THE HONG KONG
UNIVERSITY OF SCIENCE
AND TECHNOLOGY

DEPARTMENT OF CHEMISTRY

The 31st Symposium on Chemistry Postgraduate Research in Hong Kong

22 March 2025

Organized by

Participating Universities

CityU

Sponsored by

ACS International LBTEK Chem Express MERYER Waters™ SCIEX

Information at: chempgsym.hkust.edu.hk

香港科技大學
THE HONG KONG UNIVERSITY OF
SCIENCE AND TECHNOLOGY

The 31st Symposium on Chemistry Postgraduate Research in Hong Kong

The Hong Kong University of Science and Technology
22 March 2025 (Saturday)

Keynote Lecture	**Professor Robert Jerard Gilliard, Jr.** **Department of Chemistry** **Massachusetts Institute of Technology** **USA**
Registration Fee	**Free**
Website:	**https://chempgsym.hkust.edu.hk/**
Organizing Committee	**Prof. Yangjian QUAN (Chairperson)** **Prof. Tengteng CHEN** **Prof. Hugh NAKAMURA** **Prof. Kenward VONG** **Mr. Jing OUYANG** **Mr. Chun Ming CHOW (Secretary)**

Institutional Representatives	**Faculty**	**Postgraduate Student**
CityU	Prof. Kenneth Kam-Wing LO	Junwen XU
CUHK	Prof. Zhifeng HUANG	Yating FANG
HKBU	Prof. Wei Shen AIK	Kin Cheung LI
HKU	Prof. Junzhi LIU	Chang WANG
HKUST	Prof. Yangjian QUAN	Jing OUYANG
PolyU	Dr. Franco LEUNG	Rick Ka-Lung HUNG

Program Rundown

Time	Event
9:00 am – 9:30 am	**Registration & Mounting of Posters (Atrium)**
9:30 am – 10:00 am	**Opening Ceremony (LTA)**
10:00am – 11:00am	**Keynote Lecture (LTA)** **The Ligand Matters: Unusual Strategies Toward the Design of Boron-Doped Molecules and Emissive Materials** **By Professor Robert J. Gilliard, Jr.** Department of Chemistry Massachusetts Institute of Technology, USA
11:00am – 11:30am	**Group Photo-taking (LTA) and** **Tea Reception (outside LTB & LTC)**
11:30am – 11:50am	**Postgraduate Student Oral Presentation 1 (LTA)** **Mechanical achiral chiral switching of a co conformationally flexible [2]catenane** By YAO Yueliang, Hong Kong University
11:50am – 12:10 pm	**Postgraduate Student Oral Presentation 2 (LTA)** **Enantioselective Zn-Catalyzed Hydrophosphinylation of Nitrones: An Efficient Approach for Constructing Chiral α-Hydroxyamino-Phosphine Oxides** By LUO Shihui, Hong Kong Baptist University
12:10pm – 12:30pm	**Postgraduate Student Oral Presentation 3 (LTA)** **Reactivity of A Hexaaryldiboron(6) Dianion as Boryl Radical Anions** By LI Shuchang, City University of Hong Kong
12:30pm – 1:45pm	**Lunch**
1:45pm – 3:15pm	**Poster Session (Atrium)**

Time	Event
3:15pm – 3:35pm	**Postgraduate Student Oral Presentation 4 (LTA)** **A Monolithically In-textile Wristband for Wireless Epidermal Biosensing** By MA Xiaohao, Hong Kong Polytechnic University
3:35pm – 3:55pm	**Postgraduate Student Oral Presentation 5 (LTA)** **Antibody Reactions and Coacervate-Mediated Delivery for Cancer Therapies** By YUAN Dingdong, The Chinese University of Hong Kong
3:55pm – 4:15pm	**Postgraduate Student Oral Presentation 6 (LTA)** **Borenium Catalyzed Chain-walking** **By ZHU Zheng, The Hong Kong University of Science and Technology**
4:15pm – 4:45pm	**Award Presentation and Closing Ceremony (LTA)**

Keynote Lecture

The Ligand Matters: Unusual Strategies Toward the Design of Boron-Doped Molecules and Emissive Materials

Professor Robert J. Gilliard, Jr.
Department of Chemistry
Massachusetts Institute of Technology
USA

Abstract

Boron, an element that attracts substantial interest from organic and inorganic chemists, has been extensively used in Lewis acid-mediated catalysis, borylation chemistry for pharmaceutical development, small-molecule activation, the development of novel reagents, and as components of luminescent molecular materials and devices. Its widespread use across multiple subfields of chemistry stems from its metalloid characteristics, possessing properties of both metals and non-metals. Boron-containing heterocycles have been of particular interest to the scientific community; of which, neutral boron(III)-incorporated polycyclic molecules are among the most studied. Understanding their redox transformations is important for applications which rely on electron transfer and charge transport (e.g., organic light-emitting diodes, field-effect transistors, chemical sensors). While relevant redox species can often be electrochemically observed, it remains challenging to isolate and characterize boracycles where the boron center and/or polycyclic skeleton feature an unpaired electron and/or charge. Our laboratory has pioneered the use of ligand-based coordination chemistry approaches toward the design of new types of boracyclic cations, anions, and radicals. Throughout our studies we have begun to extract redox-state-specific structure-function trends, and it is now possible to tailor-make unusually bonded boracycles with unique spin properties, reactivity, and photophysical properties. This lecture will cover our work on novel chemical synthons such as diazoborane, borafluorene anions, diborapentacene dianions, as well as recent results on the first examples of dicationic versions of Schlenk's and Thiele's hydrocarbons. The lecture will conclude with a discussion of the use of borenium ions as emissive materials, including an explanation of the distinct optical transitions that lead to thermochromism and luminescence.

Keynote Speaker (Biography)

Professor Robert J. Gilliard, Jr.

Prof. Robert J. Gilliard, Jr. is the Novartis Professor of Chemistry at the Massachusetts Institute of Technology (MIT). Prior to joining MIT, he was a member of the faculty at the University of Virginia. He obtained his bachelor's degree in chemistry at Clemson University where he was an undergraduate researcher in the laboratory of Prof. Rhett C. Smith. He earned his doctorate in chemistry at The University of Georgia with Prof. Gregory H. Robinson. Gilliard was a Merck Postdoctoral Fellow and a Ford Foundation Postdoctoral Fellow where he completed his studies working jointly at the Swiss Federal Institute of Technology (ETH Zürich) with Prof. Hansjörg Grützmacher and at Case Western Reserve University with Prof. John Protasiewicz. Gilliard is currently an associate editor at the *Journal of the American Chemical Society*, has served on editorial advisory board of *Angewandte Chem*ie, and is currently on the advisory board of *Chemical Science*, *Chemical Communications*, *ChemistryEurope*, *Chem Catalysis*, and *Inorganic Chemistry*. His awards and honors include: *Chemical and Engineering News* Talented 12 Scholar, Research Corporation for Science Advancement Scialog Collaborative Innovation Award, National Science Foundation CAREER Award, Alfred P. Sloan Research Fellow, *Organometallics* Distinguished Author Award, Beckman Young Investigator Award, Packard Fellowship for Science and Engineering, Lloyd N. Ferguson Award for Excellence in Research, ACS Harry Gray Award for Creative Work in Inorganic Chemistry, Presidential Early-Career Award for Scientists and Engineers, and a NIH Maximizing Investigators' Research Award.

Oral Presentation Session

The Keynote Lecture and Oral Presentation Session will be held in the Citibank Lecture Theater (LT-A), the Hong Kong University of Science and Technology. Each university will nominate one postgraduate student representative to give a 15-minute oral presentation, followed by a 5-minute question-and-answer session. Students should use the computer system (a windows PC) in the Citibank Lecture Theater (LT-A).

Poster Presentation Session

The poster session will be held in the Hong Kong Jockey Club Atrium, the Hong Kong University of Science and Technology. Posters will be displayed throughout the Symposium. Poster presenters are required to mount their posters before 9:30am using mounting materials provided at the venue, and dismount their poster by 17:30, after the closing ceremony of the Symposium. Posters not dismounted after 17:30 will be disposed. No on-site poster delivery service will be entertained.

The size of each poster board measures 1390 mm (H) × 980 mm (W). Poster presenters are suggested to prepare posters with A0 size.

Each postgraduate student can only be the presenting author of one poster but they may be listed as a co-author in other posters. Posters will be categorized into the following three major subject areas:

(1) Analytical, Biological, and Environmental Chemistry (AnaBioEnv)
(2) Inorganic and Organic Chemistry (InoOrg)
(3) Materials and Physical Chemistry (MatPhy)

The Best Oral and Poster Presenter Awards

The best oral presenters and poster presenters from the three categories will be selected by a panel of judges made up of representatives from six universities. The awards will be presented during the closing ceremony of the Symposium. The award certificates and prizes will be delivered to corresponding institutional representatives after the Symposium.

Abstract Book

Participants will receive the abstract book in PDF through email. Printed abstract book will not be provided

Lunch Arrangement

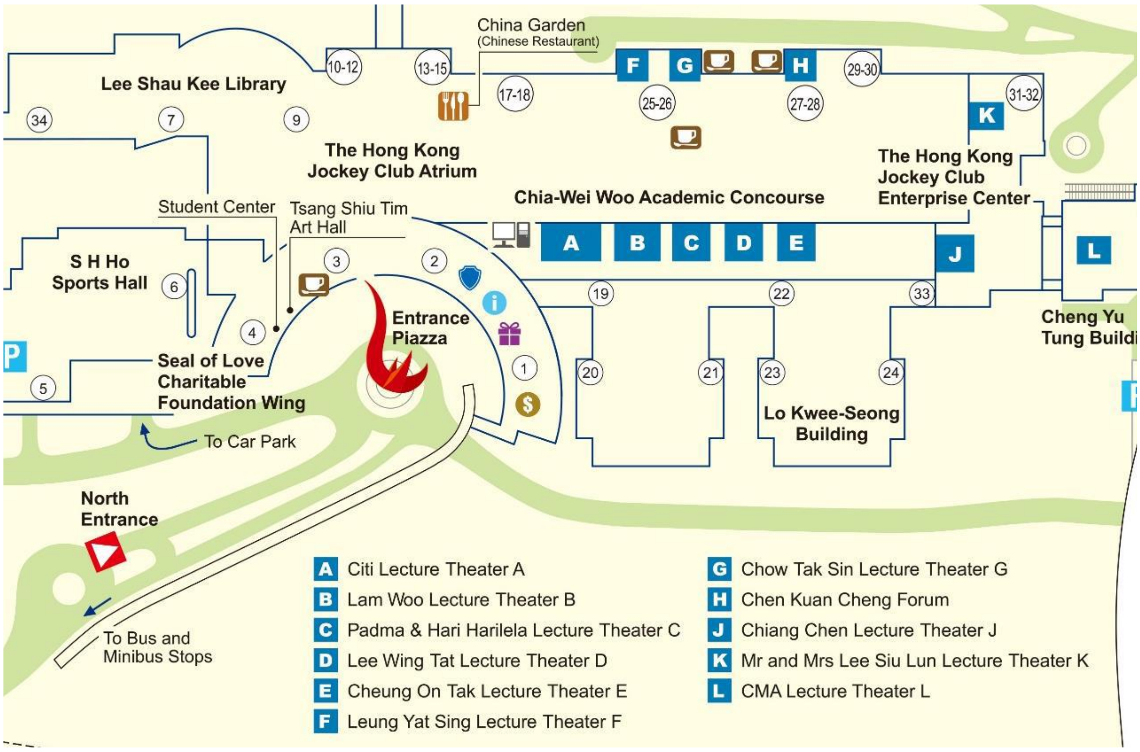
A set lunch has been arranged for faculty members in UniBistro, G/F Lo Ka Chung University Center, HKUST. There will be supporting staff giving directions to the venue. For other attendees, there are several catering outlets on campus:

- 1/F, Academic Building: American Diner, Hungry Korean, Passione
- G/F, Academic Building: China Garden, Starbucks Coffee
- LG1, Academic Building: Can.teen II
- LG5, Academic Building: McDonald's
- LG7, Academic Building: Gold Rice Bowl, Asia Pacific Catering, Oliver's Super Sandwich, TamJai SamGor

Driving to HKUST

Faculty members who wish to drive to HKUST could send the names, mobile phone number and vehicle registration number via institutional representatives to Mr. Ming Chow by email (ccming@ust.edu.hk) on or before 20 March 2025 (Thursday).

Campus Map: Atrium and LTA

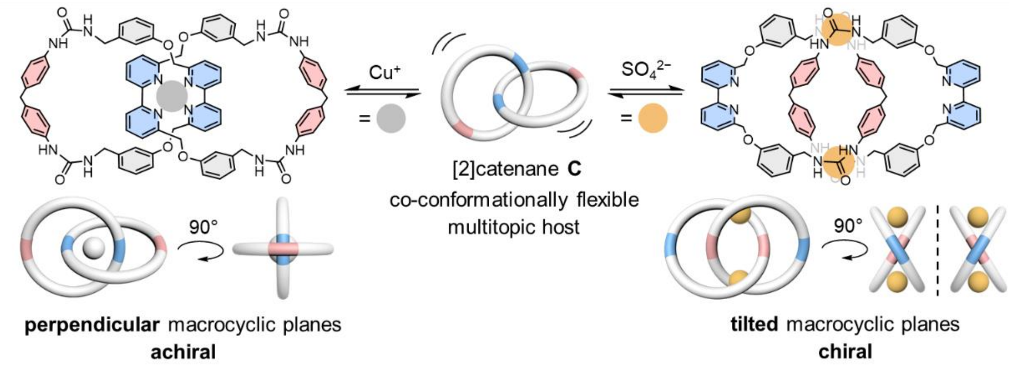


Mechanical achiral-chiral switching of a co-conformationally flexible [2]catenane

Yueliang Yao and Ho Yu Au-Yeung*
Department of Chemistry, The University of Hong Kong, Hong Kong, P. R. China
Email: hoyuay@hku.hk

Abstract

The ability of catenane-based receptors to undergo large-amplitude structural adaptation via low-energy co-conformational motions represents a unique mechanism to achieve selective and strong guest binding.[1] In this work, a heteroditopic, co-conformationally flexible [2]catenane for selective copper(I) cation or sulfate anion binding is described. The interlocked macrocycles in the catenane host can freely rotate and flip, and as such can easily adjust its co-conformation to fit for the ionic guests of opposite charge, different geometry and binding stoichiometry. Binding of the copper(I) cation and sulfate anion is strong, and respectively induces an achiral and chiral co-conformation of the catenane host, thereby rendering this work as a rare example of reversible guest-controlled mechanostereochemical switching.[2]



References

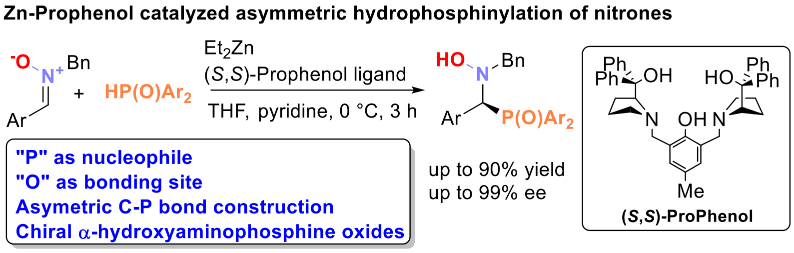
1. Au-Yeung, H. Y.; Deng, Y. *Chem. Sci*., **2022**, *13*, 3315 – 3334.
2. Yao, Y.; Tse, Y. C.; Lai, S. K.-M.; Shi, Y.; Low, K.-H.; Au-Yeung, H. Y. *Nat. Commun*., **2024**, *15*, 1952.

Enantioselective Zn-Catalyzed Hydrophosphinylation of Nitrones: An Efficient Approach for Constructing Chiral α-Hydroxyamino-Phosphine Oxides

Shihui Luo, Jun (Joelle) Wang*
Department of Chemistry, Hong Kong Baptist University, Kowloon, Hong Kong, China;
junwang@hkbu.edu.hk

Abstract

Although enantioselective hydrofunctionalization of nitrones are established for synthesis of various types of chiral hydroxylamines, the asymmetric catalytic hydrophosphinylation of nitrones remains highly challenging. Herein, an efficient asymmetric hydrophosphinylation of nitrones, catalyzed by the dinuclear zinc catalyst derived from ProPhenol, is presented, accommodating a variety of nitrones and phosphine oxides. This approach successfully addresses the long-standing challenge of catalytic hydrophosphinylation of C=N bond and offers efficient and rapid access towards chiral α-hydroxyamino-phosphine oxides. Control experiment suggests the oxide anion in the nitrone motif is crucial for the enantio-controlling.



References

1. Huang, L.; Arndt, M.; Gooßen, K.; Heydt, H.; Gooßen, L. J. *Chem. Rev.* **2015**, *115*, 2596-2697.
2. Yin, S.; Weeks, K. N.; Aponick, A. *J. Am. Chem. Soc.* **2024**, *146*, 7185-7190.

Reactivity of a Hexaaryldiboron(6) Dianion as Boryl Radical Anions

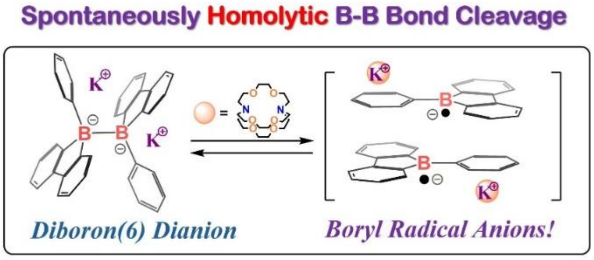
Shuchang Li, Zhenpin Lu*

Department of chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong SAR, 999077, P. R. China

Email: zhenpilu@cityu.edu.hk

Abstract

Boron-containing radical species have received tremendous research interest, which might be ascribed to their applications in chemical sensors, organic synthesis, polymer chemistry, and material science. [1-3] Our research showcases a new way to obtain boryl radicals by spontaneously breaking B-B bonds. By performing a reductive B-B coupling of 9-borafluorene, we successfully synthesized a hexaaryl-substituted diboron (6) dianion. Remarkably, it demonstrates the unique capability of undergoing homolytic B-B bond cleavage at room temperature, resulting in the formation of boryl radical anions. This phenomenon has been confirmed through EPR studies and occurs in the presence of 2.2.2-cryptand. Furthermore, it exhibits a direct reaction with diphenylacetylene, resulting in the formation of an unprecedented 1,6 diborylated allene species. DFT computational studies suggest that the preferred reaction pathway involves homolytic B-B bond cleavage, with the formation of boryl radical anions playing a crucial role in the dearomatization process. Moreover, it accomplishes the dearomative diborylation of anthracene and the activation of elemental sulfur/selenium under mild reaction conditions. The resulting borylation products have been characterized using NMR spectra, HRMS, and X-ray single-crystal diffraction.[4]



Reference

[1] Kaim, W.; Hosmane, N. S.; Záliš, S.; Maguire, J. A.; Lipscomb, W. N. *Angew. Chem. Int. Ed.* **2009**, *48*, 5082-5091.

[2] Renaud, Boron in radical chemistry. Encyclopedia of radicals in chemistry, biology and materials. John Wiley & Sons, Ltd. **2012**.

[3] Su. Y.; Kinjo, R. *Coord. Chem. Rev.* **2017**, *352*, 346-378

[4] S. Li, F. Shiri, G. Xu, S.-M. Yiu, H. K. Lee, T. H. Ng, Z. Lin, Z. Lu, *J. Am. Chem. Soc.* **2024**, *146*, 17348-17354.

A Monolithically In-textile Wristband for Wireless Epidermal Biosensing

Xiaohao Ma[1,2], Yuanjing Lin[1]*, Zijian Zheng[2]*

1. School of Microelectronics, Southern University of Science and Technology, Shenzhen 518055, China.

2. Department of Applied Biology and Chemical Technology, Faculty of Science, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR 99077, China.

E-mail: linyj2020@sustech.edu.cn; zijian.zheng@polyu.edu.hk

Abstract

Textile-based wearable electronics have attracted intensive research interest due to their excellent flexibility and breathability inherent in the unique three-dimensional porous structures. However, one of the challenges lies in achieving highly conductive patterns with high precision and robustness without sacrificing the wearing comfort. Herein, we developed a universal and robust in-textile photolithography strategy for precise and uniform metal patterning on porous textile architectures. The as-fabricated metal patterns realized a high precision of sub-100 μm with desirable mechanical stability, washability, and permeability[1]. As a proof-of-concept, a fully integrated in-textiles system for multiplexed sweat sensing was demonstrated (Fig. 1). The proposed method opens new possibilities for constructing multifunctional textile based flexible electronics with reliable performance and wearing comfort.

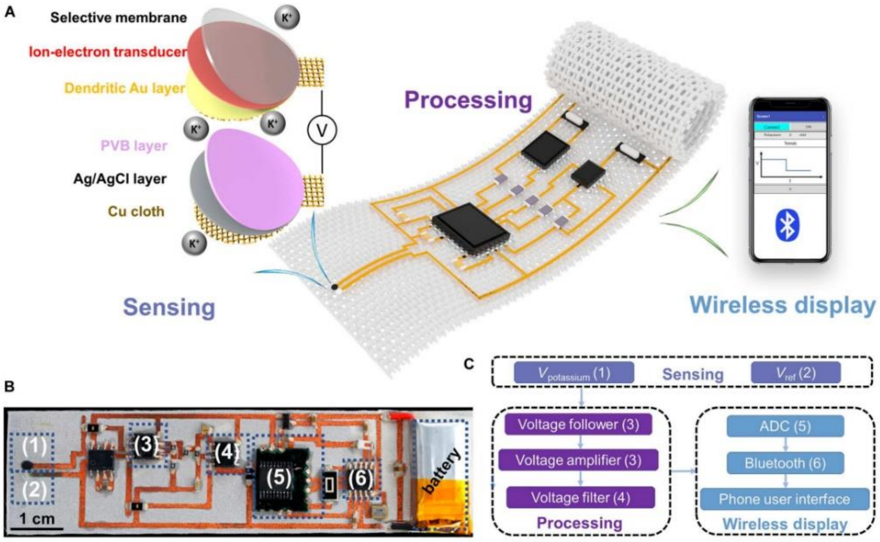


Fig. 1. Image and schematic of the monolithically integrated in-textile wristband.

Reference:

1. Ma, X. H.; Zheng, Z. J. *Science Advances*, **2023**, *9*, eadj2763.

Antibody Reactions and Coacervate-Mediated Delivery for Cancer Therapies

YUAN Dingdong, XIA Jiang*

Department of Chemistry, the Chinese University of Hong Kong; 1155165540@link.cuhk.edu.hk

Abstract

Targeted protein degradation technology plays a vital role in treating protein-related diseases, especially for those ‘undruggable’ targets in traditional drug discovery. PROTAC has been developed rapidly for intracellular protein degradation in clinical use, but membrane and extracellular protein degradation using the lysosome pathway still has challenges. Here, we designed and synthesized a lysosome sorting sequence (LSS) peptide derivative which can form the coacervates by liquid-liquid phase separation (LLPS). The LSS coacervates could successfully enrich the proteins and deliver the cargoes to the cells and achieve the lysosome targeting. We used the LSS coacervates to enrich the antibody-LSS conjugate, in which the antibody in the coacervates could bind to the targeted antigen specifically on the cell surface and the LSS coacervates could help this antibody-antigen complex enter the cells and lead to the lysosome to achieve the targeted antigen degradation. We successfully degraded the HER2 and EGFR on SK-BR-3 cells by using the commercial anti-HER2 and anti-EGFR antibodies respectively, and the mechanism studies proved the degradation using LSS coacervates followed the lysosome pathway.

References

[1] Banik, S. M., *Nature* **2020**, *584* (7820), 291-297.

[2] Zhang, H., *J. Am. Chem. Soc.* **2021**, *143* (40), 16377-16382.

Brenium catalyzed “chain-walking”

Zheng ZHU, Prof. Yangjian QUAN*
Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon, Hong Kong SAR, China
E-mail: chyjquan@ust.hk

Abstract

Remote functionalization through progressive olefin isomerization enables site-selective modification at a distal position, diversifying synthetic approaches. However, the developed protocols have long relied on transition metal catalysis.[1-2] Transition metal catalyst is deemed irreplaceable, albeit facing challenges in metal residue and catalyst poisoning. In this work, we present a pioneering approach that employs a borenium ion as a catalyst for site-selective, remote borylation, eliminating the need for metal catalysts. As the reaction progresses, borylation isomers at different positions emerge, gradually and ultimately converging into the predominant α-borylation product. This process is akin to a “walking” of boron moiety along a carbon skeleton toward an aryl terminus. Detailed mechanistic studies and DFT calculations substantiate the borenium-catalyzed, stepwise migration via a reversible B-H insertion/elimination sequence. This remote borylation exhibits good functional group compatibility, complementing those methods reliant on transition metals. Furthermore, this metal-free protocol permits the convenient synthesis of silyl-remote-boryl compounds, demonstrating an opposite regioselectivity to that observed in transition metal catalyzed tandem silylation-borylation reactions. This discovery therefore contributes to site-selective, remote di-functionalization via sequential C-B and C-Si derivatizations, exemplified by the synthesis of amino-remote-alcohol bioactive molecules.

References

1. Vasseur, A.; Bruffaerts, J.; Marek, I. *Nat. Chem.* **2016**, *8*, 209-219.
2. Sommer, H.; Juliá-Hernández, F.; Martin, R.; Marek, I. *ACS Cent. Sci.* **2018**, *4*, 153-165.

Washable Textile Biosensors Enabled by Nanostructured Oxides with Fast Ion Diffusion

Yuqing Shi[1,2], Zijian Zheng[2,3,4,5*], Yuanjing Lin[1*]

[1]School of Microelectronics, Southern University of Science and Technology, Shenzhen 518055, China

[2]Laboratory for Advanced Interfacial Materials and Devices, School of Fashion and Textiles, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China

[3]Department of Applied Biology and Chemical Technology ,Faculty of Science, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China

[4]Research Institute for Intelligent Wearable Systems, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China

[5]Research Institute for Smart Energy, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China 8Lead contact

Abstract:

Textile-based electronics, known for their comfortable skin contact, hold great promise in the field of wearable healthcare, particularly for non-invasive sweat biosensing. However, developing biosensors that maintain sensitivity and comfort while being washable remains a significant challenge. In this study, we designed and developed β-Bi_2O_3 nanosheets, which endow textile-based biosensors with remarkable washability. These nanosheets exhibit fast ionic conductivity and high moisture stability without causing a significant increase in impedance. By decorating textiles with β-Bi_2O_3 nanosheets, we fabricated ion sensors for sodium, potassium, and proton sensing. These sensors not only retained their high sensitivity but also demonstrated outstanding washability, with performance retention exceeding 90% after 20 washing cycles. Furthermore, we demonstrated a washable and reusable integrated electronic textile wristband for wireless analysis of sweat biomarkers. This strategy of using nanostructured oxides as a durable layer and fast ion conductor provides excellent washability for textile-based sensing devices and is expected to promote the practical application of electronic textiles.

