多方法，失敗的次數可謂不計其數。感謝潘伯申從大學到博班一路上的指導與幫忙，尤其在實驗遇到

瓶頸時，適時的伸出援手，甚至寄望自己未來也能成為這樣的老師。」同時，邱碩蓓也提到，實驗室成員們大方分享遇到的問題，一起討論如何解決問題的方法，是很棒的實驗團隊。

最後，潘伯申說道：「論文獲刊登要歸功於學生團隊的主動、耐心與努力。」在實驗過程中看到學長姐會帶學弟妹一起做實驗，對於研究也很有想法，「學生們會記得在實驗過程中經歷的感受，日後無論面對什麼困難都有幫助。」他更坦白說道：「老師不見得每次指導的意見與看法都是最好的。令我感到欣慰的是，同學們以實驗數據與結果來反駁老師的假設，並證明他們才是對的。能讓學生們青出於藍，應該是做老師最大的成就吧。」


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Front Cover:
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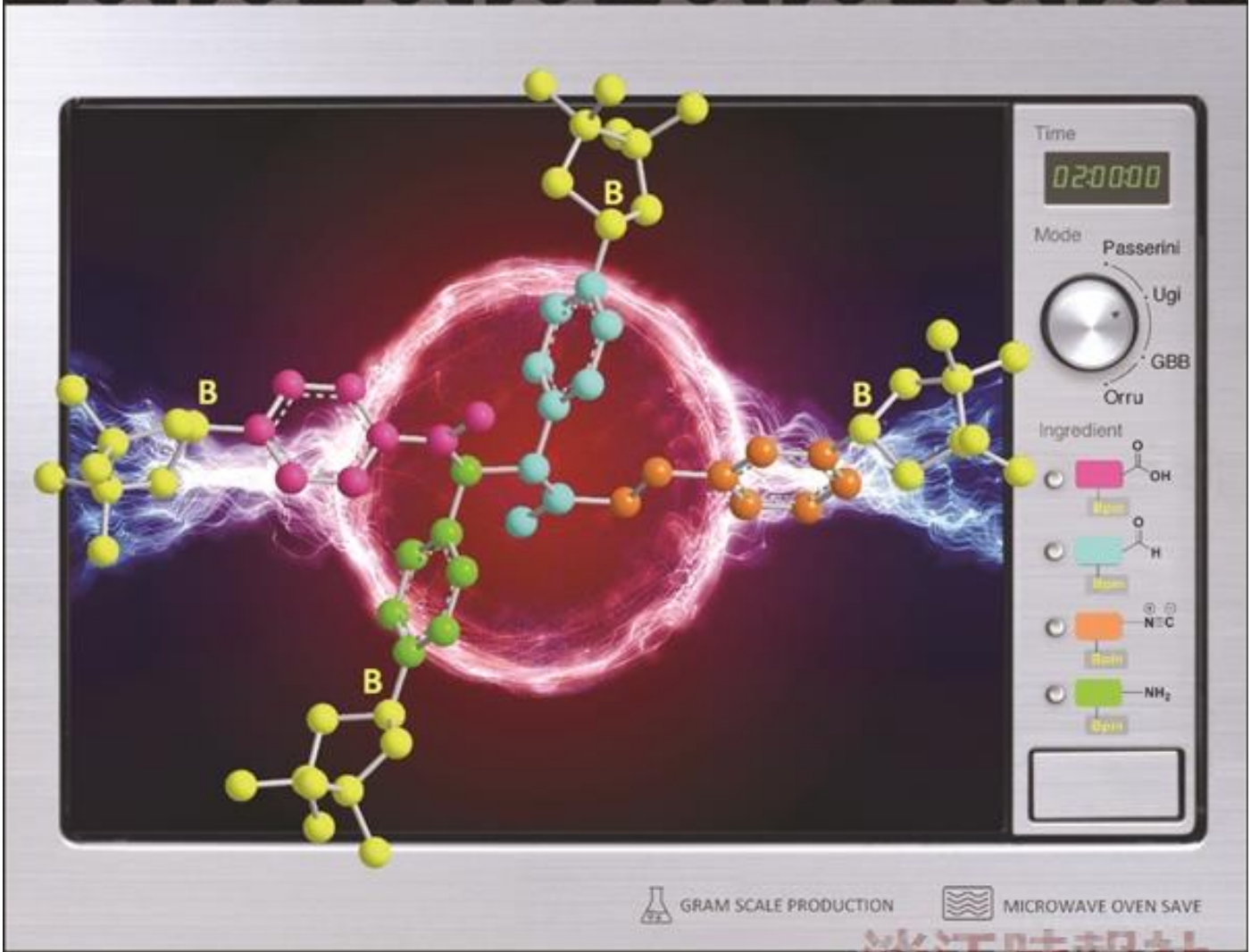
Robust Synthesis of Tetra-Boronate Esters Analogues and the Corresponding Boronic Acids Derivatives



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Protection-Free Strategy for the Synthesis of Boro-Depsipeptides in Aqueous Media under Microwave-Assisted Conditions

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Abstract: In this report, 19 boron-containing depsipeptides were synthesized via microwave-assisted Passerini three-component reaction (P-3CR) in an aqueous environment. The linker-free DAHMI fluorescent tagging approach was used on selected boron-containing compounds to study the relationship between their structures and their level of cellular uptake of HEK293 cells. The biological data retrieved from the DAHMI experiments indicated that while the structures of tested compounds may be highly similar, their bio-distribution profile could be vastly distinctive. The reported optimized one-pot synthetic strategy along the linker-free in vitro testing protocol could provide an efficient platform to accelerate the development of boron-containing drugs.

Keywords: depsipeptide(s); α-acyloxyamide; passerini; multicomponent; microwave-assisted; DAHMI; boronic acid

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1. Introduction

Boronic acids are important entities for a broad spectrum of applications [1]. Although they were widely recognized as the vital building blocks in varieties of synthetic reactions [2], boron-containing entities were also exploited as the flame retardant materials [3], semi-conducting materials [4], boron carrier agents for the boron neutron capture therapy [5], enzyme inhibitors [6], and also as the insecticide [7]. In particular, boron-based pharmaceuticals have gained much attention and success for the past decades. Unlike most pharmaceuticals that rely on non-covalent interactions with their biological targets, boron-containing compounds form a reversible covalent bond between their targets. This unique advantage makes such compounds have a high affinity toward their targets with relatively low molecular weight [6]. In 2003, the first boronic acid, Bortezomib (Velcade®), was approved by the U.S. FDA to treat multiple myeloma. Since then, a series of boron-containing molecules are either in different stages of clinical trials or have been approved by the U.S. FDA (Figure 1).