Synergistic Enhancement for Theranostic Hetero-nanocomposite for Sonodynamic and Chemodynamic Therapy with Ultrasound Contrast Imaging

Pinyou Chen, Hung Wing Li

Department of Chemistry, The Chinese University of Hong Kong, Sha Tin, New Territories

hungwingli@cuhk.edu.hk

Abstract

Sonodynamic therapy (SDT) has emerged as a promising modality due to its cost-effectiveness, non-invasiveness and high tissue-penetrating capability of ultrasound irradiation.[1] To address restricted low reactive oxygen species (ROS) generation, hypoxic conditions within tumours and lack of effective theranostic agents, a heterostructured TiO_2 framework fabricating with platinum (Pt) nanodots and linking with MnO_2-FA nanoflowers was established. TiO_2@Pt narrow the energy bandgap to improve ROS production under ultrasound while MnO_2–FA produce extra hydroxyl radical (·OH) through Fenton-like reactions. Properties of depleting glutathione of MnO_2-FA, oxygen supply from MnO_2 and Pt within tumour environment can provide an optimal condition to boost up ROS generation. Double oxygen generation from TiO_2@Pt–MnO_2 can give enhanced contrast ultrasound imaging of tumour as a theranostic agent with combined sonodynamic and chemodynamic cancer therapy. Proved by in vitro and vivo assays, TiO_2@Pt–MnO_2 yielded the highest ROS production and lowest cancer cell viability under ultrasound irradiation. The tremendous oxygen release of TiO_2@Pt–MnO_2 also highlights the potential of contrast ultrasound imaging agent. This two-in-one TiO_2@Pt–MnO_2 design illustrates the promise of heterostructured nanocomposites as theranostic platform in combined cancer therapy.

References

1. Liang, S.; Deng, X. *Adv. Funct. Mater.* , **2020**, *30*, 1908598.

Conformational dynamics of JAK2 pseudokinase-kinase domains revealed by hydrogen/deuterium exchange mass spectrometry and molecular dynamics simulation

Zhao Chang, Yao Zhongping*

zhongping.yao@polyu.edu.hk

Abstract

Janus kinase 2 (JAK2) is essential for regulating cell growth and division, particularly in blood cell production within the bone marrow. In the absence of signal stimulation, its pseudokinase (PK) domain binds to the tyrosine kinase (TK) domain, keeping JAK2 in an inactive state. Upon signal stimulation, this autoinhibition is disrupted, enabling JAK2 to an active state for catalytic activity. Pathogenic mutations constantly activate JAK2, causing overproduction of blood cells and consequently severe blood diseases. We applied hydrogen/deuterium exchange mass spectrometry (HDX-MS) to investigate the JAK2 PK-TK domains. The high sequence coverage allowed us to investigate the protein more comprehensively, including the regions that were not reported with X-ray crystallography. Most segments exhibited classical EX2 kinetic behavior, while the hinge region links the PK and TK domains showed both EX1 and EX2 kinetics, indicating interconversion between distinct conformations. Molecular dynamics (MD) simulations revealed the JAK2 PK-TK domains experienced periodic changes in torsion angle and interdomain distance, with the hinge region forming a transient 3_{10}-helix to facilitate conformational transitions. Our findings suggest that JAK2 undergoes inactive-to-active transitions under physiological conditions, and the pathogenic mutations may induce diseases via disrupting this dynamics equilibrium.

Chiral Recognition by Mass Spectrometry with the Combinations of Two Chiral Selectors

YI Qi, SHENG Yiqi, SIU Chi-Kit, YAO Zhongping

victoria.yi@connect.polyu.hk, zhongping.yao@polyu.edu.hk

Chiral recognition by mass spectrometry (MS) has advantages in its speed, sensitivity, and specificity, it also allows gas-phase investigations without solvent interference and offers insights into the intrinsic properties of chiral recognition. This project explores a novel approach using combinations of two chiral selectors. Nineteen chiral amino acids were selected as analytes and selectors for their biological relevance and diverse side chains, with their complex ions formed under ESI conditions with the presence of Cu(II).

Chiral selector pairs were tested for the chiral recognition of 19 proteinogenic amino acids, with Pro and aromatic amino acid combinations showing superior chiral recognition effects. ln(CR) value was introduced for the first time to quantitatively indicate chiral discrimination, with larger deviations from zero indicating a higher degree of chiral recognition. It was found that the two chiral selectors could play distinct roles, with one determining the chiral discrimination tendency while the other one only contributing to the chiral discrimination degree.

Computational modelling was employed to elucidate ion structures, energetics, and chiral discrimination mechanisms. The most promising geometry of $[\mathrm{Cu^{II}(Pro)(Phe)(Tyr)-H}]^+$ exhibited a penta-coordinated structure with a square-planar base (Cu-N/O: 1.94–2.06 Å) and an elongated axial coordination (Cu-O: 2.34 Å). Three spatial arrangements, where amino acids occupy the axial position, had comparable energies, suggesting their coexistence as precursor species. Only the amino acid at the axial position dissociates to form the corresponding dimer. Chiral selectivity was shown to depend on diastereomeric dimer stability, influenced by side-chain spatial hindrance in the square-planar structure.

Investigation of conformational dynamics of inhibitor-resistant β-lactamases and their interactions with inhibitors

Elena Bolonova, Tsz-Fung Wong, Pui-Kin So and Zhongping Yao
PolyU, 11 Yuk Choi Road, Hong Kong; zhongping.yao@polyu.edu.hk

Antibiotic resistance has become a major threat to public health. One of the most efficient mechanisms of resistance in bacteria is the production of special enzymes, such as β-lactamases (BLs), which can hydrolyze the β-lactam ring, a structural element shared by all β-lactam antibiotics. Combining β-lactam antibiotics with β-lactamase inhibitors has been a strategy to overcome the antibiotic resistance caused by the BL production.

Nevertheless, BLs have developed inhibitor-resistant properties through point mutations in specific sites, most commonly Met69, Ser130 and Arg244 in TEM-1 and SHV-1 BLs. Inhibitor-resistant variants of TEM and SHV BLs are posing significant challenges in the treatment of bacterial infections in clinics. However, the molecular mechanism for inhibitor-resistant properties of BLs is still poorly understood.

In this study, hydrogen/deuterium exchange mass spectrometry (HDX-MS) is used to investigate the relation between the dynamics changes and inhibitor-resistance properties of TEM and SHV BLs. The effects of Met69Leu, Ser130Gly and Arg244Ser mutations on the overall protein flexibility, the flexibility of protein backbone in specific catalytically important regions, and the relation between the conformational dynamics of TEM and SHV BLs and their resistance to 2 inhibitors, clavulanic acid and tazobactam, were studied. The HDX-MS results interestingly revealed that the inhibitor binding increased the overall flexibility of the proteins, especially the wild-type proteins. Upon clavulanic acid and tazobactam binding, major changes happened in the residues corresponding to the active site and interdomain hinge regions. It was proposed that the flexibility of these protein regions in the apo-state affects the binding affinity, which can be characterized by the inhibitory constant. At the same time, lower deuterium uptake in the catalytical center of the inhibitor/inhibitor-resistant BL complexes compared to the complexes of wild-type BLs signifies more stable hydrogen bonding, which leads to improved deacylation efficiency.

Abstract:

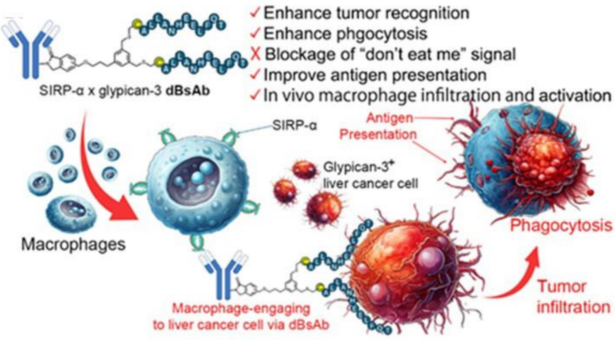
Mitochondria are essential organelles of living cells to produce energy, and they also maintain the cellular homeostasis and regulate cell death pathways. Mitochondrial dysfunction is also known to activate several mitochondrial retrograde signaling and mitochondrial stress response pathways, which promote cancer progression to malignancy. Therefore, targeting mitochondrial function has emerged as a potential therapeutic strategy against cancer. G-quadruplex (G4) is a unique secondary structure of nucleic acid. DNA G4s are also found in the human mitochondrial genome (mtDNA) and around 170 putative G4-forming mtDNA sequences have been identified, but how G4-mtDNA regulates the biological process is still unclear. To understand more about the biofunction and regulatory roles of the G4-mtDNA that causes diseases, we need to develop cell-permeable and target-specific fluorescent ligands to visualize the intracellular G4-mtDNA for chemical biology study and to interrupt the abnormal cellular function of G4s to achieve therapeutic aims such as anticancer. In this study, we reported a new small-sized di-cationic lipophilic ligand **(9)** to target MMP and mitochondrial DNA G4s to enhance drug delivery for anticancer. The ligand can induce mitochondrial dysfunction, DNA damage, cellular senescence, and apoptosis, which exhibited high anticancer activity against HCT116 cancer cells.

Chemical Assembling of Glypican-3 x SIRP-*α* IgG-like Dendritic Bispecific Macrophage-Engager for Immunotherapy Against Liver Cancer

Authors: Bo Tang, Clarence T. T. Wong*
Email address: clarence-tt.wong@polyu.edu.hk

Abstract

Traditional production methods of bispecific antibody face challenges such as heavy and light chain mismatching, complex manufacturing, and quality control. Here, we demonstrate a novel chemical strategy to generate a first-in-class bispecific antibody targeting glypican-3 and SIRP-α for immunotherapy against liver cancer. Our approach uses a bifunctional linker to conjugate multiple glypican-3-targeting peptide dimers onto an anti-SIRP-α monoclonal IgG, forming a dendrimer-like bispecific structure termed dendritic bispecific antibodies (dBsAb). We hypothesize that bringing macrophages into proximity with cancer cells could promote immune synapse formation, enhancing macrophage activation and phagocytosis. Our data showed that dBsAbs enhanced macrophage recognition, phagocytosis of cancer cells, and antigen presentation for downstream immune activation in vitro. In vivo studies validated the therapeutic potential of dBsAbs, showing significant tumor regression and enhanced macrophage infiltration and activation without noticeable toxicity. This approach demonstrates the potential of chemically engineered dBsAbs to advance cancer immunotherapy, offering a simple, robust, and flexible alternative to traditional bispecific production methods.



Design mitochondria-specific fluorescent turn-on probes targeting G-quadruplexes for live cell imaging and mitophagy monitoring study

Meng-Ting She and Wing-Leung Wong*

[1] State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China

Introduction

Mitochondria are the essential organelles in eukaryotic cells and regulate critical cellular functions such as respiration and apoptosis. Understanding their dynamic behavior is crucial across biomedical disciplines such as anti-aging and anticancer. Mitophagy is an important cellular process that selectively removes the damaged mitochondria. Currently, it has emerged as a crucial point in biomedical research due to its implications in many human diseases such as diabetes, Alzheimer and cancer. However, the study of mitophagy in live cells necessitates advanced tools for real-time visualization and monitoring of mitochondrial dynamics. Existing fluorescent probes for mitochondria imaging show limitations for target-specificity. We thus developed mitochondria-specific and G-quadruplex DNA (G4-DNA) targeting probes for real-time imaging of mitophagy in live human cells. In this study, we report a mitochondria-specific fluorescent probe BYM with a fluorescent turn-on mechanism upon binding to mitochondrial G4-DNA. BYM offers enhanced sensitivity, selectivity and biocompatibility, and facilitates real-time monitoring of mitophagy processes in live cells. Our findings shed light on mitochondrial biology and disease mechanisms, and provide valuable insights into the clinical research and therapeutic interventions targeting mitophagy.

In vitro Interaction of BYM and Mitochondrial G4-DNA

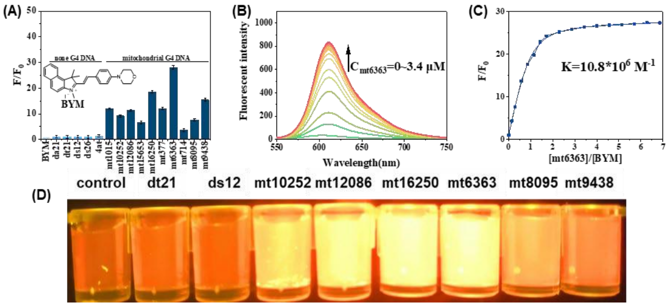


Figure 1. (A) The fluorescence intensity induced upon **BYM** binding to different DNA substrates. (B) Fluorescence titration spectra of **BYM** (0.5 μM) with mtG4 (mt6363, 0-3.4 μM) in a Tris-HCl buffer (10 mM, pH 7.4, containing 60 mM KCl). (C) The equilibrium binding constants of **BYM** and mtG4 (mt6363), (D) Different nucleic acids (280 μg/mL) were separately added to **BYM** (5 μM) and incubated for 1 h (Tris-HCl =10 mM, pH 7.4,

containing 60 mM KCl). The fluorescence signals were subsequently observed under a laboratory UV light (wavelength 302 nm).

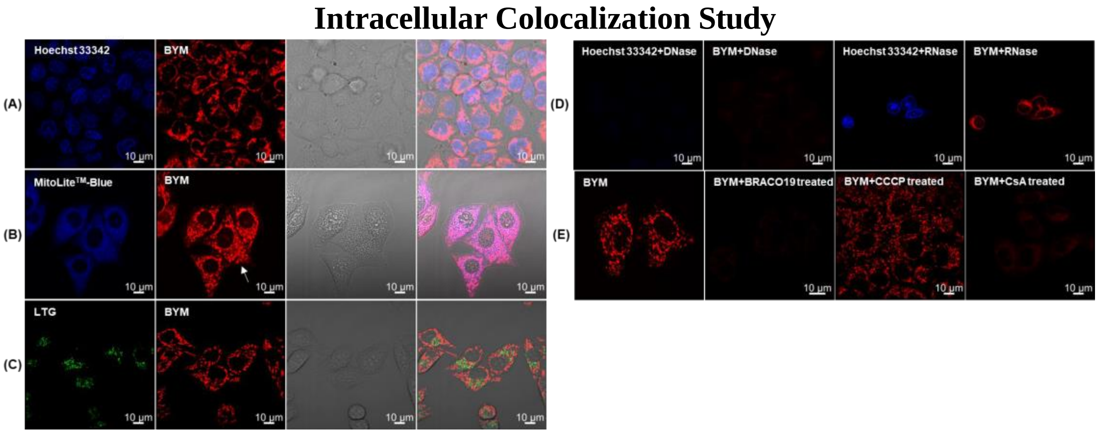


Figure 2. Confocal imaging of live HeLa cells. (A) Staining of the cells with 5 μM **BYM** and Hoechst 33342, (B) Staining of HeLa cells with MitoLiteTM-Blue and 5 μM **BYM**. (C) Staining of the cells with 5 μM **BYM** and Lyso-Tracker Green (LTG). (D) Confocal enzymatic digestion imaging of fixed cells stained with **BYM** (5 μM) and Hoechst 33342 with the DNase or RNase treatment. (E) Confocal competitive imaging of live HeLa cells stained with **BYM** (5 μM) and a commercial G4-ligand BARCO-19, 3- chlorophenylhydrazone (CCCP, to decrease the mitochondrial membrane potential) and cyclosporin (CsA, to block the permeability transition pore).

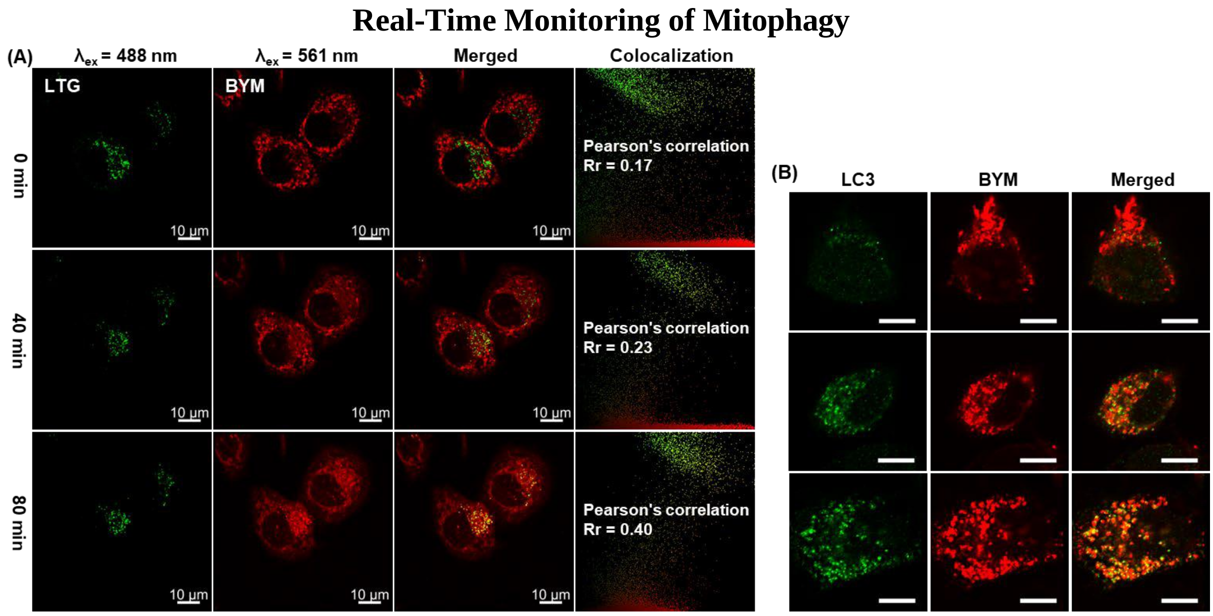


Figure 3. (A) Confocal images for the co-localization analysis. HeLa cells were treated with 50 μg/mL rapamycin and co-stained with **BYM** (5 μM) and Lyso-Tracker Green (LTG, 50 nM) from 0 to 80 min. (B) Immunofluorescent colocalization of autophagosome protein LC3

(green) and **BYM** in HeLa cells. HeLa cells were exposed to 50 μg/mL rapamycin for 0 min, 40 min, 80 min to induce mitophagy. The scale bar is 10 μm.

Conclusion

1. **BYM** is mitochondria-specific and interacts with mtDNA G4s in live HeLa cells.
2. The delivery of **BYM** to mitochondria is independent on mitochondrial membrane potential, and is primarily through the permeability transition pore on the mitochondrial inner membrane.
3. **BYM** is able to monitor mitochondrial autophagy dynamics real-time in live HeLa cells.

Acknowledgments

This project was supported by Research Grants Council [GRF Project No. 15300522], Health and Medical Research Fund [19200231], and PolyU Startup Fund [P0035712]. We also acknowledge the support received from the University Research Facilities on Life Sciences and Chemical and Environmental Analysis of The Hong Kong Polytechnic University.

LMP2A-Selective Peptide-based Agents for Enhancing Diagnostic Precision for EBV-Associated Gastric Cancer

Zhengxiao Liu, Ho-Fai Chau*, Yue Wu, Ka-Leung Wong *

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, PR China

(E-mail: mail: ho-fai.chau@polyu.edu.hk, klgwong@polyu.edu.hk)

Abstract

Gastric cancer is the fifth most common cancer and the fourth leading cause of cancer-related deaths worldwide. Epstein-Barr virus (EBV)-associated gastric cancer (EBVaGC) is recognized as a distinct subtype due to its unique molecular characteristics and virus-involved tumorigenesis[1]. Following EBV infection, a series of viral gene products are expressed, with latent membrane protein 2A (LMP2A) detected in approximately 50% of EBVaGC cases[2]. Despite clinicopathological distinctiveness and membranous protein profiling of EBVaGC, no specific diagnostic methods are currently available.

In this study, we aim to develop an EBVaGC-specific diagnostic tool using a peptide-based LMP2A-targeted imaging probe. We employed the Ph.D.^{TM}-12 Phage Display Peptide Library to obtain an enriched phage pool with LMP2A affinity. Next-generation sequencing was utilized to identify peptide sequences following three rounds of panning. The binding specificity of selected peptides to LMP2A-positive EBVaGC cells was assessed using immunofluorescence, surface plasmon resonance (SPR) assays, and flow cytometry.

We identified six LMP2A-selective peptide candidates from the phage display, with the one the peptide DR exhibiting the highest binding affinity (kD = 5.462 μM) and selected for further validation. Our findings demonstrated that peptide DR can selectively bind to LMP2A-positive EBVaGC cells while showing no affinity for normal gastric epithelial cells. Moreover, no significant cytotoxicity of it towards both EBVaGC cells and normal cells, suggesting its potential for developing LMP2A specific diagnostic agents for EBVaGC.

This work was supported by NSFC/RGC Joint Research Scheme (N_PolyU209/21)

Reference

1. Cancer Genome Atlas Research Network (2014). Comprehensive molecular characterization of gastric adenocarcinoma. *Nature, 513(7517),* 202–209. https://doi.org/10.1038/nature13480
2. Han, J., Chen, J. N., Zhang, Z. G., Li, H. G., Ding, Y. G., Du, H., & Shao, C. K. (2012). Sequence variations of latent membrane protein 2A in Epstein-Barr virus-associated gastric carcinomas from Guangzhou, southern China. *PloS one, 7(3),* e34276. https://doi.org/10.1371/journal.pone.0034276

Unearthing the Mechanism for Switching Cell Death Pathway from Apoptosis to Photoimmunogenic Pyroptosis with Porphyrin-based Photosensitizer

Xiaomin Li,[a] Yik-Hoi Yeung,[a] Ho-Fai Chau,[a,*] Ka-Leung Wong [a,*]

[a] Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, PR China

(E-mail: ho-fai.chau@polyu.edu.hk, klgwong@polyu.edu.hk)

Abstract

Pyroptosis is an attractive form of immunogenic cell death (ICD) towards promising cancer immunotherapy, which can be triggered by reactive oxygen species (ROS) using a photodynamic strategy.[1] However, the non-inflammatory apoptotic and pro- inflammatory pyroptotic cell death can both be induced upon light irradiation and thereby the precise control or switching to the desired cell death pathway is important yet challenging.[2] To date, rare inducers have been reported where specific organelle targeting or sophisticated design was required.[3] In this work, we found a simple approach to regulate the cell death pathway from apoptosis to pyroptosis by varying the concentration and light dose applied to the photosensitizer, using an easy-to-prepare porphyrin-cell- penetrating peptide conjugate **K206D** as a proof-of-concept. Upon lysosomal localization, with a low concentration of **K206D** and light dosages, only caspase-3/PARP1-mediated apoptosis was induced. Interestingly, when ≥ 4 μM **K206D** with ≥ 0.5 J/cm^2 light dose was employed, the cell death switched to the caspase-3/gasdermin-E(GSDME)-related pyroptotic pathway with ICD marker exposure. It is believed that ROS played a major role in altering the caspase-3 activation and thus the cell death pathway selection. This work demonstrates the feasibility of modulating cell death through the control of drug concentrations and light dosage, in which the switching mechanism will be unearthed in the short future, providing general guidance to induce pyroptosis for all photosensitizers.

This work was supported by NSFC/RGC Joint Research Scheme (N_PolyU209/21)

References

1. Bergsbaken, T.; Fink, S. L.; Cookson, B. T. *Nat. Rev. Microbiol.* **2009**, 7, 99–109.
2. Bertheloot, D.; Latz, E.; Franklin, B. S. *Cell Mol. Immunol.* **2021**, 18, 1106–1121.
3. Yi, Z.; Qin, X.; Zhang, L.; Chen, H.; Song, T.; Luo, Z.; Wang, T.; Lau, J.; Wu, Y.; Toh, T. B.; Lee, C.-S.; Bu, W.; Liu, X. *J. Am. Chem. Soc.* **2024**, *146*, 9413–9421.

Mitochondria-targeted Photosensitizers with High Thermal Stability and Potency for Anti-tumor Therapy

Yakun Wang[1], Wing-Leung Wong[1]

[1]Department of Applied Biology and Chemical Technology, The Hong Kong
Polytechnic University, Hung Hom, Hong Kong SAR, China

Abstract

In recent years, there has been a significant focus on photothermal and photodynamic therapies for tumor treatment, which utilize photosensitizers to specifically target and kill tumor cells. However, traditional photosensitizers have limitations, such as lack of specificity and ability to accumulate inside cells, which limits their clinical potential. Mitochondria are vital in cell function and have been targeted for tailored photosensitizer delivery in cancer cells to enhance treatment effectiveness while minimizing damage to normal cells. This study aimed to develop a mitochondria- targeting photosensitizer, P6-COOH, which demonstrated high selectivity and potency in dual-module photothermal and photodynamic antitumor therapy. The *in vitro* study explored the photothermal and photodynamic properties of P6-COOH through light modulation and photosensitizer concentration. Co-localization experiments showed efficient accumulation of P6-COOH in human tumor cell mitochondria with minimal cytotoxicity without light irradiation. Under laser irradiation, P6-COOH generated reactive oxygen species and caused photothermal to synergistically kill tumor cells.

Research progress

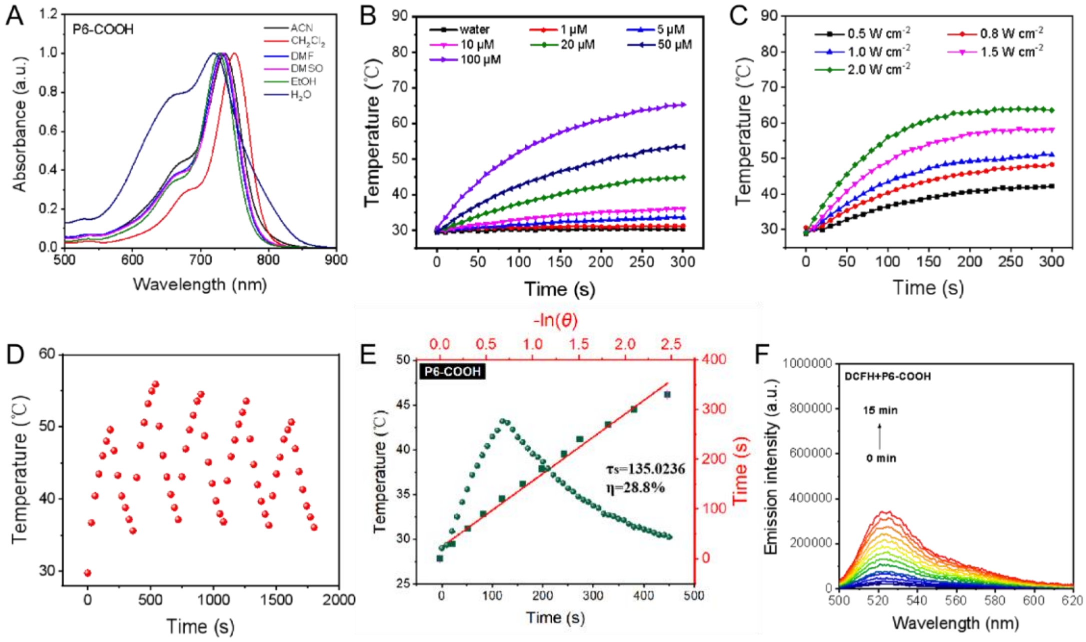


Figure 1. (A) Normalized absorption spectra of P6-COOH in various solvents. (B) Temperature profiles of P6-COOH at different concentrations (0-100 μM) in water under 808 laser irradiation. (C) Temperature profiles of P6-COOH in water under 808 laser irradiation at various laser densities (0.5-2.0 W cm-2). (D) Investigation of the photothermal stability of P6-COOH under 808 nm laser irradiation. (E) Calculation of the photothermal conversion efficiency (PCE) of P6-COOH. (F) Photoluminescence

(PL) spectra of DCFH (1 µM) in the presence of 1 µM P6-COOH after different durations of 808 laser irradiation.

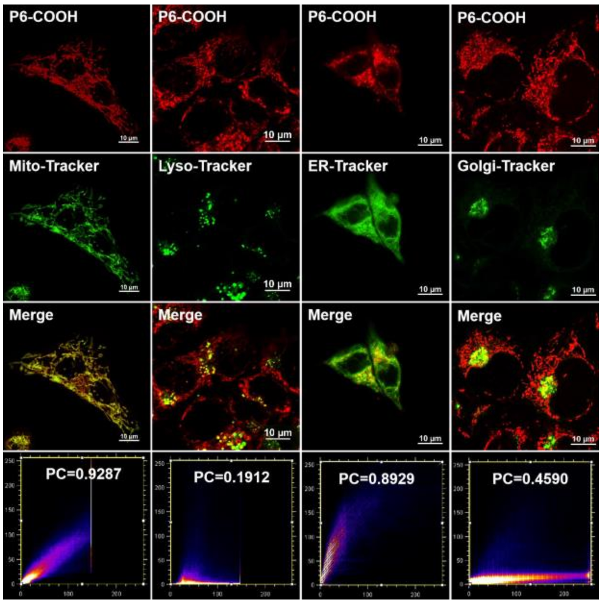


Figure 2. Co-localization CLSM images of HCT116 cells stained with P6-COOH (10 µM) and commercial dyes including Mito-Tracker Green (100 nM), Lyso-Tracker Green (50 nM), ER-Tracker Green (500 nM), and Golgi-Tracker Green (27 M). Scale bar: 10 µm.

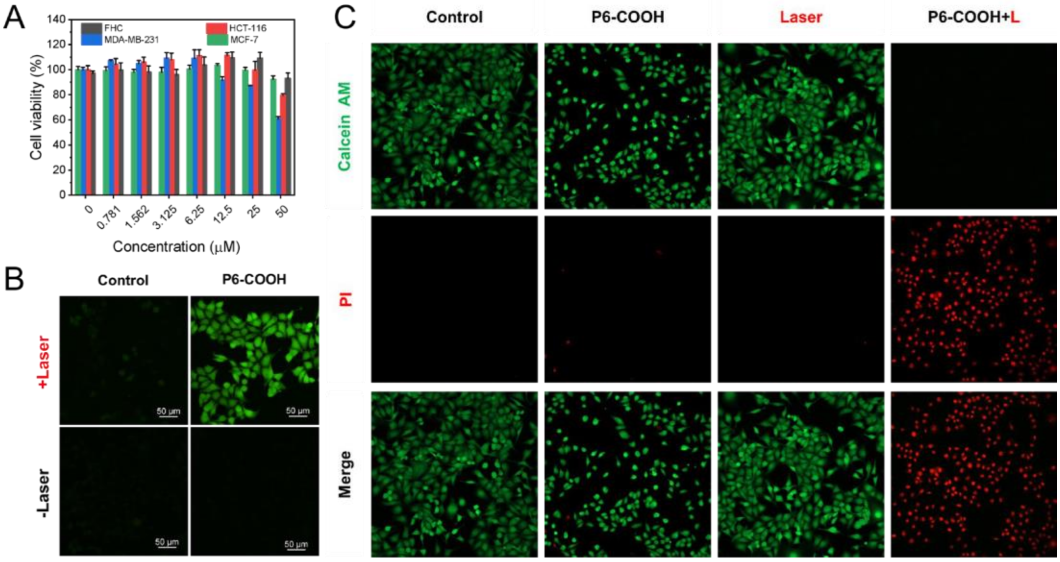


Figure 3. (A) Cell viability at various concentrations of P6-COOH on FHC (non-cancerous cells), HCT-116, MDA-MB-231, and MCF-7 (cancer cells) under dark conditions. (B) Intracellular reactive oxygen species generation using DCFH-DA (50 µM) following treatment with P6-COOH (50 µM) with/without exposure to laser irradiation (808 nm, 0.8 W cm^{-2}, 5 min). (C) Calcein AM-PI staining in MDA-MB-231 cells treated with P6-COOH (50 µM) with/without laser irradiation (808 nm, 0.8 W cm^{-2}, 5 min).

Acknowledgments

This project was supported by Health and Medical Research Fund [19200231], Research Grants Council [GRF Project No. 15300522], and PolyU Startup Fund [P0035712]. We also acknowledge the support received from the University Research Facilities on Life Sciences and Chemical and Environmental Analysis of The Hong Kong Polytechnic University.

Development of inhibitors targeting bacterial transcription antitermination complex

Tiankuang Liu[1], Yangyi Qiu[1], Xiao Yang[2], Cong Ma[1]
[1]State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR, China; cong.ma@polyu.edu.hk
[2]Department of Microbiology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR, China; xiaoyang@cuhk.edu.hk

Abstract

Discovery of antimicrobial agents with a novel mechanism is in urgent need for multidrug-resistant bacterial infections. NusB and NusE belong to the N-utilization substances (Nus) factor family, a family of transcription factors involved in the RNA bacterial transcription. In our research, protein-protein interactions (PPIs) between NusB and NusE have been proven to be essential to cell viability, making them potential target for rational drug design[1].

A hit compound, **MC4**, was obtained through virtual screening and subsequently optimized to yield several inhibitors with excellent antibacterial activity[2]. Mechanism studies of representative compounds were conducted to gain insights into the binding interactions between the compounds and the target protein[3]. The results for both cellular and molecular effects showed that **MC4** derivatives can effectively inhibit the NusB-NusE PPI, leading to reduced levels of RNA. Moreover, the result of *in vivo* test demonstrated the potential of MC4 compounds as antibiotic candidates.

References

1. Yang, X.; Luo, M. J.; Yeung, A. C.; Lewis, P. J.; Chan, P. K.; Ip, M.; Ma, C. *Biochemistry,* **2017**, *56 (38),* 5049-5052.
2. Qiu, Y.; Chan, S. T.; Lin, L.; Shek, T. L.; Tsang, T. F.; Barua, N.; Zhang, Y.; Ip, M.; Chan, P. K.-s.; Blanchard, N. *European journal of medicinal chemistry,* **2019**, *178,* 214-231.
3. Qiu, Y.; Chu, A. J.; Tsang, T. F.; Zheng, Y.; Lam, N. M.; Li, K. S. L.; Ip, M.; Yang, X.; Ma, C. *Bioorganic Chemistry,* **2022**, *124*, 105863.

Arsenic-based Fluorescent Probe for Mining Intracellular Arsenic-proteome

Hongyu Zhao[a], Hongyan Li[a], Hongzhe Sun[a,*]
[a]*Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong SAR, China.*
Email: u30008669@connect.hku.hk

Abstract

Arsenic trioxide (ATO) is a potential therapeutic agent for treating ALK-positive anaplastic large cell lymphoma (ALCL) [1]. Although enormous efforts have been made, the underlying mechanism of action of ATO remains unclear. Due to the complexity of arsenic-protein interactions in cells, tracking arsenic-binding proteins, particularly live cells, is a considerable challenge. Previously, we designed a series of fluorescent probes that have been successfully utilized to track metal-related proteins in different cells [1,2]. Nevertheless, the amount of proteins identified by the probes are limited due to low fluorescence enhancement after activation.

Herein, we report a novel fluorescent probe NI-As, enabling the arsenic-binding proteins to be anchored upon photoactivation and subsequently identified through high-throughput proteomics. Moreover, NI-As shows excellent selectivity of arsenic-binding proteins and exhibits 20-fold fluorescence enhancement after UV irradiation within 15 min, allowing 116 arsenic-related proteins to be identified in OCI-Ly7, a human DLBCL cell line. Bioinformatics analysis reveals that ATO influence multiple physiological processes, for example, sumoylation and Interleukin-1 Family Signaling. The study provides an approach to understanding the biological and pathological mechanisms of ATO at the cellular level.

We thank the Research Grants Council (R7070-18, 17308921, 2122-7S04) of Hong Kong SAR, Innovative Technology Commission of Hong Kong SAR, and the University of Hong Kong (URC and Norman & Celia Yip Foundation) for financial support.

References

[1] Aliya T., Zhao H., Li H., Sun H. *JACS Au.* **2024**, *12*, 4628-4638.

[2] Hu X., Sun H., et al. *Chem. Sci.* **2021**, *5*, 10893-10900.

Bismuth (III) compounds sensitize *Pseudomonas aeruginosa* to multiple antibiotics via disruption of iron homeostasis

Xueying Wei [ab], Yushan Xia [a], Hongyan Li [a] and Hongzhe Sun [a]*
Department of [a] Chemistry and [b] Microbiology, CAS-HKU Joint Laboratory of Metallomics on Health and Environment, The University of Hong Kong, Hong Kong, P.R. China
(e-mail: hsun@hku.hk)

Abstract

Antimicrobial resistance (AMR) bacterial infections have become a serious problem threatening human health around the world[1, 2]. *Pseudomonas aeruginosa* a high-priority pathogen listed by World Health Organization (WHO) posing the greatest threat due to rapid development of antibiotic drug resistance. As a result, it’s urgent to develop the novel antibiotics or therapies to battle with AMR.

The synergistic combination of already-in-use drugs is an alternative to developing new antibiotics to combat antibiotic-resistant bacteria[3]. Here, we demonstrate that bismuth-based drugs in combination with different classes of antibiotics (e.g. tetracyclines, macrolides, quinolones) can effectively eliminate multidrug-resistant *P. aeruginosa* and do not induce development of antibiotic resistance[4]. We found that Bi (III) disrupts iron homeostasis and demonstrated that Bi (III) binds *P. aeruginosa* siderophores. We further the efficacy of orally administered bismuth compounds to restore antibiotic activities in the bacterial infected mice. Our findings highlight the potential of bismuth- based drugs to be repurposed to combat *P. aeruginosa* infections in combination with clinically used antibiotics.

*We thank the RGC (SRFS2122-7S04, 17318322, 17304323, **17306323, 17307724**) of Hong Kong SAR; and the University of Hong Kong for support.*

References

1. A. Frei, J. Zuegg, M. A. T. Blaskovich., et al, *Nat. Rev. Chem*, **2023**, *7*, 202-224.
2. R. Wang, T. P. Lai, P. Gao, H. Li, H. Sun., et al. *Nat Commun*, **2018**, *9*, 439.
3. C. Wang, Y. Xia, H. Li, H. Sun., et al. *Nat. Commun*, **2023**, *14*, 5311.
4. Y. Xia, X. Wei, P. Gao, H. Li, R. Cebrian, O. P. Kuipers, H. Sun., et al. *Nat Microbiol*, **2024**, *9*, 2600-2613.

Accelerated Synthesis of Multiplex Metal Encoded Classifier Beads for Sensitive Prediction of Cytokine Release Syndrome

Keyuan Pu[1], Hongyan Li[1], Eric Tse[2], Hongzhe Sun[1*]

1. *Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P.R. China*
2. *Department of Medicine, The University of Hong Kong, Hong Kong, P.R. China*

(E-mail: kypu@connect.hku.hk)

Abstract

Chimeric antigen receptor T cell (CAR-T) therapy has shown remarkable efficiency in treating a variety of hematological malignancies in recent years. Cytokine Release Syndrome (CRS) is the most common adverse event induced by CAR-T therapy, with an incidence rate above 54%[1]. Prediction of the occurrence and severity of CRS may benefit safety and therapeutic efficiency of CAR-T therapy.

Herein, we developed a multiplex bead-based immunoassay for cytokines detection using mass cytometry. The metal-encoded polystyrene beads with high stability and batch-to-batch reproducibility were prepared by swealing method. By decorating the surface of beads with high-density antibodies, we can efficiently capture targeted cytokines in liquid samples. Utilizing gold nanoparticles as reporter tags, the sensitivity of this assay achieves as low as 1 fg/mL for IFNγ. This method theoretically allows the simultaneous detection of up to 10^{21} analytes, offering high multiplexing capacity and throughput for clinical applications. Significantly, five novel biomarkers were discovered via topology analysis and employed to construct a machine-learning-based prediction model in combination with 14 cytokines. This technique has potential to benefit the risk assessment of CRS in clinical setting.

We thank the Research Grants Council (RGC) of Hong Kong SAR (SRFS2122-7S04, C7034-20E, 17306323), and the University of Hong Kong (URC and Norman & Cecilia Yip Foundation) for support.

References

1. Galli E, Sora F, Hohaus S, Fresa A, Pansini I, Autore F, et al. Br J Haematol. ***2023****, 201:86–94.*

Elucidating the Roles of Chromium in Modulating Cellular Senescence in MEFs

Jiaxing Guo[1], Xueying Wei[1], Chun-Lung Chan[1], Sheung Kin Ken Wong[2], Zhongjun Zhou[2], Hongyan Li[1], Hongzhe Sun[1]*

1. Department of Chemistry, The University of Hong Kong

2. School of Biomedical Sciences, LKS Faculty of Medicine, The University of Hong Kong.
(jxguo@connect.hku.hk)

Abstract

Cellular senescence, characterized by the regression of physiological functions, contributes to chronic inflammation, disrupted molecular homeostasis, and ultimately cell death. Mitochondria dysfunction is recognized as a critical hallmark of cellular senescence. Previous studies have demonstrated that suppression of ATP synthase and activation of AMPK signaling can delay cellular aging[1,2]. Trivalent chromium (Cr III) has shown potential in rescuing fragmented mitochondria and activating AMPK by inhibiting ATP synthase activity, thereby alleviating diabetic phenotypes in both *in vitro* and *in vivo* models[3]. Given the similarity in cellular targets and mechanisms between Cr and lifespan-extending compounds, this project aims to investigate whether Cr (III) exerts comparable anti-senescence effects. Ionizing radiation (IR) and hydrogen peroxide (H_2O_2) treatments, which induce genomic instability and oxidative stress respectively, were utilized to trigger cellular senescence in mouse embryonic fibroblasts (MEFs). Preliminary results indicate that specific Cr compounds can delay senescence in these models by enhancing cell proliferation, reducing SA-β-gal activity, and reversing typical senescent markers at both mRNA and protein levels.

We thank the Research Grants Council (R7070-18, 17308921, 2122-7S04), ITF (ITS/278/20) and The University of Hong Kong (Norman & Celia Yip Foundation and URC) for financial support.

References

(1) Qu, Q.et al. *Nature* **2024**. 638(8050):E6.

(2) Chin, R. et al. *Nature* **2014**, *510* (7505), 397–401.

(3) Wang, H.; Sun, H. *Nat. Commun.* **2023**, *14* (1), 1738.

An Unexpected Fe-S Cluster in Nsp14 of SARS-CoV-2: A New Target of Antivirals

Jingxin Chen, Edmund C.M. Tse, Hongyan Li and Hongzhe Sun*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China; Email: cjxchen@connect.hku.hk

Abstract

Proteins with Fe-S clusters always favor cysteine and histidine ligands, which is very similar to zinc-fingers.[1] Due to the susceptibility to destabilization and degradation of Fe-S clusters, zinc can replace Fe-S cofactors under aerobic environment, perhaps explaining why some annotated zinc-finger proteins were found to be Fe-S co-factored proteins.[2] SARS-CoV-2 nsp14 functions both as an N-terminal 3’ to 5’ exoribonuclease stimulated and a C-terminal N7-methyltransferase in the virus life cycle. Crystallography studies show that SARS-CoV-2 nsp14 also possesses three important zinc-fingers, which are critical to the enzyme activity as well as architecture integrity.[3] Herein, we surprisingly found that SARS-CoV-2 nsp14 ligates an Fe-S cluster in the sites annotated as a zinc finger under an anaerobic environment, which can promote the enzyme activity by enhancing its substrate binding affinity. Moreover, Bi(III)-based antiviral compounds[4], were found to significantly inhibit dual activities of nsp14 regardless of whether the enzyme is in the Fe-S or Zn form. This study illustrates an authentic mechanism of action of the Bi(III)-based SARS-CoV-2 nsp14 inhibitors and highlights the potential of a labile Fe-S cluster of nsp14 as an important target for the development of anti-SARS-CoV-2 agents.

References

1. Pritts J. D., Michel S. L. J. *J. Inorg. Biochem.* **2022**, *230*, 111756

2. a) Shimberg G. D., Michalek J. L., Michel S. L. J., et al. *Proc. Natl. Acad. Sci. USA.* **2016**, *113*, 4700-4705. b) Maio N., Rouault T. A., et al. *Science* **2021**, *373*, 236-241. c) Maio N., Rouault T. A., et al. *Proc. Natl. Acad. Sci. USA.* **2023**, *120*, e2303860120.

3. Lin S., Chen H., Lu G., et al. *Nucleic Acids Res.* **2021**, *49*, 5382-5392.

4. Chen J., Li H., Sun H. et al. *ACS Infect. Dis.* **2023**, *10*, 858-869

Visualizing Lead(II) Proteomes in Cells with NIR Fluorescence

Aliya Tiemuer, Hongyan Li, Hongzhe Sun*

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P.R. China (E-mail: u3009300@connect.hku.hk)

Abstract

Lead (Pb), as one of the most serious toxicants for public health, has been revealed to exert a concerning effect on vital organs like the liver, kidney, and central nervous system where it causes significant neurophysiological and neurophysiological deficits.[1-2] Hence, mapping out the comprehensive Pb-binding protein would help understand how the Pb inserts their toxicity. In this regard, fluorescent imaging has emerged as a useful tool for in situ visualization of metalloproteins. For it not only can localize the protein in interest but also monitors the protein dynamics in a highly complex cellular environment.

To this end, fluorescence probe QM-NH_2 was designed and synthesized. QM-NH_2 exhibits weak fluorescence around 650–750 nm, which further diminishes upon coordination with Pb(II). However, after incubating with the albumin and exposure to UV light, the fluorescence was able to restore and enhance by 10-fold. Further, QM-Pb (coordination product between QM-NH_2 and Pb) can be taken up by HT22 (mouse hippocampal neuronal cells) cells and can be photoactivated in cell environment while restoring fluorescence. Further, SDS-PAGE analysis confirms the selective binding of certain protein with Pb(II). Overall, our work has demonstrated great potential in understanding how lead inserts its toxicity in the brain and may also offer a powerful tool for metalloproteome in vivo.

We thank the Research Grants Council (RGC) of Hong Kong SAR (SRFS2122-7S04, C7034-20E, 17306323), and the University of Hong Kong (URC and Norman & Cecilia Yip Foundation) for support.

References

1.Collin MS, Venkatraman SK, Vijayakumar N, et al.. *J Hazard Mater.* **2022**, *7*(2), 100094.

2. Mason LH, Harp, JP, Han DY. *Biomed Res Int.* **2014**, *2014*(10), 840547.

Unveiling a CAAX Protease-Like Protein Involved in Didemnin Drug Maturation and Secretion

Xiaolin Zou[1, 2], Yong-Xin Li [2], and Xiaoyu Tang[1*]
1. Institute of Chemical Biology, Shenzhen Bay Laboratory, Shenzhen, China
2. Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong,

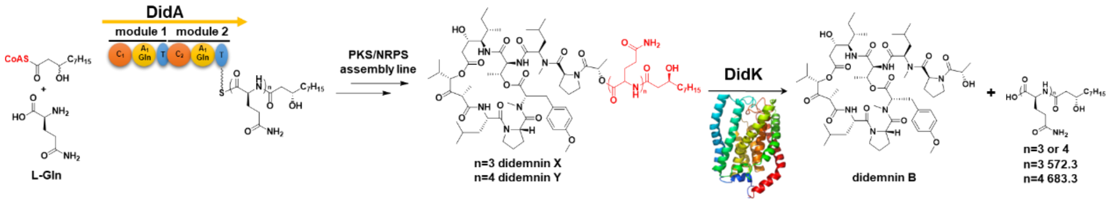
China

Email: xtang@szbl.ac.cn or xtang@microbechembio.org

Abstract

The biosynthesis of the anticancer-antiviral didemnin cyclic peptides is proposed to follow a prodrug release mechanism in Tristella bacteria. In this study, an exploration of the enzymes responsible for both the assembly and cleavage of the acylated peptide prodrug scaffolds is provided. This process involves the assembly of N-acyl-polyglutamine moieties orchestrated by DidA and the cleavage of these components at the post-assembly stage by DidK.

The findings shed light on the complex prodrug mechanism that underlies the synthesis and secretion of didemnin compounds and offer novel insights into the expanded role of CAAX hydrolases in microbes.



- DidA drives the initiation of didemnin biosynthesis through the formation of N-acyl-polyglutamine ester moieties.
- DidK, the membrane-bound CAAX hydrolase-like protein, is responsible for catalyzing the hydrolysis of the ester bond.

Reference

1 Velilla, J. A., Kenney, G. E. & Gaudet, R., Structure and function of prodrug-activating peptidases. **205**, 124-135 (2023).

2 Zou, X. *et al.* Unveiling a CAAX Protease-Like Protein Involved in Didemnin Drug Maturation
and Secretion. 2306044 (2023).

3 Pei, J. & Grishin, N., J Trends in biochemical sciences. Type II CAAX prenyl endopeptidases belong to a novel superfamily of putative membrane-bound metalloproteases. **26**, 275-277 (2001).

Targeting α-Synuclein Aggregation with a Novel Peptide: Unveiling PD-6 as a Promising Therapeutic Agent for Parkinson's Disease

Haiyan Zhou[1], Zhaohui Liang[2], Chenyin Wang[3], Wai Lok Ngai[1], Michael K. Chan[2], Chaogu Zheng[3], Xuechen Li[1]

[1] Department of Chemistry, The University of Hong Kong, Hong Kong SAR, P. R. China, [2] School of Life Sciences, The Chinese University of Hong Kong, Hong Kong SAR, P. R. China, [3] School of Biological Sciences, The University of Hong Kong, Hong Kong SAR, P. R. China. E-mail: xuechenl@hku.hk

Parkinson's disease (PD) is a prevalent neurodegenerative disorder characterized by the loss of dopaminergic neurons in the brain, leading to debilitating motor and non-motor symptoms. Despite advances in symptomatic treatments, a definitive cure or disease-modifying therapy for PD remains to be elusive. Recent studies have suggested that the pathogenesis of PD is intricately linked to the α-synuclein, with oligomerization and fibrils being identified as key neurotoxic species, which could be a promising therapeutic target for developing more effective treatments. Here, we present high throughput phage display approach for identifying peptides that specifically target to α-synuclein. Using diverse peptide libraries constructed based on truncated SUMO1 scaffold[1], we identified a potent peptide inhibitor, PD-6, with good solubility and strong binding affinity to α-synuclein (Kd = 26.85 ± 7.45 nM), which is 96-fold stronger than that of the truncated SUMO1(Kd = 2.60 ± 0.98 μM) reported in the previous study. *In vitro* studies confirmed PD-6's ability to mitigate α-synuclein-induced cytotoxicity in SH-SY5Y cells and reduce fibril formation. Furthermore, *in vivo* assessments in a C. *elegans* PD model expressing human α-synuclein A53T mutants revealed dose-dependent improvements in completely restoring locomotion and increased ADE survival rates with PD-6 supplementation, accompanied by a significant reduction (120 μM) and even elimination (240 μM) of α-synuclein aggregate signal. Taken together, these findings highlight PD-6 is a promising drug-lead compound for further development of therapeutic treatment targeting α-synuclein in Parkinson's disease.

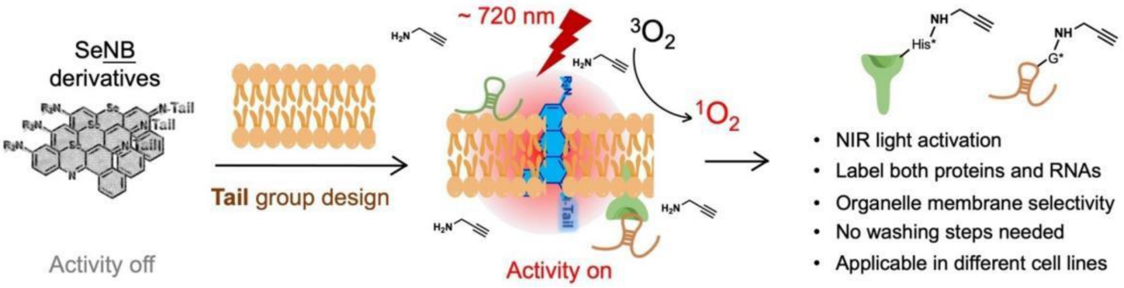
(1) Liang, Z.; Chan, H. Y. E.; Lee, M. M.; Chan, M. K. *Cell Chem. Biol.* **2021**, *28*, 180-190.

Small-Molecule Benzo-Phenoselenazine Derivatives for Multi-Subcellular Protein Profiling and Localization

Han Jia, Jinghua Han, Kaiyun Zhao, and Ying Li*
yingli0e@hku.hk

Abstract

To better understand protein localization and interactions in living cells, we employed a proximity labeling strategy utilizing SeNB derivatives, which are activated by near- infrared (NIR) light. This approach enables specific labeling of proteins near organelle membranes, without the need for washing steps. Through fluorescence confocal imaging, we identified key protein localization in the endoplasmic reticulum (ER), mitochondria, and lysosomes. By optimizing the CuAAC reaction and using cleavable biotin linkers, we successfully biotinylated proteins and confirmed their membrane-proximal localization using western blotting and cell fractionation techniques. Proteomic analysis identified a variety of membrane-associated proteins, including ER-localized proteins (RPN2, RPN1, PDIA3) and inter-organelle proteins, providing insight into the molecular interactions between organelles. Our study highlights the utility of SeNB-based proximity labeling for proteomics, offering a powerful tool for exploring cellular dynamics, protein translocation, and inter-organelle communication.



Reference

1. Jia, H., Han, J., Qi, Y., Liu, J., Leung, Y. T., Yau, H. T., Chu, Y., Wang, T., Fung, Y. E., Wang, Y., Li, Y. *Angew. Chem. Int. Ed.* **2025**, *64*, e202419904

Microtubule inner protein profiling by Taxol-based photoaffinity probe

Wanzhang Zhang, Xiang David Li*

The University of Hong Kong, Hong Kong, China

xiangli@hku.hk

Abstract

Microtubules play a significant role in cell mitosis and intracellular transportation, with the functions realized by the assistance of various kinds of microtubule binding proteins (MTBP)[1]. However, almost all the MTBPs are reported to interact with the outer surface, and very few MTBPs located inside the lumen have been discovered[2]. Here we established a proteomics method of the identification of microtubule inner proteins (MIPs), based on a photo-affinity probe modified from Paclitaxel, which is a famous drug targeting inner lumen[3]. Taking advantage of the proximity labeling ability of the probe, the MIPs can be captured through photo-crosslinking and identified based on proteomics techniques.

References

1. Goodson, H. V.; Jonasson, E. M., Microtubules and Microtubule-Associated Proteins. *Cold Spring Harb Perspect Biol* **2018,** *10* (6).

2. Nihongaki, Y.; Matsubayashi, H. T.; Inoue, T., A molecular trap inside microtubules probes luminal access by soluble proteins. *Nat Chem Biol* **2021,** *17* (8), 888-895.

3. Kellogg, E. H.; Hejab, N. M. A.; Howes, S.; Northcote, P.; Miller, J. H.; Diaz, J. F.; Downing, K. H.; Nogales, E., Insights into the Distinct Mechanisms of Action of Taxane and Non-Taxane Microtubule Stabilizers from Cryo-EM Structures. *J Mol Biol* **2017,** *429* (5), 633-646.

Unlocking the Existence of Demethylase through Genetic Code Expansion

Siqin Yu, Xiang David Li Department of Chemistry, HKU
Corresponding e-mail: xiangli@hku.hk

Abstract

Histone methylation is a pivotal epigenetic modification that plays a critical role in regulating gene expression, chromatin structure, and essential cellular processes[1]. While multiple methyltransferases (writers) and demethylases (erasers) have been identified for various lysine methylation sites on histones H3 and H4, H3K79 methylation remains a notable exception[2]. This modification occurs within the core of histone H3 and is catalyzed solely by the methyltransferase Dot1L[3], with no known demethylase identified in human cells to date. Here, we employed genetic code expansion combined with UV irradiation to site-specifically incorporate monomethylated H3K79 into histones in HEK293T cells[4]. Through proteomics analysis, we failed to detect unmodified H3K79 peptides, suggesting the absence of a demethylase for H3K79 methylation in HEK293T cells. However, we identified that some demethylase could cleave histone H3 by recognizing H3K79 monomethylation *in vivo* and *in vitro*, leading to a reduction in H3K79 monomethylation levels. These findings provide new insights into the mechanisms regulating H3K79 methylation and highlight alternative pathways that may modulate this epigenetic mark.

References

1. Kouzarides T. *Cell*, **2007**, *128*, 693–705.
2. Hyun K, Jeon J. *Exp Mol Med*, **2017**, *49*, e324.
3. Feng Q, Wang H. *Curr Biol*, **2002**, *12*, 1052–1058.
4. Groff D, Chen PR. *Chembiochem*, **2010**, *11*, 1066-1068.

Semi-synthesis of trifunctional histone H4K20me2 and H3K36me3

Mao Xin, Xiang David Li*

Department of Chemistry, University of Hong Kong, China. Email: xiangli@hku.hk

Abstract

H4K20me2 and H3K36me3 are two histone modifications that are crucial for the maintenance of whole genome integrity and transcription regulations. Great efforts have been put to investigate these histone modifications, including the discovery of H4K20me2 / H3K36me3 effector proteins. Given that traditional methods of PTM effector proteins identification are limited owning to their lack of whole chromatin context or the low binding affinity between binders and modified histone, significant information could be lost. To solve that, a trifunctional nucleosome-based probe has been developed [1], which has the whole context of nucleosome and can convert weak interaction into covalent bond upon UV irradiation. To prepare a nucleosome probe, the trifunctional histones need to be synthesized. Here we report the synthesis strategies of H4K20me2 and H3K36me3, preparing for the profiling of their effector proteins in nucleosome context.

Reference:

1. Liu Z, Wu Y, Mao X, Kwan KC, Cheng X, Li X, Jing Y, Li XD. Development of multifunctional synthetic nucleosomes to interrogate chromatin-mediated protein interactions. *Science Advances*, **2023**, 9(18):eade5186.

Chemical proteomics approach to identify the reader of Histone H3P16oh

Xiang Li, Xiang David Li*
Department of Chemistry, The University of Hong Kong, Hong Kong
Email: xiangli@hku.hk

Abstract

Histone post-translational modifications (PTMs) recruit effector proteins ("readers") to regulate essential biological processes, including transcriptional activation and repression. Proline hydroxylation (Poh) at histone H3P16 (H3P16oh) is an emerging epigenetic mark linked to gene regulation, yet its specific reader proteins remain unidentified. Here, we employ our previously established chemical proteomic platform (CLASPI) to identify Protein X as a selective binder of H3P16oh. Biochemical assays demonstrate that Protein X directly recognizes H3P16oh with high specificity. Genome-wide CUT&Tag profiling further reveals co-localization of Protein X and H3P16oh at promoter regions, suggesting a role in gene regulation. Collectively, our study identifies Protein X as the first bona fide reader of H3P16oh, unveiling a novel mechanism by which histone proline hydroxylation couples to gene regulation and expanding the functional landscape of Protein X in epigenetic signaling.

References

1. Kaelin, W. G. Jr & Ratclife, P. J. Oxygen sensing by metazoans: the central role of the HIF hydroxylase pathway. Mol. Cell 2008, 30, 393–402.
2. Semenza, G. L. Hypoxia-inducible factors: mediators of cancer progression and targets for cancer therapy. Trends Pharmacol. Sci. 2012, 33, 207–214.
3. Liu X, Wang J, Boyer JA, Gong W, Zhao S, Xie L, Wu Q, Zhang C, Jain K, Guo Y, Rodriguez J, Li M, Uryu H, Liao C, Hu L, Zhou J, Shi X, Tsai YH, Yan Q, Luo W, Chen X, Strahl BD, von Kriegsheim A, Zhang Q, Wang GG, Baldwin AS, Zhang Q. Histone H3 proline 16 hydroxylation regulates mammalian gene expression. Nat Genet. 2022, 54(11):1721-1735.

Biocatalytic oxidative cross-coupling reaction for peptide biaryl cyclization

Runze Liu[1], Rongyu Ren[2], Gengfan Wu[1], Beibei He[1], Zhuanglin Shen[2], Jing Liu[1], Jiahai Zhou[2,3*] and Yong-xin Li[1*]

1 Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, China

2 Shenzhen Institute of Synthetic Biology, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, China

3 School of Food Science and Pharmaceutical Engineering, Nanjing Normal University, Nanjing210023, China

Abstract

Macrocyclic peptides, including nonribosomally produced peptides (NRPs) and ribosomally produced post-translationally modified peptides (RiPPs), are promising for developing chemical probes and therapeutic agents like vancomycin and arylomycin. Transition-metal-catalyzed biaryl cross-coupling offers benefits, but its efficiency and selectivity depend on substrate characteristics. With biosynthesis insights, we explore RiPPs P450s as biocatalysts for peptide biaryl cyclization. Global genome mining and big data analysis helped map RiPPs P450s landscape and utilize P450 for in vitro biocatalysis. P450-catalyzed peptide biaryl cyclization displayed specificity and efficiency, with surprising substrate versatility. P450 showed promiscuity on amino acids and inner cycle amino acids. This P450 discovery highlights its catalytic potential for peptide biaryl crosslinking and presents a strong candidate for future engineering.

Reference

[1] RZ Liu#, HY Ren#, GF Wu, BB He, ZL Shen, J Liu, ZM Song, JH Zhou*, YX Li*. *biorxiv https://doi.org/10.1101/2024.10.06.616194* (**2024**)

Oncogenic mechanisms of G34W onco-mutation in giant cell tumor of bone

Derui Li, Gaofei Tian, Xiang David Li

The University of Hong Kong, Hong Kong, China Email: deruili@connect.hku.hk

Abstract

The histone H3.3 G34W mutation is a key driver in giant cell tumor of bone [1], but its molecular mechanism in suppressing tumor suppressor genes through epigenetic regulation remains unclear[2]. This study utilized Amber suppression technology to incorporate a photo- crosslinking unnatural amino acid into the G34W mutant, combined with pull-down experiments, and for the first time identified MRG15 as a key interacting protein of G34W. Binding site mapping and site mutation studies showed that MRG15 specifically recognizes the G34W mutation through its Chromo domain and recruits the Sin3B complex via the MRG domain. We hypothesize that Sin3B complex carries HDAC1/2, which mediates histone deacetylation (such as H3K14ac, H3K18ac, H3K27ac), thereby suppressing target gene expression. Enzymatic assays confirmed that the binding of MRG15 to G34W will facilitate the enzymatic activity of HDAC1/2 and could be crucial for the epigenetic reprogramming of tumor cells. To further elucidate the functional targets of the G34W-MRG15-Sin3B- HDAC1/2 complex, we plan to use CUT&Tag technology to map its binding sites and histone modification dynamics across the genome, with a focus on changes in the acetylation of tumor suppressor genes (such as those related to the p53 pathway). This study may reveal a new mechanism by which the G34W mutation inhibits tumor suppressor gene expression by recruiting the MRG15-Sin3B-HDAC1/2 complex, providing a theoretical basis for developing precise therapeutic strategies targeting epigenetic complexes.

References

1. Khazaei, S.; Jay, N. de; Deshmukh, Cancer discovery 2020, 10 (12), 1968–1987.
2. Mitchener, M. M.; Muir, T. W. Molecular Cell 2022, 82 (16), 2925–2938.

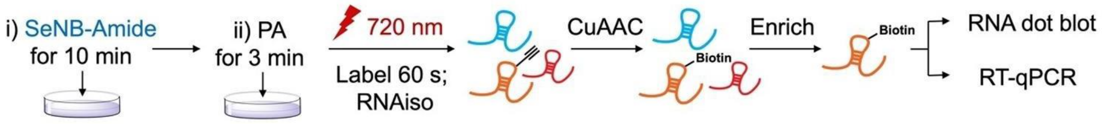
Application of Benzo-Phenoselenazine Derivatives on Transcriptomics

Han Jia, Jinghua Han, Yajing Qi, Jie Liu, Yuen Ting Leung, Yau Hei Tung, Yuanyuan Chu, Tong Wang, Yi-Man Eva Fung, Yi Wang, and Ying Li

Postal address(es): yingli0e@hku.hk

Abstract

The development of proximity labeling (PL) to understand the cellular functions of RNAs and proteins has been getting more advanced over the decade. The mainstream PL methods usually involve genetically encoded proteins or enzymes that express the labeling probe at a protein of interest. A downside of these methods is that they can only be applied to specific cell lines. Given the limited exploration of cell line-independent PL methods in the past, we developed a novel method that uses a series of small molecule benzo-phenoselenazine derivatives as photocatalytic probes to achieve PL. With near-infrared (NIR) light activation, the selenium-containing Nile Blue (SeNB) motif, attached to the cellular component of interest, can generate singlet oxygen and achieve labeling in both RNAs and proteins. In the case of RNA, the generated singlet oxygen, as a reactive oxygen species, would rapidly oxidize RNA guanosine bases within a proximal range. When cells were incubated with propargylamine (PA), the oxidized G would then be susceptible to PA labeling. Given the flexibility of allowing targeted binding of the SeNB derivatives to locations of interest and the reduced nonspecific background noises resulting from NIR light irradiation, SeNB probes are useful in labeling RNA in different cell lines with high spatiotemporal accuracy. Facilitated with copper-catalyzed azide-alkyne cycloaddition (CuAAC), RNAs labeled with PA can be clicked with fluorophores and biotin, allowing downstream analysis, such as imaging and RT-qPCR, thereby making locational and RNA profiling on less conventional cell line possible with high resolution[1].



References

1. Jia, H., Han, J., Qi, Y., Liu, J., Leung, Y. T., Yau, H. T., Chu, Y., Wang, T., Fung, Y. E., Wang, Y., Li, Y. *Angew. Chem. Int. Ed.* 2025, *64*, e202419904

A novel reader of H3K9 methylation in *Arabidopsis*

Xinyu Dong, Sha Liu, Xiang David Li

University of Hong Kong, Hong Kong, China

xiangli@hku.hk

Abstract

H3K9 methylation is a crucial epigenetic mark in *Arabidopsis thaliana*, playing a central role in gene silencing, heterochromatin formation, and genome stability. Key discoveries include the identification of SUVH4 as a major H3K9 methyltransferase, which establishes H3K9me2/me3 marks and links DNA methylation to histone modification[1]. Additionally, the Jumonji C domain-containing protein IBM1 has been identified as an H3K9 demethylase, regulating gene expression and stress responses[2].

Despite the well-characterised functions of these proteins, the full spectrum of the H3K9 methylation-associated readers remains incomplete. In this study, we discovered a novel H3K9 methylation reader, protein X, through the TMT (Tandem Mass Tags)-based proteomics. This protein consists of two DUF3444 (Domain of Unknown Function 3444) domains, which only the first domain can specifically recognise the H3K9 methylation. This finding provides new insight into the mechanisms by which H3K9me1/2/3 mediates chromatin dynamics and gene regulation, expanding our understanding of the regulatory network controlling this epigenetic mark, and offering potential targets for further exploration in epigenetic research in plants.

References

1. Jackson, J. P., et al.. Control of CpNpG DNA methylation by the KRYPTONITE histone H3 methyltransferase. *Nature*, **2002**, 416(6880), 556-560.
2. Saze, H., etal.. Control of Genic DNA Methylation by a jmjC Domain-Containing Protein in Arabidopsis thaliana. *Science*, **2008**, 319(5862), 462-465.

Identification of eEF1A methylation “readers” in living cells

DING Yuzhen, HUANG Siyue, TIAN Gaofei, Xiang David Li
Department of Chemistry, The University of Hong Kong
Email: xiangli@hku.hk

Abstract

eEF1A1 is involved in delivering aminoacyl-tRNAs during mRNA translation. Lysine methylation occurs at 5 sites (K36, K55, K79, K165, and K318) on eEF1A1, mediated by specific lysine methyltransferases (KMTs). These KMTs are dedicated to methylating eEF1A1 exclusively. Methylation events on eEF1A1 have been linked to the regulation of protein synthesis elongation. However, the precise molecular mechanisms and implications in cellular processes and disease remain unknown. To gain insights, we aim to identify the "readers" of eEF1A1 methylation. To capture the transient and weak interactions in living cells, we have developed two strategies: SILAC-based TurboID and iCLASPI (in vivo crosslinking-assisted and stable isotope labeling by amino acids in cell culture [SILAC]-based protein identification). Our pull-down assays showed that both TurboID and iCLASPI can capture binders of eEF1A. Once we have identified the "readers" of eEF1A1 methylation, we will proceed to verify and characterize the interaction through Co-IP, FPLC, and ITC assays. Additionally, we aim to understand the binding mechanisms using crystallography or Cyro-EM techniques. Finally, we will explore the biological significance of eEF1A methylation.

References:

1. Liu, S., Hausmann, S., Carlson, S. M., Fuentes, M. E., Francis, J. W., Pillai, R., et al. (2019). Mettl13 methylation of eEF1A increases translational output to promote tumorigenesis. *Cell*. 176, 491-504 e21.

2. Mealey-Farr, R., Jeong, J., Park, J., Liu, S., Hausmann, S., Francis, J. W., et al. (2023). Antibody toolkit to investigate eEF1A methylation dynamics in mRNA translation elongation. *J Biol Chem*. 299, 104747.

Exploring Linear Azole Containing Peptides (LAPs) from Archaea

Cunlei Cai, Zhiman Songand Yong-xin Li

Email: ccunlei@connect.hku.hk

Abstract

Archaea are microorganisms that are commonly found in extreme environments, characterized by extreme temperatures, high salinity, and other challenging conditions. Due to their ability to withstand such harsh conditions, enzymes and metabolites derived from archaea have great potential for use in biotechnology. Genomic analysis of archaea revealed that they encoded most of the known classes of secondary metabolites, but exact characterization of archaeal natural products is still far lagged behind. In this study, we target at a group of azol(in)e-modified RiPPs - linear azole containing peptides (LAPs). These compounds feature thiazole and oxazole heterocyclic rings within their core peptide structures and have been reported to exhibit a wide variety of bioactivities. Our ultimate goal is to explore novel enzymatic mechanisms involved in the biosynthesis of these compounds and identify potential new drug candidates.

References

1. Burkhart, Brandon J., et al. *Chemical reviews*, **2017**, *117*, 5389-5456.
2. Collin, Frederic, and Anthony Maxwell. *Journal of molecular biology*, **2019**, *431*, 3400-3426.

BOOST: a robust ten-fold expansion method on hour-scale

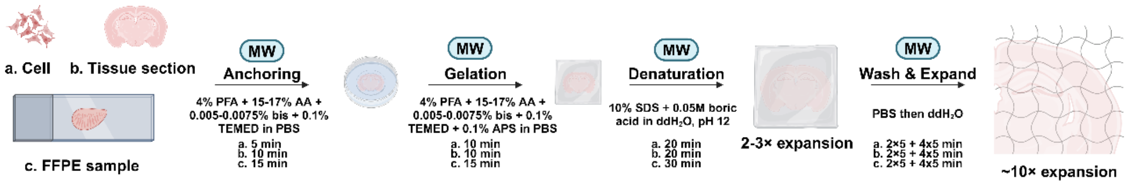
Jinyu Guo[a], *Hui Yang*[a], *Chixiang Lu*[a], *Di Cui*[a], *Murong Zhao*[a], *Weihua Chen*[a], *Qian Yang*[a] *and Haibo Jiang*[a,*]

[a]Department of Chemistry, The University of Hong Kong, Hong Kong SAR, China

[*]Correspondence: Haibo Jiang, hbjiang@hku.hk

Abstract

Expansion microscopy (ExM) enhances the microscopy resolution by physically expanding biological specimens and improves the visualization of structural and molecular details. Numerous ExM techniques and labeling methods have been developed and refined over the past decade to cater to specific research needs. Nonetheless, a shared limitation among current protocols is the extensive time required for sample processing, particularly for challenging-to-expand biological specimens (e.g., formalin-fixed paraffin-embedded (FFPE) sections and large three-dimensional specimens). Here, we have developed a rapid and robust ExM workflow, named BOOST, leveraging a series of novel microwave (MW)-accelerated ExM chemistry. Specifically, BOOST enables a single-step 10-fold expansion of cultured cells, tissue sections, and even the challenging-to-expand FFPE sections under merely 90 minutes. It employs microwave-assisted proteomic staining and immunostaining to facilitate high-resolution visualization of structural and molecular details with significantly enhanced throughput. Notably, BOOST has pioneered a 10-fold expansion of large millimeter-sized three-dimensional specimens that was not possible before. The workflow is also easily adaptable based on stable and common reagents, thus boosting the potential adoption of ExM for applications.



References

1. Guo, J. et al. *bioRxiv* **2024**, *doi:https://doi.org/10.1101/2024.07.11.603043*

Tool to Resolve Distortions in Elemental and Isotopic Imaging

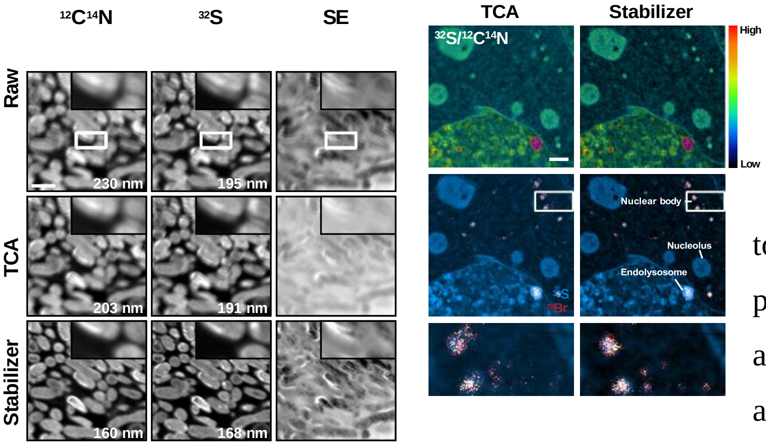
Chixiang Lu[a,†], Gu Chen[a,†], Xiaojuan Qi[b,*], and Haibo Jiang[a*]

Department of [a]Chemistry, and [b]Electrical and Electronic Engineering, The University of Hong Kong;

[*]Correspondence: Haibo Jiang, hbjiang@hku.hk; Xiaojuan Qi, xjqi@eee.hku.hk

Abstract

Nanoscale secondary ion mass spectrometry (NanoSIMS) enables high-resolution chemical imaging of sample surfaces with a lateral resolution of up to 40 nm. The NanoSIMS instrument bombards samples with a primary ion beam (e.g., $^{133}Cs^+$), and images are created, pixel by pixel, from secondary ions (e.g., $^{2}H^-$, $^{13}C^-$, $^{79}Br^-$, and $^{127}I^-$). However, persistent challenges include distortion from instrumental (e.g., electromagnetic, acoustic, and mechanic) and sample interferences compromise imaging fidelity and resolution.



To address this challenge, we developed the NanoSIMS Stabilizer, a computational tool based on the recurrent all-pairs field transforms (RAFT) algorithm for correcting rigid and nonrigid distortions in the NanoSIMS image series. The NanoSIMS Stabilizer has a superior registration capability for correcting multiple types of distortions for synthetic and real data compared with translation-counter balancing algorithms (TCAs), built-in registration modules in OpenMIMS, ImageJ and other NanoSIMS software. The NanoSIMS Stabilizer preserves localization and signal ratio data and is available in a code-free, open-source, ready-to-use ImageJ plugin. Leveraging the deep learning-based optical flow registration model, the NanoSIMS Stabilizer ensures high-fidelity visualization of drug-related isotopes and elements at cellular and subcellular levels, enabling researchers to extract reliable data from complex biological systems.

Reference

Lu, C.; Chen, G.; *Journal of the American Chemical Society* **2024**, *146* (29), 20221-20229.

Fabrication of a Simple and Efficient Reactor for Online Derivatization of Aristolochic Acids to Facilitate the Detection by Liquid Chromatography Coupled Fluorescence Detection

Man-Lung CHIN, Wan CHAN*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon,
Hong Kong SAR
E-mail: chanwan@ust.hk

Abstract

Aristolochic acids (AAs) are a group of naturally occurring carcinogenic and nephrotoxic compounds produced by plant species of the *Aristolochia* and *Asarum* genera. Strong evidence in the toxicological and clinical research carried out over the past decades suggested the close correlation of AA-intake through consumption of herbal remedies composed of AA-containing plants with the development of aristolochic acid nephropathy (AAN), a rapidly progressive renal fibrosis and leads to high incidence of urothelial malignancy developed at the upper urinary tract. [1] In the meantime, environmental studies demonstrated AA is an emerging class of environmental contaminants originating from the decay of the widespread *Aristolochia* species that include *A. clematitis*.[1] The event of contamination by AA resulted in AA-tainted food that includes food grains and vegetables grown at the site of contamination, as well as underground water source.[1],[2] It is believed that prolonged exposure to AA through consumption of these food and water involved in the aetiology of a variant of AAN that named Balkan endemic nephropathy (BEN). Liquid chromatography coupled with fluorescence detection or mass spectrometry, with enhanced sensitivity and selectivity by incorporating a pre-column offline derivatization procedure, were employed as the tools to determine AA at low ng/g level in complex matrices of environmental and food samples.[2],[3] In these methods, aristolactam (AL), the derivative of AA formed by nitroreduction of AA with zinc dust under acidic condition was detected and quantified. However, due to the natural occurrence of AL from the same source of AA, true amount of AA can be determined only when both derivatized and underivatized samples have been analyzed, which caused complication and consumption of time, reagents and labour. To facilitate the analysis of AA, a column-based reactor was developed and optimized for post-column reduction of AA and detected using a fluorescence detector. This new method allowed simultaneous detection and quantification of AA and AL in one single run without sacrificing sensitivity, significantly enhanced the efficiency of the analysis and reduced the cost of reagents and labour. The validated method was applied to analyze wheat grains and herbal medicines for demonstration of the accuracy and precision by comparing to other reported methods.

References:

[1] S. Das et al., Aristolochic acid-associated cancers: a public health risk in need of global action. Nat. Rev. Cancer. 2022, 22, 576-591.
[2] C. -K. Chan et al., Development of a novel liquid chromatography-tandem mass spectrometric method for aristolochic acids detection: application in food and agricultural soil analyses. Food Chem. 2019, 28, 673-679.
[3] W. Chan et al., Quantitation of aristolochic acids in corn, wheat grain, and soil samples collected in Serbia: identifying a novel exposure pathway in the etiology of Balkan endemic nephropathy. J. Agric. Food Chem. 2016, 64, 5928-5934.

Wheatgrass (Triticum aestivum) as an Efficient Phytoremediation Plant for Aristolochic Acid-Contaminated Water and Arable Soil

Hong Ching Kwok, Wan Chan*
The Hong Kong University of Science and Technology, Clear Water Bay, Hong Kong
Email: chanwan@ust.hk

Abstract

Dietary exposure to aristolochic acids (AAs) through consumption of AA-contaminated foods has long been recognized as a causal factor to Balkan endemic nephropathy (BEN), a slowly progressive renal fibrotic disease that affects many individuals residing in farming communities along the Danube River in the Balkan Peninsula. Recent findings have revealed that farmland soil and groundwater in endemic regions are contaminated with AAs, which are released from the decay of *Aristolochia clematitis*, thereby heightening the risk of human exposure to these potent phytotoxins. Consequently, there is an urgent need to develop effective remediation strategies for AA-contaminated water and agricultural soil. In this study, we evaluated the efficacy of phytoextraction techniques using commonly employed phytoremediation plants to remove AAs from polluted water and soil. Our experimental results indicate that wheatgrass is particularly effective in extracting AAs from both contaminated water and soil, as well as in metabolizing these compounds into less toxic form of AAs -- aristolactams (ALs). Furthermore, we observed that an acidic environment, which is characteristic of endemic villages, enhances both the phytoextraction and metabolic efficiency of the plants, highlighting the potential applicability of the developed method in affected regions.

References

1. Chan, C. K.; Xiong, L.; Pavlović, N. M.; Chan, W. *ACS Agric. Sci. Technol.* **2021**, *1*, 522−528
2. Tung, K. K.; Chan, C. K.; Zhao, Y.; Chan, K. K. J.; Liu, G.; Pavlović, N. M.; Chan, W. *Environ. Sci. Technol.* **2020**, *54*, 1554−1561.
3. Hughes, J. B.; Shanks, J.; Vanderford, M.; Lauritzen, J.; Bhadra, R. *Environ. Sci. Technol.* **1997**, *31*, 266−271.

Year-round observation of atmospheric wet and dry deposition of inorganic and organic nitrogen at a coastal site of Hong Kong

Wing Hei Marco Wong[1], Xu Yu[2], Jian Zhen Yu[1,2,*]

[1]Department of Chemistry, The Hong Kong University of Science and Technology, Hong Kong
[2]Division of Environment and Sustainability, Hong Kong University of Science & Technology

Abstract

Atmospheric nitrogen (N) deposition serves as a significant pathway of N nutrient input to terrestrial and aquatic ecosystems. Organic nitrogen deposition has been largely under-evaluated in the past N deposition observations. Here, a year-round observation of atmospheric deposition of inorganic N (including NH_4^+-N and NO_3^--N) as well as water-soluble organic nitrogen (WSON) was performed using an automatic wet and dry deposition collection system at a coastal site of Hong Kong from September 2023 to November 2024. Annual total (wet plus dry) N deposition flux was 56.5 kgN ha^{-1} $year^{-1}$ at the site, ranking one of the highest in the developed regions of the world. The total deposition fluxes of NH_4^+-N, NO_3^--N, WSON were 14.6, 26.1 and 15.9 kgN ha^{-1} $year^{-1}$, accounting for 26%, 46% and 28% of water-soluble total nitrogen (WSTN) deposition, respectively. Notably, WSON made an appreciable contribution to WSTN, indicating that WSON should be included when monitoring N deposition. Wet and dry deposition were both significant N deposition pathways, contributing around 75% and 25%, respectively, to total N deposition during the observation period. Our study demonstrated the high level of N deposition at coastal Hong Kong and filled the knowledge gap of organic nitrogen deposition. Future efforts include investigating the sources of N in wet and dry deposition and potential impacts of N deposition on ecosystems.

What happened that night? Source apportionment of a short-term air pollution episode using half-hourly resolved GC-MS data for PMF analysis

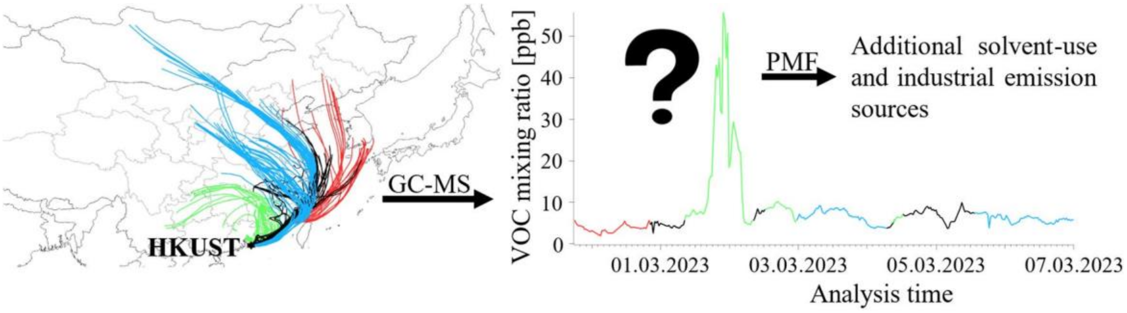
Anna Mae Vorwerk, Wing Sze Chow, Jianzhen Yu

Department of Chemistry, HKUST, Clear Water Bay, Hong Kong; chjianyu@ust.hk

Abstract

Air pollution caused by volatile organic compounds (VOCs) is an ongoing problem for human health and a major contributor to climate change. To improve air quality and decrease greenhouse gas emissions, it is important to know the local air composition and VOC emission sources.[1] However, short-term air pollution episodes are difficult to analyse. Instruments with high time resolution could enable monitoring authorities to capture short-term changes of the VOC composition in ambient air more accurately.

The Aerodyne 2-channel GC-MS at the suburban HKUST Air Quality Research Supersite Facility can obtain VOC data with a half-hour temporal resolution. From March 1st, 2023, 3 pm until March 2nd, 2023, 7 am we recorded a sudden increase in VOC mixing ratios during a shift of the air mass origin to the northern vicinity of Hong Kong. Applying the positive matrix factorization (PMF) model on one-week data of 25 source-indicating VOCs, we identified seven factors. Through their respective time series, two factors were attributed to the pollution episode. The VOC profiles of both factors hint towards solvent use and industrial emission sources. Our findings highlight the importance of high time- resolution VOC monitoring for source identification of short-term air pollution episodes.



References

Mai, Y.; Cheung, V.; Louie, P. K. K.; Leung, K.; Fung, J. C. H.; Lau, A. K. H.; Blake, D. R.; Gu, D. *Journal of Environmental Sciences (Beijing, China)*, **2025**, *151*, 424 – 440.

Anna Mae Vorwerk thanks the Hong Kong PhD Fellowship Scheme for financial support. The authors thank the Environment and Conservation Fund (grant no. ECF109/2023) for funding and the Hong Kong Environmental Protects. 22-00404) for funding and instrumentation support.

Comparison of two oxidative potential chemical assays applied to atmospheric $PM_{2.5}$ samples in an urban environment in Hong Kong

Ng Pak Hiu[1], Chen Hanzhe[1], Cheng Yuhuang[2], Jian Zhen Yu[1,2,*]

[1]Division of Environment and Sustainability, [2]Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong

*Corresponding Author: chjianyu@ust.hk

Abstract:

Ambient particulate matter (PM) is known to be the reason for generation of reactive oxygen species (ROS) within the human body. To quantify the rate of PM generating ROS in the human body, oxidative potential (OP) is used. However, there are multiple assays that are commonly used for OP measurement, including acellular assays such as dithiothreitol (DTT), ascorbic acid (AA), glutathione (GSH), and different cellular assays. Different assays have different reaction mechanisms. Thus, the OP value, which can be expressed in volume- normalized and mass normalized OP, will vary with different assays. This research compared two commonly used acellular assays DTT and AA, with the use of samples of urban HK in 2021, which showed different levels of correlation with chemicals and seasonal variation. Volume-normalized DTT showed a V-shaped variation, which is high in winter, reduced in spring and summer, and increased in fall and winter, mass-normalized DTT does not show a clear variation, with minor increase from winter to spring, and a minor level of decrease from spring to summer and fall. While both volume-normalized and mass-normalized AA does not show a significant trend of seasonal variation, which both showed a trend of low in winter, and highest in summer, and then decreased gradually from fall to winter. While both mass and volume-normalized DTT showed a moderate correlation with water soluble Manganese, Iron and organic carbon, the mass and volume normalized AA showed high correlation with water soluble Copper.

Accurate Quantification of Multifunctional $C_{2–3}$ Organosulfates in Atmospheric Aerosols Using Liquid Chromatography-Electrospray Ionization Mass Spectrometry: Overcoming Matrix Effects and Underestimation

Shumin Liang[1], Yuchen Wang[2], Hanzhe Chen[3], Wan Chan[1], Jian Zhen Yu[1,3]*

[1] Department of Chemistry, The Hong Kong University of Science & Technology, Clear Water Bay, Kowloon, Hong Kong, China

[2] College of Environmental Science and Engineering, Hunan University, Hunan, China

[3] Division of Environment & Sustainability, The Hong Kong University of Science & Technology, Clear Water Bay, Kowloon, Hong Kong, China

*Corresponding author: jian.yu@ust.hk

Abstract

Reversed-phase liquid chromatography (RPLC) coupled with electrospray ionization-mass spectrometry (ESI-MS) is widely used to analyze polar organic compounds in atmospheric particulate matter (PM). However, its efficacy for small, polar multifunctional C_2–C_3 organosulfates ($C_{2–3}$OSs)—conceivably key products of isoprene oxidation—is questionable. Notable matrix effects are anticipated to arise from poor retention and co-elution with abundant salts in PM samples. Here, we systematically evaluated RPLC versus hydrophilic interaction liquid chromatography (HILIC) coupled with ESI-Orbitrap MS in quantifying PM-bound $C_{2–3}$OSs. We synthesized three $C_{2–3}$OSs, including glycolic acid sulfate, hydroxyacetone sulfate, and lactic acid sulfate. The availability of authentic standards enabled the first quantitative assessment of measurement bias for $C_{2–3}$OSs using RPLC-ESI-Orbitrap MS method, revealing an underestimation of these compounds by 1–2 orders of magnitude. The measurement bias primarily stemmed from matrix effects arising from co-existing bisulfate in ambient PM. In contrast, HILIC notably outperformed RPLC in retentive capacities and peak resolving abilities, effectively avoiding matrix suppression effects. Additionally, the HILIC-ESI-MS method uncovered four previously unreported $C_{2–3}$OSs, expanding our knowledge of atmospheric OSs. This work enhances our capability of accurate quantification of aerosol components, thus helping reduce constraints on studies of aerosols and their impacts.

Characteristics and Sources Appointment of Water-soluble Organic Carbon in $PM_{2.5}$: One-year Analysis in Hong Kong

Ryan Lee[1], Tao Li[1], Jian Zhen Yu[1,2]

[1] Division of Environment and Sustainability, [2] Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon, Hong Kong, China

Corresponding author : jian.yu@ust.hk

Abstract:

As an important fraction of organic carbon in $PM_{2.5}$, WSOC plays a crucial role in climate change, atmospheric chemistry, and is associated with adverse health effects. While fossil fuel combustion and secondary formation are common sources of WSOC, the temporal variations and sources of WSOC in Hong Kong remain unclear. In this study, we conducted a field measurement of daily $PM_{2.5}$ composition at Tsuen Wan, an urban residential area in Hong Kong, over a one-year period from 2023 to 2024. In addition to WSOC, carbonaceous species, saccharides, inorganic ions, and metal concentrations were determined to trace the sources of WSOC.

The results showed that the annual average concentration of WSOC was 1.6 ± 1.0 µgC/m³, with the highest concentration observed in winter (2.1 ± 1.0 µgC/m³) and the lowest in summer (1.1 ± 0.8 µgC/m³) among four seasons. WSOC accounted for 40% of the total OC throughout the study period, with the following seasonal contributions: winter (44.2%) > fall (42.5%) > summer (37.2%) > spring (35.2%), suggesting increased pollution levels during the winter months. A Positive Matrix Factorization (PMF) analysis was performed to identify the sources of WSOC, revealing that primary sources such as coal combustion and biomass burning contributed more than 50% to WSOC levels. These findings could inform strategies for mitigating WSOC-related health impacts and improving air quality in Hong Kong.

Reference:

1. Du, Z., He, K., *Atmospheric Environment*, **2014**, *92*, 514–521.

Cupric Ion Induced L-glutathione Depletion in Surrogate Lung Fluid: A Quasi-Michaelis-Menten Mechanism

Yuhuang Cheng[1] and Jian Zhen Yu[1,2]

[1] *Department of Chemistry, Hong Kong University of Science & Technology, Hong Kong, China*

[2] *Environmental Science Programs, Hong Kong University of Science & Technology, Hong Kong, China*

Postal address: ychengbn@connect.ust.hk

Abstract

The inhaled ambient fine particulate matter ($PM_{2.5}$) can release morbific chemicals to human respiratory system. Among them, the highly catalytical transition metals (TMs) can contribute to antioxidant depletion and reactive oxidative species (ROS) formation. These can increase the adverse oxidative potential (OP) to the human body, causing multiple health issues. Previous studies have assessed OP of different samples based on glutathione (GSH) assay, as GSH is an essential antioxidant applied inside human body. Equations between OP and TM concentration have also been generated by different regression models. However, these empirical equations could hardly explain the catalytical effect of TM in OP generation processes as no underlying chemical mechanisms were proposed to support them.

In this study, we measured the cupric ion induced GSH loss rate with controlled Cu concentration and GSH initial concentration respectively. The reaction rate not only shows a Michaelis-Menten like trend with increasing Cu concentration but is also first ordered with respect to GSH concentration. Based on these results, we proposed a modified quasi-Michaelis-Menten mechanism to explain the catalytical effect of Cu during the GSH oxidation process in the surrogate lung fluid. In addition, the synergistic effect of ambient organics during Cu-induced GSH oxidation is also tested and discussed. Our work proposed a detailed chemical mechanism for Cu induced GSH depletion in the acellular GSH assay. This lays the foundation for understanding OP generation in the more complicated human respiratory system, providing valuable reference for OP calculation and modeling based on measured chemical composition of ambient $PM_{2.5}$.

Bioorthogonal release and synthesis of anticancer drugs via propargylbenzoxime (PBO) precursors

Jing Huang, Yiling Liu, and Kenward Vong*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, Hong Kong, China. E-mail: kvong@ust.hk

Abstract

Currently, dissociative biorthogonal metal-catalyzed reactions used for developing prodrugs have largely centered on the release of amines, alcohols, and certain aryl groups. To add to the growing list of these reactions, this study develops what is described as the propargylbenzoxime (PBO) group. When exposed to Au(III) catalysts, the PBO group was found to undergo hydroamination, followed by spontaneous N–O bond cleavage to release aldehydes/ketones under mild and physiological conditions.[1] Further adaptation of the PBO group was then explored so that carbonyl release could elicit the synthesis of an indole core. To highlight their applications for anticancer prodrug therapies, this study also developed PBO-masked prodrugs that can undergo the gold-triggered synthesis of indole-based drugs.

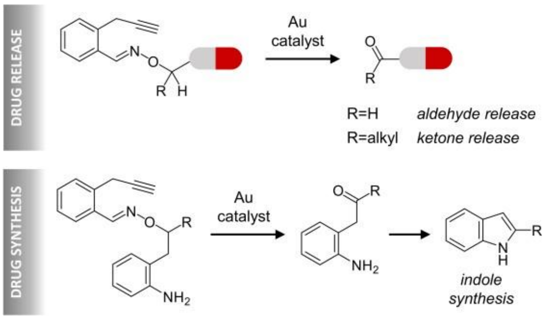


Figure 1. Development and adaptation of PBO groups for drug release (carbonyl release) and drug synthesis (indole forming)

References

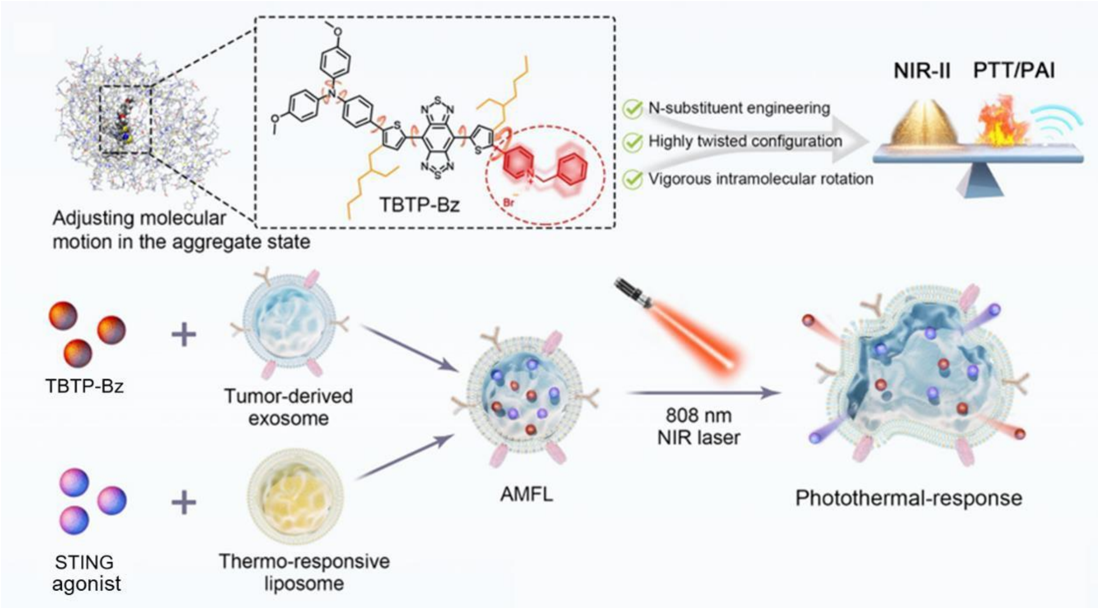
[1] Huang, J.; Liu, Y. and Vong, K. *Submitted.*

NIR-II photothermal agent for STING activation and multimodal image-guided cancer immunotherapy

Xinyan Zhu[+]., …Tianfu, Zhang*., Ben Zhong, Tang*.
zhangtf@gzhmu.edu.cn, tangbenz@cuhk.edu.cn.

Abstract

The immunosuppressive tumor microenvironment in triple-negative breast cancer could hinder response to thorough immunotherapy and diminish the antitumor efficacy[1]. Here, we manifest a novel phototheranostic agent with aggregation-induced emission property that guided pharmacological activation of a STING agonist for photothermal-immunotherapy to create an immunologically "hot" tumor[2]. A pyridinium rotor strategy is proposed to develop a positively charged TBTP-Bz which is stably co-incorporated with STING agonist into thermal-responsive exosome-liposome hybrid nanoparticles for tumor-targeting delivery. Significantly, single-dose photoimmunotherapy effectively suppresses abscopal tumor growth and provokes an immune memory effect to inhibit postsurgical recurrent and rechallenged tumors.



References

1. Harbeck, N.; Cardoso, F. *Nature Reviews Disease Primers* **2019**, *5*, 66.
2. Xinyan, Z.; Benzhong, T. Journal of American Chemical Society **2024**, submitted.

AIEgen-Based System for Smart Theranostic and Photocatalytic Therapy

Kun Zhou, Ryan T. K. Kwok, Jacky W. Y. Lam, Jianwei Sun and Ben Zhong Tang
Department of Chemistry, The Hong Kong University of Science and Technology,
Kowloon 100071 Hong Kong, China

E-mail: tangbenz@ust.hk

Abstract

Drug-resistant microbial infections have become a global public health issue, necessitating early detection and intervention. Current in vitro clinical diagnostic methods typically require sampling and culturing, processes that are cumbersome and time-consuming. In response, we have developed a smart, portable system that integrates AIEgens (fluorescent sensors), a mini dual-light channel on a cellphone, and intelligent software. This system can monitor infections within seconds and provide photodynamic therapy within minutes using low-power white light irradiation, achieving antimicrobial activity rates of over 96% and enabling wound healing within a week. The system is further enhanced with remote communication and image analysis software, allowing for wireless data transmission, infection analysis, and medical advice from doctors via the Internet. This innovation addresses the global antibiotic resistance crisis and lays the groundwork for the development of smart wound dressings with potential applications in preclinical research and diagnostics.[2, 3]

Additionally, traditional photodynamic therapy (PDT) faces challenges in treating anaerobic bacterial infections due to the need for oxygen. To overcome this, we have constructed an exceptionally potent photocatalytic system, TBSMSPy$^+$, which exhibits high catalytic activity through photo-induced intramolecular multi-step electron transfer. TBSMSPy$^+$ effectively catalyzes the oxidation of NADH, disrupting normal metabolism and leading to cell death. We term this mechanism "photoinduced redox imbalance" (PIRI) and have demonstrated its effectiveness in oxygen-free periodontitis treatment.[1]

References

1. Zhou, K., Du, L., Ding, R., Xu L., Shi, S., Wang, S., Wang, Z., Zhang, G., He, G.,* Zhao, Z.,* Tang, B. Z.**Nat. Commun.* **2024**, *15*, 10551.
2. Zhou, K., Yu, Y., Xu, L., Wang, S., Li, Z., Liu, Y., Ryan T. K. Kwok, Sun, J., Jacky W. Y. Lam*, He, G.,* Zhao, Z.,* Tang, B. Z.* *ACS Nano* **2024**, *18*, 29930.
3. Zhou, K., Wang, S., Xu L., Li, H., Wang, Y., Qiu, Z., Zhang, G., Zhao, Z.,* Tang, B. Z.* *Matter* **2023**, *6*, 3449.

Rational Design of NIR-II AIE Probes for High-Contrast Bioimaging and Photodynamic Therapy

Xinyuan Wang[a], Xueqin Yang[a], Jacky W. Y. Lam[a], Jianwei Sun[a*], and Ben Zhong Tang[a,b*]

[a] Department of Chemistry, The Hong Kong Branch of Chinese National Engineering Research Center for Tissue Restoration and Reconstruction, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong *Email: sunjw@ust.hk

[b] School of Science and Engineering, The Chinese University of Hong Kong, Shenzhen, Guangdong 518172, China *Email: tangbenz@ust.hk

Abstract

Near-infrared-II (NIR-II) fluorescence imaging and photodynamic therapy (PDT) hold immense potential for precision medicine, yet existing probes struggle to simultaneously achieve high brightness, efficient reactive oxygen species (ROS) generation, and organelle-specific targeting. This work presents two molecular engineering strategies to address these challenges. Utilizing dithieno[3,2b:2′,3′-d]pyrrole and indolium, the designed ionic aggregation-induced emission (AIE) photosensitizer DTP-In redshifted absorption/emission to 620/970 nm while reducing the singlet-triplet energy gap (ΔE_{ST} = 0.78 eV) for enhanced ROS production. Through intramolecular S-N electrostatic locks, the AIEgen TSEH showed boosted NIR-II quantum yield (QY = 1.22% in water) and brightness. Therapeutically, DTP-In enables real-time NIR-II-guided PDT with 78% tumor growth inhibition, whereas TSEH visualizes sub-millimeter metastatic lung tumors (<1 mm) for surgical navigation. These findings collectively advance NIR-II probes toward clinical translation, offering dual solutions for image-guided cancer therapy (DTP-In) and point-of-care diagnostics (TSEH), with broader implications for designing multifunctional nanomaterials through rational electronic and steric control.

Reference

Yang, X., Wang, X., *Advanced Materials*, **2024**, *36*, 2402182

Wang, X., Yang, X., *Angewandte Chemie International Edition*, **2024**, *63*, e202404142

Discovery of a Novel Marine Bacterial AIEgen for Fluorescent Visualization of Specific G-Quadruplexes

Wenkang Ye#[1], Xinnan Wang#[2], …… Guang Zhu*[3], Ben Zhong Tang*[2,4], Pei-Yuan Qian*[1]

1. Department of Ocean Science, The Hong Kong University of Science and Technology, HKSAR, P.R. China
2. Department of Chemistry, The Hong Kong University of Science and Technology, HKSAR, P.R. China
3. Department of Life Science, The Hong Kong University of Science and Technology, HKSAR, P.R. China
4. Shenzhen Institute of Aggregate Science and Technology, School of Science and Engineering, The Chinese University of Hong Kong, Shenzhen (CUHK-Shenzhen), Guangdong, 518172, P.R. China

*Corresponding authors: boqianpy@ust.hk, tangbenz@cuhk.edu.cn, gzhu@ust.hk

Abstract

The emergence of aggregation-induced emission (AIE) two decades ago marked a significant advancement in chemical science, spurring the booming development of novel AIEgens for bioimaging, optoelectronics, and biochemical sensing. Limited by constrained chemical space, environmental concerns, and uncertain biocompatibility, synthetic AIEgens face application challenges, making the pursuit of naturally derived BioAIEgens a promising strategy for next-generation development.[1] Here, we report the first AIEgen derived from a marine bacterial metabolite, 2-(2-hydroxy-6-methoxy-3-propionylphenyl)quinazolin-4(3H)-one (HMPQ). HMPQ exhibits a unique fluorescence mechanism via excited-state intramolecular proton transfer and displays diverse emissions in various solvents and solid-state polymorphic forms. Notably, HMPQ selectively binds to G-quadruplexes (G4s), enabling fluorescence visualization of these non-canonical nucleic acid structures without altering their conformation. Its excellent biocompatibility and precise cellular imaging of G4s highlight its potential in biological applications, paving the new way for BioAIEgens as novel G4 probes.

Reference

1. Gu, Y.; Zhao, Z.; *et al*. *CHEM. SCI*, **2018**, *9*, 6497-6502.

Lab-in-cell: A Covalent AIE Photosensitizer Reverses Hypoxia and Evokes Ferroptosis and Pyroptosis for Enhanced Anti-tumor Immunity

Bingnan Wang,[a] Ryan T. K. Kwok*,[a] Jacky W. Y. Lam*,[a] Anjun Qin*[b] and Ben Zhong Tang*[a,c]

[a] *Department of Chemistry, The Hong Kong University of Science & Technology, Clear Water Bay, Kowloon, Hong Kong,*
[b] *State Key Laboratory of Luminescent Materials and Devices, South China University of Technology, Guangzhou, China.*
[c] *School of Science and Engineering, The Chinese University of Hong Kong, Shenzhen, China.*
**E-mail: chryan@ust.hk; chjacky@ust.hk; msqinaj@scut.edu.cn; tangbenz@cuhk.edu.cn*

Abstract

Photodynamic immunotherapy presents a non-invasive strategy characterized by spatiotemporal control and minimal side effects to induce immunogenic cell death (ICD). This approach significantly enhances the release of tumour-associated antigens and damage-associated molecular patterns, thereby improving cancer immunotherapy outcomes. However, hypoxia and antioxidant defences at tumour sites considerably diminish the efficacy of photodynamic immunotherapy. In this work, we introduced a covalent warhead, alkyneamide, into an AIE photosensitizer to develop a novel covalent photosensitizer, MBTP-PA, which targets redox systems and facilitates ferroptosis- and pyroptosis-mediated photodynamic immunotherapy by thiol-yne click reactions. The covalent photosensitizer interacts with intracellular thiol compounds such as cysteine and glutathione, disrupting the intracellular antioxidant system and alleviating hypoxia. This results in enhanced photodynamic therapy (PDT) efficacy compared to the non-covalent photosensitizer MBTP-A. Furthermore, in conjunction with PDT, this reaction therapy can activate ICD through ferroptosis and pyroptosis, thereby enhancing anti-tumor immunity. Notably, in vivo injection of MBTP-PA nanoparticles at the tumour site led to the elimination of primary tumours, inhibiting distal tumours and exhibiting minimal side effects. Therefore, this work not only integrates the thiol-yne click reactions into cellular systems, significantly enhancing the efficacy of photodynamic immunotherapy but also paves the way for developing novel photosensitizers.[1,2]

References

1. Tang, Y.; Bisoyi, H. K.; Chen, X.-M.; Liu, Z.; Chen, X.; Zhang, S.; Li, Q. *Adv. Mater.* **2023**, *35*, 2300232.
2. Wang, B.; Li, C.; He, D.; Ding, K.; Tian, Q.; Feng, G.; Qin, A.; Tang, B. Z., *Small* **2024**, *20*, 2307309.

Trigger inducible tertiary lymphoid structure formation using covalent organic frameworks for cancer immunotherapy

Liang Zhang, Boxin Zhang, Meng-Jie Zhang, Wenlang Li, Hao Li, Yantian Jiao, Qi-Chao Yang, Shuo Wang, Yuan-Tong Liu, An Song, Hai-Tao Feng, Jianwei Sun, Ryan T. K. Kwok, Jacky W. Y. Lam*, Ben Zhong Tang*, Zhi-Jun Sun*

Research Center for Tissue Restoration and Reconstruction, The Hong Kong University of Science and Technology, Hong Kong 999077, China. chjacky@ust.hk; tangbenz@cuhk.edu.cn; sunzj@whu.edu.cn

Abstract

The discovery of tertiary lymphoid structures (TLS) within tumor tissues provides a promising avenue to promote the efficacy of cancer immunotherapy. Yet, the lack of effective strategies to induce TLS formation poses a substantial obstacle. Thus, the exploration of potential inducers for TLS formation is of great interest but remains challenging. Here, inspired by the mechanism of artificially cultivated pearls, a covalent organic framework (COF) is employed to induce TLS formation[1]. Single-cell sequencing analysis reveals that this is achieved by promotion of cytokine hypersecretion, which facilitates the maturation, proliferation, and migration of T and B cells, critical for triggering TLS formation. Furthermore, the efficacy of COF-mediated phototherapy in inducing TLS formation is validated in both the MC38 and 4MOSC1 female tumor models. Notably, a strong synergistic effect between COF-mediated phototherapy and αCTLA-4 is observed, resulting in the effective eradication of both primary and distant tumors, while also inhibiting tumor recurrence.

References

1. Zhang, L.; Zhang, B.; Zhang, M.J.; Jiao Y. *et al. Nat. Commun.*, **2025**, *16*, 1-14.

Engineering a Near-Infrared Spiro-Based AIEgen for DNAzyme-Sensitized Photothermal Therapy with High Efficiency and Accuracy

Yingying Chen[1], Sheng-Yi Yang[1], Xinwen Ou[1], Wenqian Yu[2]*, Fuan Wang[2]*, Jacky W. Y. Lam[1]*, Ben Zhong Tang[1]*

[1] Department of Chemistry, The Hong Kong University of Science and Technology; chjacky@ust.hk; tangbenz@cuhk.edu.cn;

[2] College of Chemistry and Molecular Sciences, Wuhan University; wenqianyu@whu.edu.cn; fuanwang@whu.edu.cn

Abstract

Aggregation-induced emission luminogens (AIEgens)-based photothermal therapy (PTT) has grown into a sparkling frontier for tumor ablation. However, challenges remain due to the uncoordinated photoluminescence and photothermal properties of classical AIEgens, along with hyperthermia-induced antiapoptotic responses in tumor cells, hindering satisfactory thera-peutic outcomes. Herein, a near-infrared (NIR) spiro-AIEgen TTQ-SA was designed for boosted PTT by auxiliary DNAzyme-regulated tumor cell sensitization. With the combination of spiro-AIEgen-based PTT and DNAzyme-based gene silencing, the as-designed nanosystem showed promising NIR and photothermal imaging abilities for tumor targeting, and demonstrated significant cell apoptotic, antitumor, and anti-metastasis effects against both orthotopic and spontaneous breast cancer. These findings offer new insights into AIEgen-based photothermal theranostics and DNAzyme-regulated tumor cells sensitization, paving the way for synergistic gene silencing-PTT nanoplatforms in clinic.

Reference

1. Chen, Y., Yang, S. Y., Ou, X., Wang, H., Kong, F.-C., Chow, P. C. Y., Wang, Y., Jiang, Y., Zhao, W., Sun, J., Kwok, R. T. K., Zheng, D.-W., Yu, W.,* Wang, F.,* Lam, J. W. Y.,* Tang, B. Z.*. *J. Am. Chem. Soc.*, **2024**, *146*, 35462−35477.

2. Yang, S. Y., Wang, J., Deng, Z., Xu, Y., Su, X., Zhang, L., Yang, S., Kwok, R. T., Lam, J. W., Tang, B. Z. *Matter*, **2024**, *7*, 3390.

Alpha Synuclein Forming Liquid-Liquid Phase Separation with Mitochondrial Genome DNA via The Nucleoid Protein TFAM.

Xiaohui Ma[1], Vince St. Dollente[1], Shuqin Zheng[2], Zhixiao Wu[3], Jin Wang[3], Dac Hieu Nguyen[3], Tongle Xu[1], Lan Wang[3], Lingxiang Jiang[2], Toyotaka Ishibashi[3], Jinqing Huang[1]

1 Department of Chemistry, HKUST, Hong Kong. 2 South China Advanced Institute for Soft Matter Science and Technology, School of Emergent Soft Matter, South China University of Technology, Guangzhou 510640, China 3 Department of Life Science, HKUST, Hong Kong.

Corresponding author: maxhuq@ust.hk

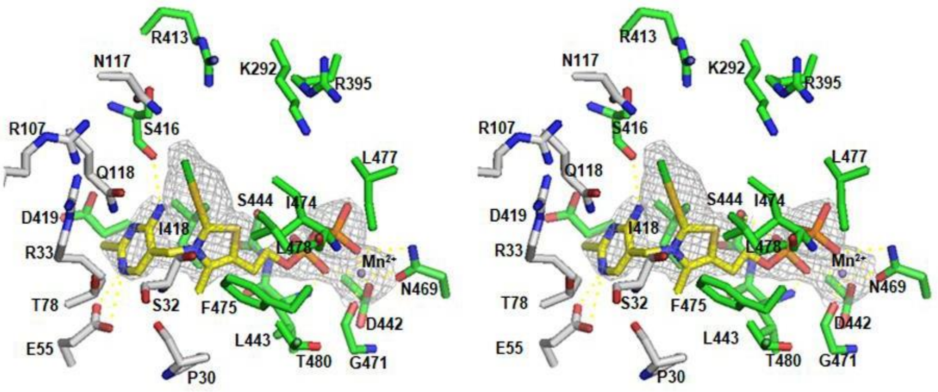
α-synuclein is an intrinsically disordered protein (IDP). The aggregation of α-synuclein is associated with several neurodegenerative diseases Like Parkinson Disease (PD). During the process of aggregation, α-synuclein will form the condensate membranelles organelles with other proteins, DNA, or RNA, which is defined as liquid-liquid phase separation (LLPS) The condensate of α-synuclein can be found in almost whole cells including mitochondria.

Mitochondria provide more than 90% of energy to support bioreactions inside cells. Mitochondria genome DNA (mtDNA), which is always covered by mitochondrial nucleoid proteins like TFAM, is a double-strand circular DNA, with various copies in the mitochondrial matrix. In PD models, α-synuclein has been reported to locate in the outer membrane, inner membrane, and matrix of mitochondria. However, the relationships among α-synuclein, mtDNA, TFAM and PD remains unclear. Our study first shows α-synuclein is colocalized with TFAM and mtDNA in Hela cells and could form LLPS with mtDNA and TFAM in vitro. With the single molecule optical tweezers, we find TFAM is essential core of the LLPS droplet whose DNA binding function is force dependent. Finally, our study also proves calcium is also the key of LLPS forming. Our study shed light on PD studies with novel methods in single molecule level. Furthermore, combination between biochemical and biophysics methods also fill the gap in molecule dynamics and processing from molecule level to cell level.

Gold-dependent artificial metalloenzymes from native thiamine enzymes

Hong Dai, Ke Du, Lingfeng Zhang, Luning Tian, Zhihong Guo*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR
E-mail: chguo@ust.hk

Many artificial metalloenzymes have been created to convert the versatile transition metal catalysts into environment-friendly biocatalysts. Here we report a new strategy to create artificial metalloenzymes from native thiamine enzymes. We use the thiamine-diphosphate cofactor as a carbene ligand to coordinate transition metals and incorporate the metalated cofactor into the active site for use as a transition metal cofactor. Using gold (I) as example, we have successfully synthesized the gold (I) cofactor and incorporated it into the thiamine enzyme MenD from E. coli (see below). The holo-metalloenzyme retains the catalytic activities of the gold complex with a very high substrate specificity. Increase of its catalytic efficiency by molecular evolution is in progress. This new strategy of forming artificial metalloenzymes promises to transform a significant portion of transition metal catalysis into green chemistry.



Acknowledgement

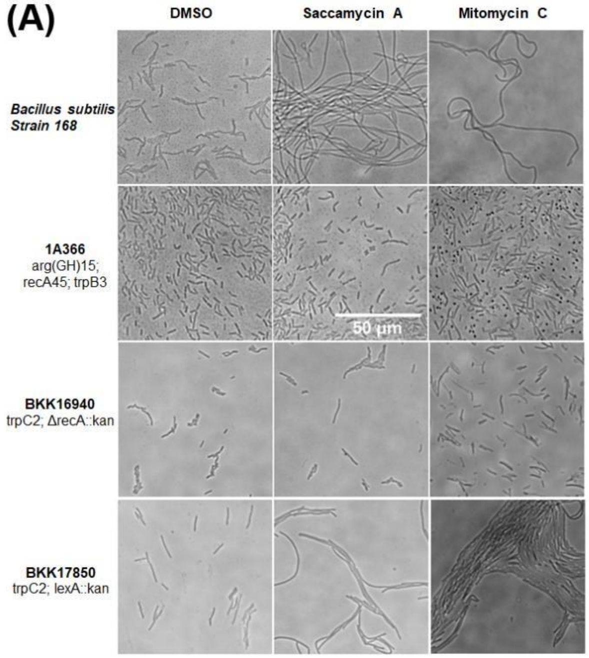
This work was financially supported by the General Research Fund (GRF16301922) from the Research Grants Council of the Hong Kong SAR Government.

Saccamycin A exhibits high antibiotic and antitumor potency by targeting DNA

Ke Du, Lingfeng Zhang, Zixu An and Zhihong Guo*

Department of Chemistry, Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong.
E-mail: chguo@ust.hk

Saccamycin A (SacA) is C_2-symmetric cyclodepsipeptide natural products recently isolated in our laboratory from *Saccharothrix syringae*. It exhibits high antibiotic activities against Gram-positive bacteria and nanomolar potency against cancer cells. Here we show that it achieves these biological activities by targeting DNA in a new mode of action. It is found to trigger SOS response (Figure 1A), resulting in release of the SPβ prophage from *Bacillus subtilis*. Intact SacA is readily recovered from the genomic DNA isolated from drug-treated bacteria, indicating that the natural product tightly binds to DNA without covalent interaction. *In vitro*, SacA progressively binds supercoiled or linear plasmid DNA and causes dose-dependent shift in electrophoretic mobility. It forms multiple complexes with distinct size with 33-37 bp DNA duplexes, which are unambiguously manifested in the dose-dependent pattern in polyacrylamide gel electrophoresis (Figure 1B). Using even shorter DNA duplexes, SacA is found to bind DNA with very low sequence specificities. Interestingly, SacA is also found to be capable of saturating plasmid DNA at a ratio of approximately one molecule to four base pairs. SacA-sacturated DNA is resistant to cleavage by restriction enzymes, demonstrating that the tight drug binding disables the biological activity of DNA. Taking together, these results show that SacA disables DNA functions by random, noncovalent binding that successfully evade the robust DNA repair mechanism in the host cells. This new mode of action suggests that SacA is a promising candidate in the development of new antibiotics and new cancer chemotherapies.



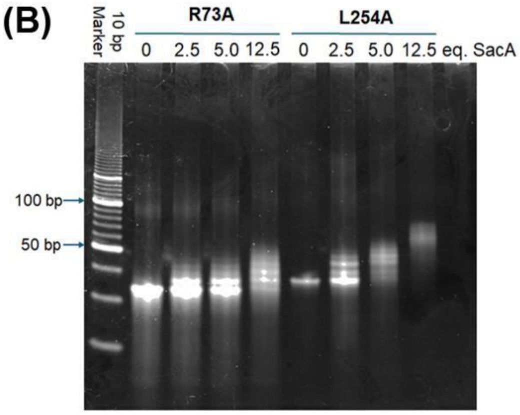


Figure 1. (A) SacA-induced filamentation indicative of the SOS response in *Bacillus subtilis*. Mitomycin C is a positive control. The SOS activator protein RecA is mutated or knockout in 1A366 and BKK16940, whereas the recA repressor protein LexA is disabled inBKK17850. (B). Oligomeric DNA duplexes R73A (37 bp) and L254A (33 bp) form multiple complexes with SacA. In the assay, 50 pmol of R73A or 5 pmol of L254A was mixed with SacA in 10 mM Tris. HCl buffer at pH 7.35 and incubated for 1h at 37℃ before loading for electrophoresis on a polyacrylamide gel.

Acknowledgement

This work was supported by the Collaborative Research Fund C6022-22WF and C6026-19GF from the Research Grants Council of the Hong Kong SAR.

Constitutive human heterochromatin domains and their ultrastructure

Hong Dai,[1, 2] Ke Du,[1, 2] Shihong Chen,[1] Zixu An,[1, 2] Lingfeng Zhang,[1, 2] Rongbiao Tong,[1] Benzhong Tang,[1, 2, 3] Haibin Su,[1] Zhihong Guo[1, 2,] *

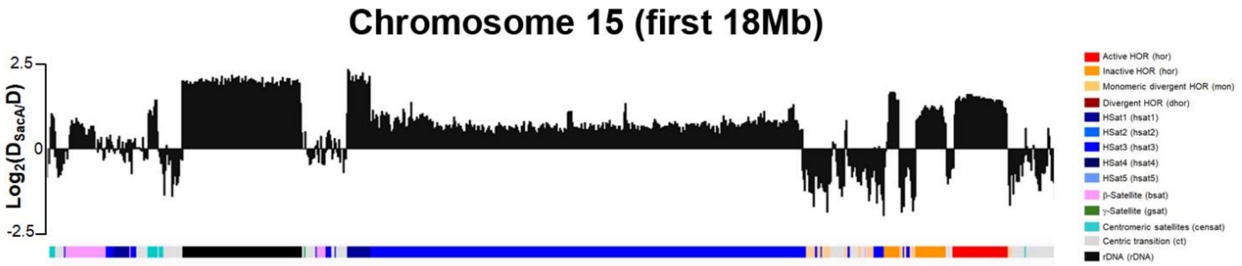
[1]*Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China*

[2]*Chinese National Engineering Research Centre for Tissue Restoration and Reconstruction (Hong Kong Branch), The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China*

[3]*School of Science and Engineering, Shenzhen Institute of Aggregate Science and Technology, The Chinese University of Hong Kong, Shenzhen (CUHK-Shenzhen), Shenzhen, 518172, China.*
E-mail: chguo@ust.hk

Abstract

Condensed, transcriptionally inert genomic regions are present as constitutive heterochromatin at telomeres, centromeres and pericentric regions of human chromosomes. The internal structure of these heterochromatic regions has remained a mystery for a long time. Here we use the small-molecule natural peptide product Saccamycin A to probe these regions and find that they are divided into domains with a distinct accessibility profile according to the underlying tandem repeats. Discrete heterochromatic domains are formed on all telomeric tandem repeats, most □-satellite higher order repeats in centromeres or pseudocentromeres with a low size cutoff, all megabase classical satellite tandem repeats, select centromeric satellite arrays and smaller classical satellites with specific repeating units, and hybrid regions containing at least one small satellite array and often together with non-satellite sequences, while many small satellite arrays and gene-coding regions are accessible. Each domain is unique in ultrastructure as indicated by the distribution of inaccessibility peaks, which rarely present a periodic pattern despite the highly repetitive underlying sequence. Interestingly, the enrichment of trimethylated histone 3 lysine 9 (H3K9me3) is neither necessary nor sufficient for a constitutive heterochromatic domain, contrary to the belief that the repressive histone mark is essential for constitutive heterochromatin. These findings suggest that multiple factors are involved in the formation of the centromeric and pericentric heterochromatin domains, including at least epigenetic modifications as well as the sequence, organization and size of the underlying tandem repeats.



Acknowledgement

This work was supported partially by C6022-22WF from the Research Grants Council and ITC-CNERC14SC01 from the Hong Kong Branch of Chinese National Engineering Research Centre for Tissue Restoration & Reconstruction.

Novel Natural Cyclodepsipeptide Products from *Saccharothrix syringae*

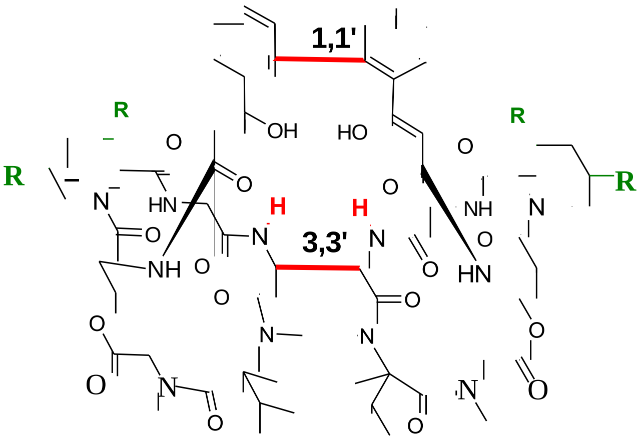
Lingfeng Zhang,[1] Zixu An,[1] Weijian Ye,[1] Ke Du,[1] Abdalla Alia,[1] Sheng Chen,[2] Rongbiao Tong,[1]
Haibin Su,[1] and Zhihong Guo[1], *

[1]*Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong.*

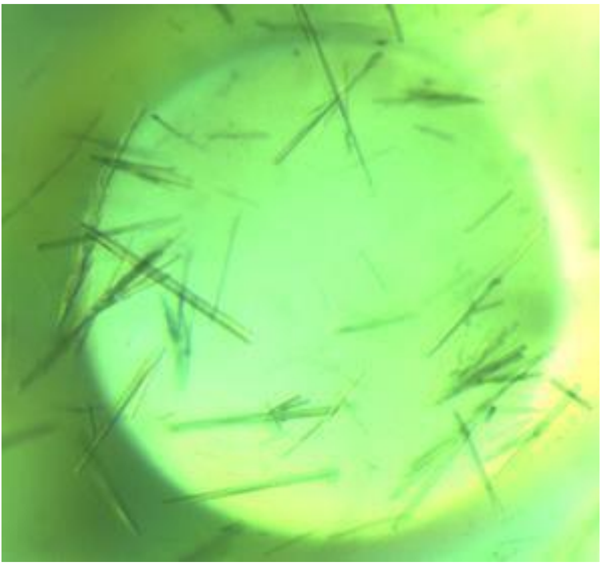
[2]*Department of Food Science and Nutrition, Faculty of Science, The Polytechnic University of Hong Kong, Kowloon, Hong Kong.*
E-mail: chguo@ust.hk

Abstract

Natural products offer an unparalleled chemical diversity that synthetic libraries often cannot match. Here we report the isolation and identification of Saccamycin A and B from *Saccharothrix syringae*. Their structure is tentatively determined as novel, *C*2-symmetric 7-residue cyclodepsipeptide dimers (below) by one- and two-dimensional NMR spectroscopy. Determination of their three-dimensional structure is in progress. These natural peptide products exhibit nanomolar potencies against some Gram-positive bacterial strains and various cancer cell lines and are promising leads for development of new antibiotics and antitumor chemotherapies. A biosynthetic gene cluster in the bacterial genome is proposed to be responsible for their biosynthesis by non-ribosomal peptide synthetase (NRPS), which interestingly contains only six synthetic modules with trans-acting acyltransferase (AT) and adenylation (A) domains. These findings show that Saccamycins represent a new class of natural peptide products with a unique mode of biogenesis.



Saccamycin A: R = CH_3COO
Saccamycin B: R = H



Acknowledgement

This work was supported by the Collaborative Research Fund C6022-22WF and C6026-19GF from the Research Grants Council of the Hong Kong SAR.

Bisphenol A in Disposable Face Masks: A Novel Human Exposure Pathway and Impact on the Aquatic Environment

Hei-Tak Tse, Chun-Kit Au, and Wan Chan *

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong.

E-mail: chanwan@ust.hk

Abstract

We conducted a study to identify and quantify bisphenol A (BPA), a known endocrine disruptor, in disposable face masks collected from Hong Kong. Our findings indicate that BPA is a prevalent contaminant in these masks, with concentrations reaching up to 2 μg per mask. While polypropylene, the primary material used in mask production, is usually regarded as BPA-free, the contamination likely stems from additives like flame retardants that are added during the manufacturing process. With a dermal absorption coefficient of 0.59,[1] BPA can be readily absorbed through the skin. Alarmingly, 8 out of 85 samples tested could lead users to exceed the tolerable daily intake of BPA established by the European Food Safety Agency, which is set at 0.0002 μg/kg body weight per day.[2] Furthermore, BPA fully dissolves in landfill leachate within 70 days, presenting significant health and environmental risks. Given the widespread use of face masks during the pandemic, their critical role in protecting medical professionals, and the absence of regulations concerning BPA levels in masks, it is essential to explore regulatory measures to protect both mask users and the environment.

References

1. Ge, J.; Wang, J.; Wu, C.; Bao, L.; Zeng, E. Y. *Sci. Total Environ.* 2021, *795*, 148827.
2. Lambré, C.; Barat Baviera, J. M.; Bolognesi, C.; Chesson, A.; Cocconcelli, P. S.; Crebelli, R.; Gott, D. M.; Grob, K.; Lampi, E.; Mengelers, M.; Mortensen, A.; Rivière, G.; Silano, V.; Steffensen, I.; Tlustos, C.; Vernis, L.; Zorn, H.; Batke, M.; Bignami, M.; Corsini, E.; FitzGerald, R.; Gundert-Remy, U.; Halldorsson, T.; Hart, A.; Ntzani, E.; Scanziani, E.; Schroeder, H.; Ulbrich, B.; Waalkens-Berendsen, D.; Woelfle, D.; Al Harraq, Z.; Baert, K.; Carfi, M.; Castoldi, A. F.; Croera, C.; Van Loveren, H. *EFSA J.* 2023, *21*, e06857.

C=C Bonds Positional Determination of Unsaturated Fatty Acids Via Potassium Permanganate Oxidation in Combination with Tandem Mass Spectrometry

DANNA HU; Tak Wah Dominic Chan

Department of Chemistry, The Chinese University of Hong Kong, Hong Kong SAR
999077, P. R. China

Email address of the corresponding author: twdchan@cuhk.edu.hk

Abstract: Positional characterization of C=C bonds is crucial for elucidating the structure of unsaturated fatty acids. Chemical derivatization of C=C bonds prior to tandem mass spectrometry (MS/MS) has proven to be an effective approach for producing diagnostic fragments that enable precise determinaion of C=C locations. This study employed neutral potassium permanganate to convert C=C bonds of unsaturated fatty acids into α-hydroxy ketones, which were subsequently analyzed by low-energy collision-induced dissociation (CID). Negative ion mode CID of the deprotonated oxidized FA anions generated diagnostic fragment ions alongside abundant false-positive peaks. Various metal ions were then evaluated as charge carriers of mono-oxidized fatty acids. Notably, positive ion mode CID of lithium adduct ions, $[(M+2O)+Li]^+$, produced abundant diagnostic fragments for identifying C=C bond positions in polyunsaturated fatty acids, without any interference from false-positive fragments. For monounsaturated fatty acids, diagnostic fragment ions were also observed, although they were accompanied by some false-positive fragments.

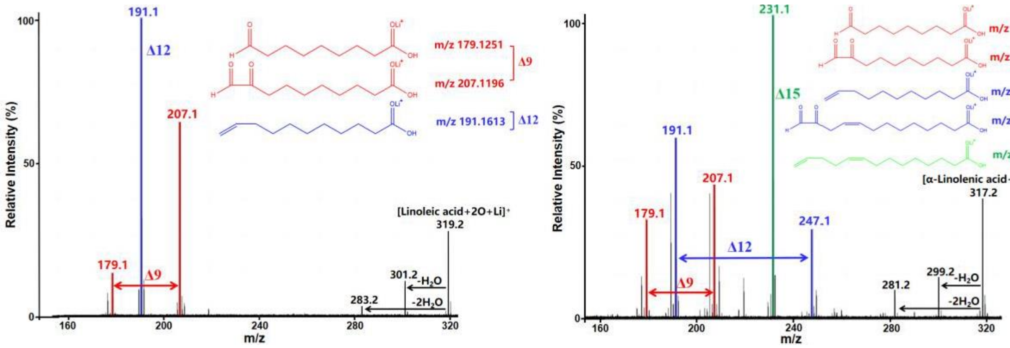


Figure: Positive ion mode MS/MS spectrua of lithium adduct ions mono-oxidized linoleic acid (18:2 cis-9,12) and mono-oxidized α-linolenic acid (18:3 cis-9,12,15)

Probing Oligomerization of Glucagon-Like Peptide-1 Analogues Using Mass Spectrometry-based Techniques

Tin Yi Lui[1], Si Huang[2], Yuye Zhou[2], Ri Wu[2], Tak Wah Dominic Chan[1], Renato Zenobi[2]*

[1]Department of Chemistry, The Chinese University of Hong Kong, Hong Kong SAR 999077, P. R. China

[2]Laboratory of Organic Chemistry, Department of Chemistry and Applied Biosciences, ETH Zurich, CH-8093 Zurich, Switzerland

E-mail address of the corresponding author: zenobi@org.chem.ethz.ch

Abstract

Semaglutide, a lipidated analogue of glucagon-like peptide-1, remains one of the most widely prescribed medications worldwide. Since oligomerization is a critical quality attribute for drug safety and efficacy, oligomerization of semaglutide was studied using various mass spectrometry-based approaches in this study. Native mass spectrometry was first used to assess the effects of a series of factors, including peptide concentration, number of freeze-thaw cycles, incubation time and the presence of metal ions, on the oligomerization extent of semaglutide. Remarkably, it was found that copper (II) ions significantly promote semaglutide's oligomerization. Temperature-controlled nanoelectrospray ionization-mass spectrometry was then applied to compare the thermal stability of the copper-bound and copper-free semaglutide multimers. It was found that semaglutide dimers demonstrated a much more significant stabilization effect than trimers and tetramers upon copper binding. This implied that the copper (II) ions might have promoted semaglutide oligomerization by enhancing its dimerization. Finally, hydrogen/deuterium exchange mass spectrometry was used to localize the stacking interface of the copper-bound semaglutide dimers.

This study demonstrated the application of mass spectrometry methods for characterizing the oligomerization behaviour of peptide candidates, which is an important consideration during the development of a safe, long acting, and stable drug.

Effects of Heavy Metals on the Formation of Aristolochic Acid-DNA Adduct and its Association to Balkan Endemic Nephropathy

Chun-Kit Au, Stefan Nagl, Wan Chan*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR

E-mail: chanwan@ust.hk

Abstract

Balkan endemic nephropathy (BEN), a chronic kidney fibrotic disease diagnosed in more than 10,000 individuals living in villages alongside Danube River,[1] is associated to chronic exposure to aristolochic acid (AA) through contaminated crops or water.[2] Recently findings showed that AA and common environmental pollutants, e.g., polycyclic aromatic hydrocarbons and phthalate ester, exert combined genotoxicity, as indicated by the elevated DNA adduct levels through co-exposure.[3] Yet, the combined toxicity of AA and another common class of environmental pollutants, heavy metals, remains uncleear. In this study, we investigated the formation of AL-DNA adducts, quantified by LC−MS/MS, in cellular DNA induced by concomitant exposure to aristolochic acid I (AA-I) and ten metal species. Results showed that AL-DNA adduct level increases in cells co-exposed to AA and As(III)/Cd(II)/Fe(III) in time- and concentration- dependent manner. Meanwhile, slower elimination kinetics of AL-DNA adducts was also observed, which may be due to the effects of nucleotide excision repair enzymes impairment and AA detoxification enzymes inhibition by metals. The results of this study revealed a previously unaware causative role of heavy metals in BEN development.

References

1. Das, S. *et al. Nat. Rev. Cancer*, **2022**, *22*, 576 − 591.

2. Ivić, M. *Lijec. Vjesn.*, **1969**, *91*, 1273 – 1281.

3. Guo, W. *et al. Envion. Sci. Technol*, **2021**, *55*, 9024 − 9032.

Amyloid-β Guided Responsive Theranostic Fluorescent Probe for Imaging of Endogenous Hydrogen Peroxide in Alzheimer Disease

Yang Yuncong, Man Shing Wong.

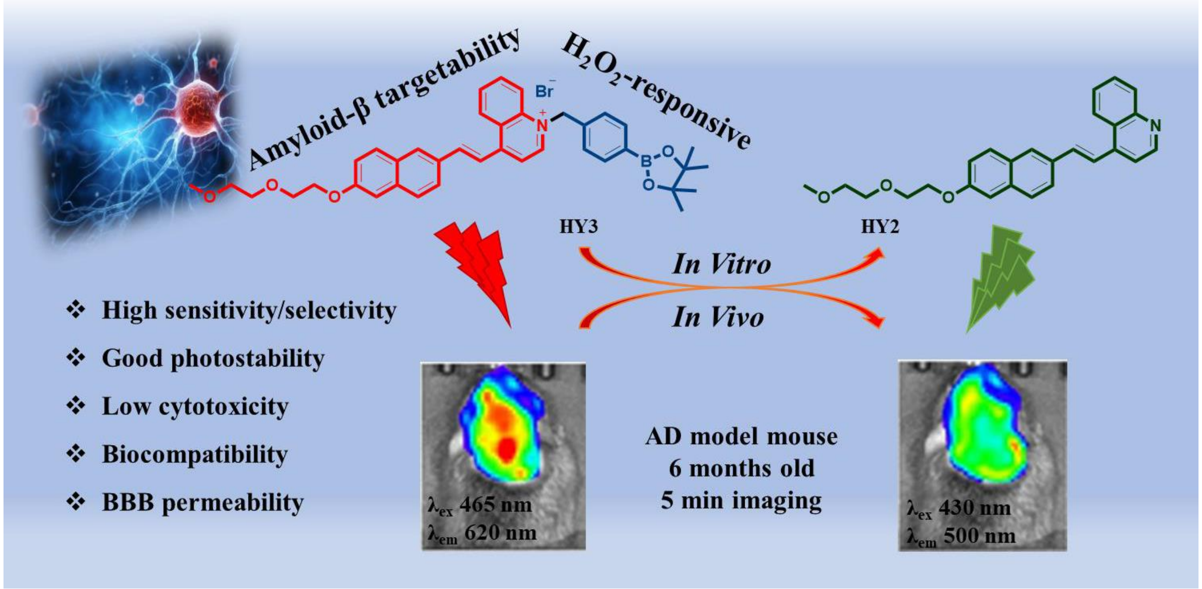
HongKong Baptist University; mswong@hkbu.edu.hk

Abstract

Alzheimer disease (AD) is a severe neurodegenerative disorder marked with a series of pathological changes. Among them, deposition of amyloid-*β* (A*β*) plaque is the most well-known hallmarks of AD, which is formed from the aggregation of misfolded A*β* peptides leading to neuroinflammatory, neuronal dysfunction, cell death and ultimately dementia. Meanwhile, oxidative stress is widely observed in AD brain due to the overproduction of reactive oxygen species (ROS) such as hydrogen peroxide (H_2O_2), leading to the peroxidation of lipids, proteins, and DNA, exacerbating lesions of brain. Currently, magnetic resonance imaging (MRI) and positron emission tomography (PET) are the primary imaging technique applied in the clinical diagnosis of AD. Due to their inherent limitation, optical imaging utilizing fluorescent dye as a label for the visualization of pathological changes is potentially promising to be an alternative diagnostic technique clinically. However, effective fluorescent probes for diagnosis of AD are still lacking.

A*β* and H_2O_2 are the widely used biomarkers in developing probes and drugs for the detection, diagnosis, and therapy of AD. Herein, we report the design and development of a dual-target fluorescent probe (HY3) constructed by the D-π-A structural based fluorophore and H_2O_2-responsive moiety for detection of A*β* and H_2O_2 in AD cell and mouse models. HY3 exhibits a large emission wavelength shift of ~130 nm upon reacting with H_2O_2 and ~180 nm in the presence of A*β*, concomitant with a strong fluorescence enhancement. HY3 shows outstanding sensitivity and selectivity towards A*β* and H_2O_2 compared with other biologically related proteins and ions. This biocompatible and nontoxic sensing probe is able to detect exogenous/endogenous H_2O_2 and differentiate N2a and N2aSw cells. *In-vivo* imaging studies also show that HY3 is BBB-permeable and can successfully transform to its oxidative product (HY2) in the brain giving rise to dual emission. The remarkable difference

in fluorescence intensity between the wild-type and transgenic mice of different age groups suggests that HY3 is a highly sensitive probe to detect and monitor Aβ plaque and H_2O_2 in the brain of AD mouse model. Thus, HY3 is promising to be a useful tool in the detection and diagnosis of AD.



References

1. Yang, Y.; Wang, C.; Xue, H.; Chen, P.; Li, H.W.; Wong, M.S. *Sensors and Actuators B: Chemical*, **2024**, 406, 135452

2. Wang, X.; Iyaswamy, A.; Xu, D.; Krishnamoorthi, S.; Sreenivasmurthy, S.G.; Yang, Y.; Li, Y.; Chen, C.; Li, M.; Li, H.W.; Wong, M.S. *ACS Appl Mater Interfaces*, **2023**, 15, 39-47.

3. Wang, C.; Wang, X.; Chan, H.N.; Liu, G.; Wang, Z.; Li, H.W.; Wong, M.S. *Advanced Functional Materials*, **2020**, 30, 1909529.

Peroxynitrite and Amyloid-β Dual-Activated Near-Infrared Theranostic Probe for Oxidative Stress Monitoring in Alzheimer's Disease

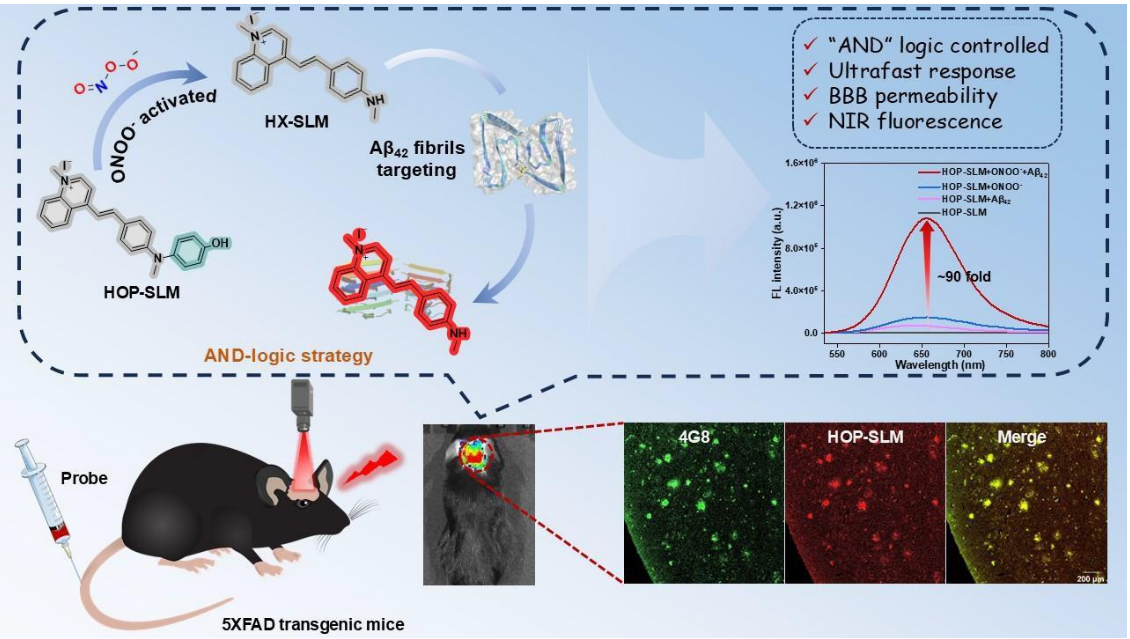
Huanxin Xue[1, b], Xueli Wang[1, *, a], Qiuyan Jiang[a], Jiale Ma[a], Man Shing Wong[*, b]

[a]*College of Pharmaceutical Sciences, College of Chemistry & Environmental Science, Key Laboratory of Medicinal Chemistry and Molecular Diagnosis, Ministry of Education, Hebei University, Baoding 071002, China. E-mail: xueliy0322@163.com*

[b]*Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong SAR of China. E-mail: mswong@hkbu.edu.hk*

Abstract

Amyloid-β (Aβ), a key biomarker of Alzheimer's disease (AD), is known to induce reactive oxygen species, including peroxynitrite ($ONOO^-$), which play a critical role in the disease's pathogenesis and progression. However, developing tools for directly detecting and monitoring Aβ-induced $ONOO^-$ remains a significant challenge. Herein, we design a near-infrared (NIR) fluorescent probe, **HOP-SLM**, which is synergistically activated by both Aβ and $ONOO^-$, enabling highly selective imaging of Aβ-induced $ONOO^-$ levels *in vivo*. Impressively, **HOP-SLM** exhibits a substantial fluorescence enhancement at 655 nm when reacting with $ONOO^-$ in the presence of Aβ, demonstrating high sensitivity down to 13 nM with minimal interference. The strong affinity for Aβ and low cytotoxicity make it suitable for detecting and visualizing endogenous $ONOO^-$ levels induced by Aβ in AD cell models. Notably, this $ONOO^-$-responsive probe can effectively detect, monitor, and differentiate varying $ONOO^-$ levels induced by Aβ in AD mice of different ages, where cerebral $ONOO^-$ levels increase with age and Aβ plaque accumulation. Moreover, the $ONOO^-$-reaction product of **HOP-SLM** offers significant neuroprotection against Aβ-induced toxicity and exhibits anti-Aβ aggregation effects, providing an additional therapeutic advantage. Thus, this multifunctional theranostic probe serves as a highly sensitive and specific imaging tool for visualizing and monitoring $ONOO^-$ levels in the presence of Aβ in vivo, facilitating more accurate early diagnosis and treatment of AD.



Scheme 1. Graphical abstract. Cited by ref. 1

References

1. Xue, H. X.; Wang, X. L.; Jiang, Q. Y.; Ma, J. L.; Wong, M. S. *Biosens. Bioelectron.*, **2025**, 275, 117201.

Europium Probe Binding to Human Serum Albumin and *α*-1-AGP:

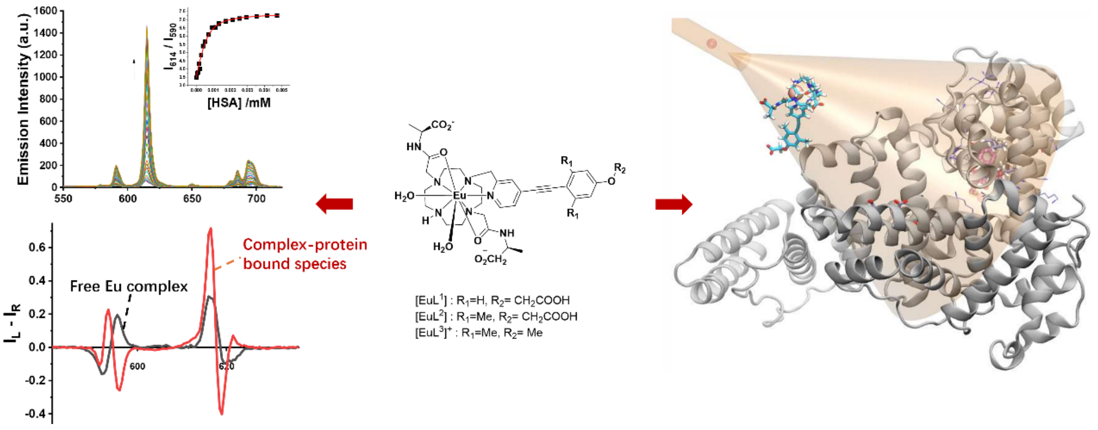
Key Importance of Configuration, Charge and Size Complementarity

Huishan Li, [a] Dominic J. Black, [b] Wei Han [a], Sally Lok-Wan Ng [a], Robert Pal [b], David Parker *[a]

a. Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong; davidparker@hkbu.edu.hk

Abstract

We have observed remarkable selectivity behaviour in protein binding with three structurally related Eu di-aqua complexes, [EuL$^{1-3}$]. Circularly polarized luminescence studies and stochastic molecular dynamics binding pocket simulations confirm and add additional detailed stereochemical information regarding the nature of the selective protein binding interaction between drug site 1 in HSA with [EuL^{2}], and between [EuL^{3}]$^{+}$ and α-1-AGP. In each case, both charge and size complementarity are critically significant, enabling these probes to be utilized in competitive assays for drugs that exhibit strong interactions with the specified protein binding site.



References

1. S. Shuvaev, R. Pal, D. Parker, *Chem. Commun.*, **2017**, *53*, 6724-6727.
2. S. Shuvaev, E. A. Suturina, K. Mason and D. Parker, *Chem. Sci.*, **2018**, *9*, 2996–3003.
3. D. Parker, J. D. Fradgley, and K-L. Wong, *Chem. Soc. Rev.* **2021**, *50***,** 8193-8213.
4. D. F. De Rosa, M. Starck, R. Pal, D. Parker, *Chem. Eur. J.* **2024**, *30*, e20233227.

Fluorinated liquid crystal monomer (FLCM) induces kidney dysfunction by disrupting PPARα-mediated fatty acid oxidation

Lin Peng, Zongwei Cai*

State Key Laboratory of Environmental and Biological Analysis, Hong Kong Baptist University; Prof. Zongwei Cai (zwcai@hkbu.edu.hk)

Abstract

Fluorinated liquid crystal monomers (FLCMs) are ubiquitous in our daily life as being the units of liquid crystal displays, yet their toxicological impacts remain largely unexplored. Herein, this study presents a comprehensive investigation into the hazardous effects of 3,4-difluoro-4′-(trans-4-ethylcyclohexyl)-biphenyl (DFECB), a representative biphenyl FLCM, using in vivo, in vitro, and in silico approaches. Mice exposed to human-relevant concentrations of DFECB for 30 days exhibited renal dysfunction, characterized by interstitial inflammation, glomerular morphological changes and metabolic disorders. Metabolomic profiling revealed inhibited fatty acid β-oxidation as a key factor in renal impairment, correlating with significant downregulation of peroxisome proliferator-activated receptor α (PPARα). In vitro assays demonstrated DFECB-induced cytotoxicity, oxidative stress, inflammation and energy deficit in renal cells. Importantly, pretreatment with the PPARα agonist mitigated the adverse effects of DFECB, underscoring the central role of PPARα in DFECB-induced nephrotoxicity. Molecular docking simulations elucidated strong halogen and hydrophobic interactions between DFECB and PPARα, providing mechanistic insights. Collectively, these results suggested that DFECB could act as a disruptor of the PPAR α-mediated fatty acid metabolism pathway, leading to renal dysfunction. This study highlights the potential health risks associated with FLCMs and emphasizes the need for their scientific regulation and further toxicological investigation.

Impacts of Rhizodeposition of Chinese fir (*Cunninghamia lanceolata*) on Soil Organic Matter Characteristics and Microbial Communities

Huishan LI [a, b], Zongwei CAI [a], Junjian WANG [b, *]

[a] State Key Laboratory of Environmental and Biological Analysis, Hong Kong Baptist University

[b] School of Environmental Science and Engineering, Southern University of Science and Technology

* wangjj@sustech.edu.cn

Abstract

The plant rhizodeposition plays a crucial role in the formation of stable components of soil organic matter. Rhizodeposited carbon, utilized and transformed by microorganisms, affects the carbon turnover process between plants and soil. Chinese fir (*Cunninghamia lanceolata*) is a preferred tree species for afforestation and urban greening, mainly distributed in Asia, especially in China. However, the impacts of rhizodeposition of Chinese fir on the molecular composition of soil organic matter and microbial communities remain still uncertain. By analyzing the soil organic matter compositions at different distances from the roots of potted Chinese fir, we found that the organic carbon content in root-adhered soil is 4 times higher than that in bulk soil and no-root soil. Rhizosphere carbon input significantly affects the fine particle fraction (< 20 μm) stably combined with minerals. The chemical characteristics of dissolved organic matter in rhizosphere soil are most similar to root exudates. Metagenomic analysis of soil microorganisms revealed the species composition of root-adhered soil differs from that of other soil, with specific community functions involving carbon fixation and secondary metabolite metabolism. It indicates long-term accumulative rhizodeposition significantly increases the proportion of stable soil organic matter in rhizosphere, which maybe mediated by rhizosphere microbe. The study supports the stability of soil organic matter and carbon sink estimation in Chinese fir plantations and urban greening lands.

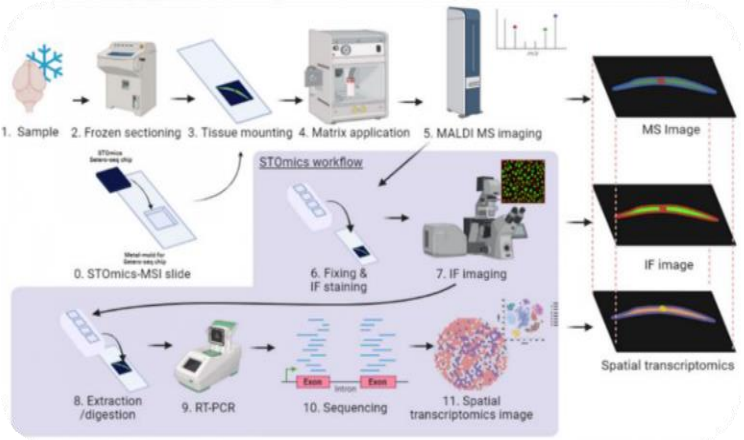
Key words: Rhizodeposits, Root exudates, Soil organic carbon, Microbial function

Single Tissue Multimodal Imaging for Cellular Spatial Omics Analysis

LAM Ka Yam Thomas⁺, ZHANG Bingxu⁺, WANG Jianing, CAI Zongwei*, XIA Yiji*,
Hong Kong Baptist University ⁺Equal contribution; *Corresponding.
Email: zwcai@hkbu.edu.hk; yxia@hkbu.edu.hk;

Abstract

The advent of omics and spatial technologies has revolutionized modern research, enabling the simultaneous study of multiple molecular layers alongside tissue architecture and in-situ distribution[2]. High-resolution spatial technologies reveal molecular crosstalk and interactions from the sub-regional to the sub-cellular level. This study presents the development of cellular-level multimodal imaging of transcriptomes and metabolomes by integrating novel spatial technologies, specifically Stereo-seq[1] and matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI). We introduce a novel protocol that combines spatial transcriptomics and metabolomics, achieving 10μm spatial resolution and molecular depth. Our integrated spatial multiomics method offers the highest spatial resolution for cellular analysis to date. This method provides a comprehensive tool for exploring complex molecular and metabolic environments in cell-cell interactions within tissues, with significant implications for research and clinical applications.



Reference

1. Chen, A.; Liao, S.; Cheng, M.; Ma, K.; Wu, L.; Lai, Y.; Wang, J. Spatiotemporal transcriptomic atlas of mouse organogenesis using DNA nanoball-patterned arrays. Cell 2022, 185, 1777-1792.
2. Vicari, M.; Mirzazadeh, R.; Nilsson, A.; Shariatgorji, R.; Bjärterot, P.; Larsson, L.; Lundeberg, J. Spatial multimodal analysis of transcriptomes and metabolomes in tissues. Nat. Biotechnol. 2024, 42, 1046-1050.

Size-dependent pulmonary toxicity and whole-body distribution of inhaled micro/nano plastic particles in male mice from chronic exposure

Leijian Chen+, Yu Liu+, Huankai Li, Siyi Lin, Xiaoxiao Wang, Jiacheng Fang, Xin Diao, Lei Wang, Zhu Yang*, Zongwei Cai*
Hong Kong Baptist University +Equal contribution; *Corresponding.
Email: zwcai@hkbu.edu.hk; zyang@hkbu.edu.hk

Abstract

In recent years, the ubiquitous presence of micro/nanoplastics (MP/NP) in the air has raised concerns about their potential toxicity, particularly under natural respiration conditions, a puzzle largely absent in existing studies. To better address this knowledge gap, our research employed a whole-body inhalation exposure system to investigate the absorption, transfer, and accumulation of inhaled polystyrene micro/nanoplastics (MP/NP) (1.5 x 10^5 particles/m^3), along with their pulmonary toxicities in ICR male mice *(n=16)*. Illuminated with fluorescent polystyrene MP/NP, our findings revealed the highest MP/NP concentration in the lung, followed by blood and spleen, and the lowest in the brain. Moreover, 80 nm nanoplastics exhibited greater inter-tissue transfer efficiency than 1 μm microplastics. Chronic inhalation exposure to MP/NP notably exacerbated oxidative stress within the extracellular environment of the lungs, impaired antioxidant defenses, and disrupted both intra- and extracellular balances of the metabolome and lipidome, leading to increased oxidative stress and inflammation. Contrary to expectations, exposure to 1 μm microplastics, instead of 80 nm nanoplastics, resulted in more severe pulmonary toxicity, including heightened oxidative stress, apoptosis, and necrosis in alveolar macrophages. These disturbances, in turn, mediated a more pronounced epithelial-mesenchymal transition in lung epithelial cells and led to fibrosis. Our research significantly advances the understanding of the health risks posed by MP/NP inhalation, offering critical insights into their various toxicities based on size and highlighting the greater toxicity of larger microplastics.

Mechanistic study of N6-methyladenosine demethylation by ALKBH5

Yingqi Lai[1], Simranjeet Kaur[1], Ivanhoe K.H. Leung[2,*] and Wei Shen Aik[1,*]

[1]Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong SAR, China;
aikweishen@hkbu.edu.hk

[2]School of Chemistry and Bio21 Molecular Science and Biotechnology Institute, The University of
Melbourne, Parkville, Victoria 3052, Australia; ivanhoe.leung@unimelb.edu.au

N6-methyl adenosine (m6A) is one of the most prevalent and abundant RNA modifications in cellular RNA. Human AlkB homolog H5 (ALKBH5) belongs to the conserved AlkB family of Fe(II)- and α- ketoglutarate-dependent oxygenases that demethylates this m6A modification. Unlike the other human m6A oxidizing enzyme, the fat mass and obesity-associated protein (FTO), which gives stable mono-oxidized N6-hydroxylmethyladenosine(hm6A) and double-oxidized N6-fomyladenosine(f6A) before they slowly degrade into the final adenosine (A), ALKBH5 quickly fragments the intermediate hm6A to the demethylated A. In our previous study, we proposed a proton shuttle between the crucial residue inside the active site of ALKBH5, Lys132 and Tyr139, and the m6A, allowing fast-track the generation of A. Here, we present the high-resolution QToF-based mass spectrometry activity assays with mutants in which either of the two crucial residues are modified. Together with our previously reported structures of ALKBH5(74-292) in complex with the 8-mer m6A-ssRNA substrate and 2OG/NOG, we verified the proton shuttling mechanisms that lead to the fast m6A demethylation by ALKBH5.

In situ Generation of Copper(II)/diethyldithiocarbamate Complex Based on Metal-organic Frameworks for Four-in-One Enhanced Synergistic Tumor Therapy

HU KAIQI, LI HUNG WING

The Chinese University of Hong Kong, Shatin, NT, Hong Kong, hungwingli@cuhk.edu.hk

Abstract

Conventional cancer treatments, including chemotherapy (CT), phototherapy, and chemodynamic therapy (CDT), have significantly advanced the fight against tumor. However, each approach faces inherent limitations that restrict their effectiveness and safety. Intracellular oxidative defense systems, low catalytic efficiency, and significant systemic toxicity pose substantial barriers to the effectiveness of CDT and CT. Herein, we developed a 4 in 1 strategy that employed an innovative DSF-loaded Fe-based near- infrared (NIR)-triggered DMTICH nanozymes for synergistic CT, CDT, photothermal therapy (PTT) and photodynamic therapy (PDT). Upon intravenous administration, DMTICH nanozymes were selectively accumulated in tumor tissues through HA- mediated endocytosis, followed by releasing DSF, Fe^{3+}, Cu^{2+}, ICG triggered by the acidic tumor microenvironment (TME). The accumulation of DSF and Cu^{2+} in situ formed a highly toxic bis(*N*, *N*-diethyldithiocarbamate) copper (II) complex (CuET), effectively achieving chemotherapy (CT), while tackling the inherent systemic toxicity of CT. DMTICH nanozymes exhibit peroxidase-like (POD-like) activities, glutathione peroxidase-like (GPX-like) activities when Fe^{3+}, Cu^{2+} facilitated the generation of hydroxyl radicals ($^{\cdot}OH$) through Fenton-like reaction, and depleted endogenous glutathione (GSH), which act like intracellular oxidative defense systems. These nanozymes activities are also boosted by ICG-generated photothermal heat triggered by 808nm laser irradiation, along with the generation of $^1O_2$ for photodynamic therapy. Excitingly, DMTICH nanozymes demonstrated significantly enhanced antitumor efficacy and favorable biosafety profiles in both in vitro and in vivo studies.

Peptide-based Phase Separation System for Intracellular Nucleic Acids Delivery

XU Zhiyi[1], Chaiyaporn Kuwentrai[2], Jian-Dong Huang[2*], XIA Jiang[1*]

[1] Department of Chemistry, the Chinese University of Hong Kong;
1155167804@link.cuhk.edu.hk
[2] School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, University of Hong Kong

Abstract

Nucleic acids are promising therapeutic biomacromolecular which could not pass through the cell membrane spontaneously. Various vehicles have been devised to deliver nucleic acids across the plasma membrane but limited by the bio-compatibility or delivery efficiency. Here we design a new peptide-based phase separation system following the spacer-sticker theory[1][2], which could recruit a wide range of nucleic acids in a high packaging rate, enter the cytoplasma spontaneously, and release the cargos by response to the natural reductant in the mammalian cells. It could deliver siRNA, different size of plasmids and also mRNA. This new system shows even a better delivery efficiency compare to the common used commerial transfection reagents in vitro and in vivo. We have already proved this peptide-based system has the potential to serve as the mRNA vaccine vehicle in the mouse model.

Keywords: phase separation, nucleic acids delivery, mRNA vaccine

References

[1] Erik W. Martin, *Science*, **2020**, 367, 694-699.

[2] Manzar Abbas, *Nat. Chem.*, **2021**, 13, 1046-1054.

Enzyme Assembly Based on Nucleoid Associated Proteins (NAPs) to Expand the Functions of *E.coli* nucleoid

Hao Jiang, Jiang Xia*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong; 1155183076@link.cuhk.edu.hk

Abstract

In eukaryotic cells, various organelles are critical for complex life activities. Although prokaryotic cells lack membrane-bound organelles, the discovery of P granule in C. elegans has attracted focus to membraneless organelles.[1]

The primary mechanism for the formation of these organelles is liquid-liquid phase separation (LLPS). These organelles provide higher local concentrations of specific proteins while enabling material exchange with the cytoplasm. Thus, Constructing artificial membraneless organelles in prokaryotic cells and recruiting key catalytic enzymes into these organelles may optimize enzyme-catalyzed reactions, metabolic pathways, and increase yield.

The main objectives were to overexpress HU proteins in E. coli, confirm their binding with nucleoids, and introduce the α-farnesene biosynthesis pathway by fusing key enzymes with HUαβ heterodimers. We aimed to modify nucleoids into α-farnesene-producing organelles and enhance α-farnesene production.

Reference

---

[1] Seydoux G. *Journal of molecular biology*, **2018**, *430*(23): 4702-4710.

Targeted Intracellular Delivery through Phase-separating Molecules

Hu Yuke, Jiang Xia*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong; 1155231363@link.cuhk.edu.hk

Abstract

Liquid-liquid phase separation (LLPS) refers to a physical process where molecules spontaneously generate condensates (also known as coacervates), which manifest as a highly concentrated liquid phase within the liquid solution. This phenomenon typically occurs in biomolecules such as proteins and nucleic acids. Recently, it has been reported that certain small molecules with low molecular weights can also assume this state. [1] Coacervates have emerged as an exciting new category of drug delivery vehicles over the past decade, serving as carriers for small molecule drugs and proteins.[2] However, the delivery specificity of such vehicles remains an issue, and strategies like photo-responsive delivery and surface modification have been explored. We discovered a novel small molecule structure capable of forming coacervates. Owing to its unique structure, a high-efficiency surface modification can be achieved.

References

[1] Y. Bao, H. Chen, Z. Xu, J. Gao, L. Jiang, J. Xia, *Angew. Chem. Int. Ed.* **2023**, 62, e202307045.

[2] Johnson NR, Wang Y. *Expert Opin Drug Deliv.* **2014** Dec;11(12):1829-32.

Multiphasic protein condensate for the enzymatic cascade reaction

Yongxu Han[1], Jiang Xia[1*]

[1] Department of Chemistry, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China; 1155165543@link.cuhk.edu.hk

Abstract

Biomolecular condensations formed by liquid–liquid phase separation (LLPS) play a crucial role in diverse cellular organization and processes. Inspired by the multicompartment subcellular organelles of a cell to achieve specific metabolic functions,[1] we reconstitute biomolecular condensations by two intrinsically disordered proteins, including RGG proteins and elastin-like proteins as scaffolds. [2,3] By tuning the mixture compositions and temperatures, the biomolecular condensations present nested and core-shell structures. Multienzyme condensates were then constructed in vitro and in E.coli by assembling two enzymes Idi and IspA through an RIAD/RIDD interaction and SpyTag/SpyCatcher covalent interaction separately. This work provides the strategy for engineering the synthetic biomolecular condensates and lays the foundation of a biosynthetic pathway by modulating multienzyme system based on LLPS-proteins.

Keywords: Multiphase • biomolecular condensate • biocatalysis

References

1. Kaur T, Raju M, Alshareedah I, et al. *Nature communications*, 2021, *12*(1): 872.

2. Schuster B S, Reed E H, Parthasarathy R, et al. *Nature communications*, 2018, *9*(1): 2985.

3. Zhang Z, Lynch C J, Huo Y, et al. *Journal of the American Chemical Society*, 2024, *146*(8): 5383-5392.

Photo-metallo-immunotherapy: Fabricating Chromium-Based Nanocomposites to Enhance CAR-T Cell Infiltration and Cytotoxicity against Solid Tumors

Qingshuang Zou,[a] Ke Liao,[b] Shuai Wang,[a] Yao Shen,[b] Dixian Luo,[b]* Dennis K. P. Ng[a]* and Quan Liu[b]*

[a] Department of Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China

[b] Department of Laboratory Medicine, Nanshan Hospital, Shenzhen, China

Corresponding author: Prof. Dennis K. P. Ng: E-mail: dkpn@cuhk.edu.hk; Prof. Dixian Luo: luodixian_2@163.com; Prof. Quan Liu: liu_quan2020@163.com

Abstract

The infiltration and cytotoxicity of chimeric antigen receptor (CAR)-T cells are crucial for effective elimination of solid tumors. [1] While metallo-immunotherapy is a promising strategy that can activate the antitumor immunity. [2] This study investigates the utilization of biodegradable polydopamine as a carrier for chromium nanoparticles (Cr NPs) in combination with CAR-T cell therapy for the treatment of solid tumors. The nanocomposites, when exposed to near-infrared light, induce mild hyperthermia. Thereby it could "warm" the "cold" tumor microenvironment and facilitating CAR-T cell migration. The administration of B7-H3 CAR-T cells into NOD/SCID gamma mice bearing human hepatoma or PIK3CA-mutated breast tumors results in significant tumor growth inhibition. The trivalent Cr^{3+} ions, as the primary degradation products, upregulate CXCL13 and CCL3 chemokine expressions, leading to the formation of tertiary lymphoid structures (TLSs) in tumor tissues, which further promotes CAR-T cell infiltration.

References

1. Sun X., Zhou X., Shi X., Abed O. A., An X., Lei Y. L., Moon J. J. *Nat. Biomed. Eng.*, **2024**, *8*, 1073-1091.

2. Mempel T. R., Lill J., Altenburger L. M. *Nat. Rev. Cancer* **2024**, *24*, 28-50.

CRISPR-Cas12a Mediated Magnetic Aptasensors for Direct Detection of Brain-derived Neurotrophic Factor

Zheng Zou, Pinyou Chen, Hung-Wing Li*
Department of Chemistry, The Chinese University of Hong Kong, Hong Kong, China;
hungwingli@cuhk.edu.hk

Abstract

Brain-derived neurotrophic factor (BDNF) is a neurotrophin essential for neuronal survival and development. Its serum levels have been identified as potential biomarkers for multiple brain diseases such as depression, schizophrenia, and Alzheimer's disease (AD). However, current methods for BDNF detection are hindered by complex instrumentation and long processing times. In this study, we developed a CRISPR/Cas12a-based magnetic aptasensor (APT-MB) for fluorescent detection of BDNF. In the presence of BDNF, BDNF was bound to the aptamer, causing the hairpin to open and expose the activation sequence. The activation sequence activated Cas12a with the help of the complementary strand (Activator). Activated Cas12a trans-cleaved the free FAM-ssDNA-quenchers (FQ-reporters), reducing the fluorescence quenching from Förster resonance energy transfer (FRET) and generating a detectable fluorescence signal. To enhance detection performance, we conjugated the aptasensors to magnetic beads (MBs), using MBs as the detection platform. MBs facilitated the capture and separation of BDNF from serum samples, minimizing interference from other proteins or nucleic acids. By incorporating a specially designed aptasensor and magnetic beads as the detection platform, APT-MB offers a straightforward fabrication process and high sensitivity, which can directly analyze BDNF in real serum samples, with an ultra-low limit of detection. The sensor's performance demonstrates its potential for clinical diagnosis in analyzing real samples of AD patients and normal people.

Reference

1. Dunn, M. R. et al. *Nature Reviews Chemistry,* **2017**, 1, 0076.
2. Swarts, D. C. et al. *Molecular cell,* **2019**, 73, 589-600.

A Nonenzymatic HCR-CHA Cascade Signal Amplification Strategy for Ultrasensitive Detection of Nucleic Acid

Ting LI, Hung-Wing LI*

Department of Chemistry, The Chinese University of Hong Kong, Hong Kong, China

hungwingli@cuhk.edu.hk

Disease-associated biomarkers, are ubiquitously distributed across diverse biofluids, including blood, urine, and saliva. These biomarkers exhibit robust correlations with many diseases, rendering their detection in bodily fluids a cornerstone of modern medical diagnostics for early disease identification. Among biomarker classes, nucleic acids—such as DNA, mRNA, and microRNA (miRNA)—are particularly prominent due to their specificity and utility in molecular diagnostics. Recent advancements have focused on isothermal, enzyme-free nucleic acid amplification strategies, including hybridization chain reaction (HCR) and catalytic hairpin assembly (CHA), which circumvent the thermal cycling limitations of conventional PCR. Nevertheless, persistent challenges, such as limited amplification efficiency, hinder their widespread application. To address these limitations, we developed a FRET-based two- layered nonenzymatic nucleic acid cascade circuit (HCR-CHA circuit). In this system, target DNA acts as the initiator of the primary HCR amplification layer, generating HCR products enriched with intermediate trigger sequences. These mediators subsequently activate the secondary CHA amplification layer, enabling iterative hybridization events. The self-assembly dynamics of the cascade were monitored in real time via Förster resonance energy transfer (FRET) signal transduction. Our results demonstrate that the **HCR-CHA hybrid circuit** exhibits accelerated reaction kinetics compared to HCR alone, achieving a detection limit as low as the picomolar (pM) range. This enhancement in sensitivity and speed underscores the circuit's potential for high-performance bioanalysis and early-stage disease diagnostics

Self-Supplying Hydrogen Peroxide-Induced Aggregation of Gold Nanoparticles for Multimodal Tumor Therapy Enhanced by Endoplasmic Reticulum Stress and Glutathione Depletion

LI Junyou, LEE Man Lung, HU Kaiqi, CHEN Pinyou, LI Ting, WANG Chengke,* LI Hung Wing.*

Department of Chemistry, The Chinese University of Hong Kong; N.T., Hong Kong.

Email: chengkewang@163.com; hungwingli@cuhk.edu.hk

Abstract

Protoporphyrin IX (PpIX), excitable by luminol (Lu) emission at 400-425 nm, has been long recognized as a Type II photosensitizer (PS) for photodynamic therapy (PDT), transferring energy directly to oxygen (O2) to form singlet oxygen ($^1O_2$), while electron-rich substrate epigallocatechin-3-*O*-gallate (EGCG), bearing the chelation ability with Cu(II), was proved to enhance PpIX electron withdrawing, shifting it to a Type I-dominant PS that generates superoxide anion radicals ($O_2 \cdot^-$), tolerancing tumor microenvironment (TME) hypoxia without the need of external light. β-Lapachone (Lap) markedly elevates hydrogen peroxide (H_2O_2) levels in tumor tissues via NAD(P)H quinone oxidoreductase-1 (NQO1)-mediated bioreduction, which not merely drastically boosts Cu(II)-mediated Haber Weiss reaction for chemodynamic therapy (CDT) to produce highly cytotoxic hydroxyl radicals (·OH), OH^- and O_2, but also alleviates TME acidosis and hypoxia, in synergy with EGCG, facilitating both PDT and Lu luminescence. Inspired by tetrazole/alkene cycloaddition and PpIX's intrinsic alkene, we hence conjugated PpIX and tetrazole onto gold nanoparticles (AuNPs) respectively to precipitate the aggregation of AuNPs for augmented photothermal therapy (PTT), triggered by the self-supplying H_2O_2-induced emission of Lu. Holistically, by further integrating Lu and Lap, a simple yet remarkably ingenious AuNP-based nanoplatform, capable of PDT, CDT, and PTT in a synergistic fashion, was thus devised.

References

1. Mao Q, Fang J, Wang A, et al. *Angewandte Chemie International Edition*, **2021**, 60(44): 23805-23811.

2. Chen W, Wang Z, Tian M, et al. *Journal of the American Chemical Society*, **2023**, 145(14): 8130-8140.

Hybrid Membrane-coated nanomotor for immunotherapy and chemotherapy of breast cancer

Lee Man Lung, Hung-Wing Li*
Department of Chemistry, The Chinese University of Hong Kong, Hong Kong, China;
hungwingli@cuhk.edu.hk

Abstract

Cancer cells adhesion and extracellular matrix penetration are important for drug delivery in cancer treatment. However, it is reported that coating nanoparticle surface with tumor-recognizing ligands can only achieve 0.7% delivery to solid tumors in preclinical animal models. The major reason for low delivery efficiency is due to the blockade by extracellular matrix (ECM) in tumor microenvironment (TME). Here, we proposed a hybrid membrane coated NO driven mesoporous silica iron oxide nanomotor ([RBC-MDA]-GDL-MSN@Fe_3O_4) for drug delivery. Red blood cells (RBCs) membrane coating can prevent the immune clearance of nanoparticles by expressing "don't eat me" signal, thus prolonging the blood circulation time. The coating of cancer cell membrane (CCM) endows the nanoparticles with tumor homogeneous targeting ability, unlike most single-ligand targeting agents, the tumor-homing properties of CCM function well despite of tumor heterogeneity. Mesoporous silica iron oxide is loaded with glucose oxidase (GOX), DOX and L-arginine(L-arg) for chemo/immunotherapy and starvation therapy. Through the conversion of L-arg to nitric oxide (NO) bubble in reactive oxygen species (ROS) overexpressed tumor microenvironment (TME), [RBC-MDA]-GDL-MSN@Fe_3O_4 can be propelled by the generation of nitric oxide gas to penetrate the extracellular matrix, thus enhancing the accumulation of nanoparticles in tumor site.

Photocatalytic Green Conversion of Methane to Methanol

Jie Yang,[1] Zhengxiao Guo[1]*
[1]Department of Chemistry, The University of Hong Kong,
Hong Kong island, Pokfulam Road, Hong Kong SAR, China
zxguo@hku.hk

Abstract

Selective CH_4 oxidation to Value-added chemicals (i.e. CH_3OH or HCHO) with O_2 in water system under mild conditions provides a desired sustainable pathway for synthesis of basic chemicals. Nevertheless, the challenge of maintaining high productivity while exhibiting sufficient selectivity in reaction remains significant, primarily due to the complexity inherent in the kinetic control of oxygenate formation in the context of overoxidation. Here, we propose a highly efficient strategy, through tuning the band structure and constructing active sites (i.e.,co-catalysts and oxygen vacancies) in our AuPd/In_2O_3 catalyst, under full-spectrum irradiation, the synergy of palladium and gold (PdAu) cocatalyst and oxygen vacancies (OVs) on In_2O_3 nanorods enables superior photocatalytic CH_4 activation by O_2. The optimized catalyst reaches ca. 200 μmol h^{-1} of C1 oxygenates, with a selectivity of primary products (CH_3OH and CH_3OOH) up to 72.5%. O_2 is proven to be the only oxygen source for CH_3OH production, while H_2O acts as the promoter for efficient CH_4 activation through ·OH production. This work thus provides new understandings on simultaneous regulation of both activity and selectivity by the synergy of metal cluster cocatalysts and oxygen vacancies.

1. Nishtha Agarwal et al.; *Science*, **2017**, *358*,223-227
2. Jiang,Y.; Tang, Z. *J. Am. Chem. Soc.*, **2023,** *145*, 2698−2707.
3. Luo,L.; Fu,L.; Liu,H.; Xu,Y.; Xing,J.; Chang,C.; Yang,D & Tang,J. *Nat Commun*., **2022**, *13*, 2930.

Development of synthetic carbohydrate-based antibacterial vaccines against Gram-negative bacteria

Xing Guo; Siyu Tang; Xuemei Yang; Han Liu; Sheng Chen; Xuechen Li
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China
siyu1210@connect.hku.hk

Considering the high immunogenicity of Pse and its key role in antibody recognition as reported by Wu et al., we hypothesized that the simple synthetic pseudaminoside without other sugar units from the CPS structure might also be capable to elicit immunogenicity against either Pse-containing *A. baumannii* CPS and protect the vaccinated animal from lethal infection caused by corresponding serotypes. This hypothesis facilitated us to design the α-pseudaminoside based conjugate vaccines Pse-CRM197 conjugates 1-7 (**Figure 1**), in which *ortho*-phthalaldehyde (OPA)-pseudaminic acid linker was bioconjugated to the protein carrier CRM197 via reaction with primary amines, aiming to scrren the optimal vaccine against different pathogens and different serotypes. To identify the immune responses, the immunization of the monovalent **Pse-I-CRM197**, **Pse-II-CRM197** and **Pse-III-CRM197** vaccines; the bivalent **Pse-I-II-CRM197**, **Pse-I-III-CRM197**, and **Pse-II-III-CRM197** vaccines; as well as trivalent **Pse-I-II-III-CRM197** vaccine were assessed by mice injection and analyzed by ELISA and flow cytometry. Even the results showed that **Pse-II-III-CRM197** vaccine triggered high responses to all 3 types of Pse derivates among all the candidates, **Pse-III-CRM197** could elicit good immune response against all three types of Pse epitopes based on the immunological performance of Pse conjugate vaccine candidates. Compared to the costs the preparation difficulties for scaleup production and application, **Pse-III-CRM197** was identified as the universal vaccine candidate against Pse-containing pathogens.

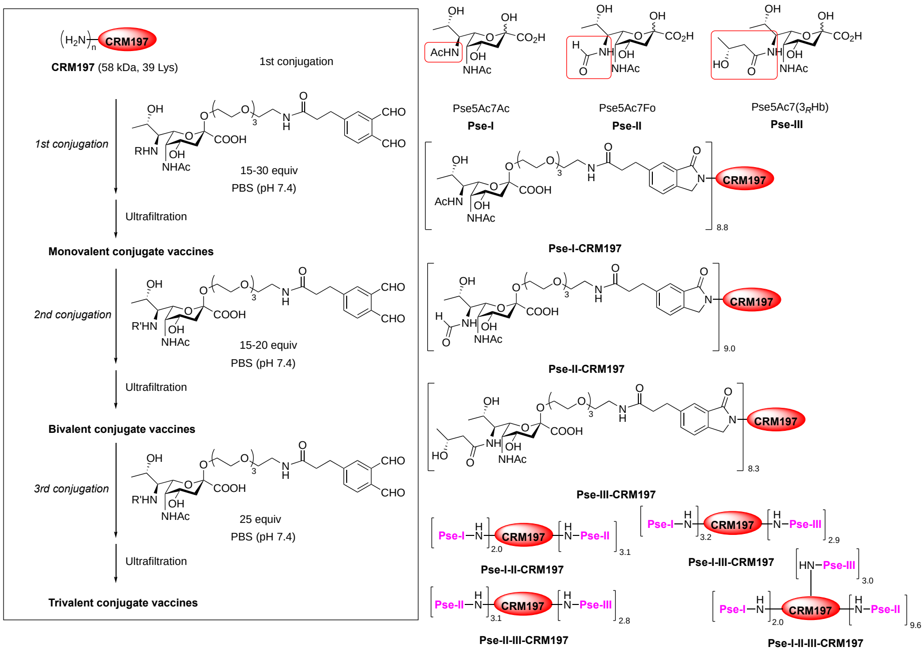


Figure 1. Mono-, di-, and tri-valent Pse-CRM197 conjugates.

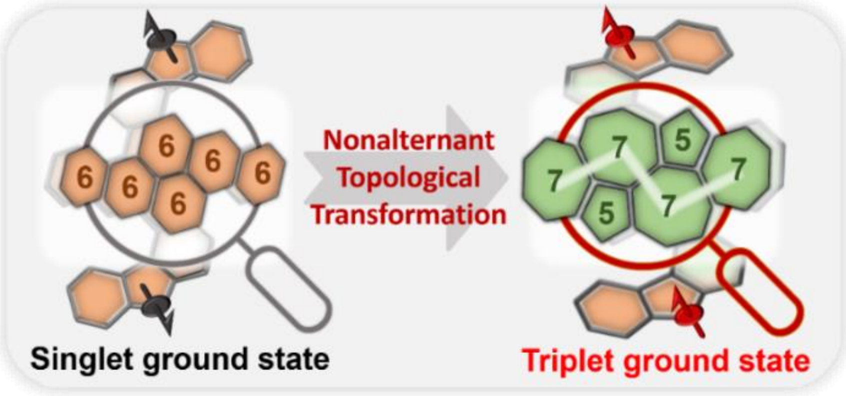
Switching the Ground State through Topological Transformation: A Highly Stable Triplet Diindeno-typed Diradicals Bearing a Di-azuleno[2,1,8-*efg*:2',1',8'-*kla*]heptalene Core

Zhaohang Lin, Yu-Shuang Zhang, Shang-Da Jiang*, and Junzhi Liu*

E-mail: jiangsd@scut.edu.cn; juliu@hku.hk

Abstract

The practical applications of carbon-based polycyclic hydrocarbons with high-spin radicals are hindered by their structural limitations and chemical instability, posing challenges for their precise synthesis.[1,2] Herein, we report an extraordinarily stable high-spin diradicals containing a diazuleno[2,1,8-*efg*:2',1',8'-*kla*]heptalene core. Compared with the structural isomer with only hexagons, which exhibits singlet open-shell diradicals feature, the ground state can be switched to triplet of diradicals through the nonalternant topologies. Experimental and theoretical results determined the triplet ground state open-shell characteristic and highly stable under ambient conditions, in which the half-life ($t_{1/2}$) is fitted as long as 109 days.



References

1. Kothe, G.; Denkel, K. H.; Sümmermann, W. *Angew. Chem. Int. Ed.* **1970**, *9*, 906-907.

2. Saha, P.; Chrysochos, N.; Elvers, B. J.; Patsch, S.; Uddin, S. I.; Krummenacher, I.; Nandeshwar, M.; Mishra, A.; Raman, K. V.; Rajaraman, G.; Prabusankar, G.; Braunschweig, H.; Ravat, P.; Schulzke, C.; Jana, A. *Angew. Chem. Int. Ed.* **2023**, *62*, e202311868.

Extension of Nonalternant Nanographenes Containing Nitrogen-Doped Stone-Thrower-Wales Defect

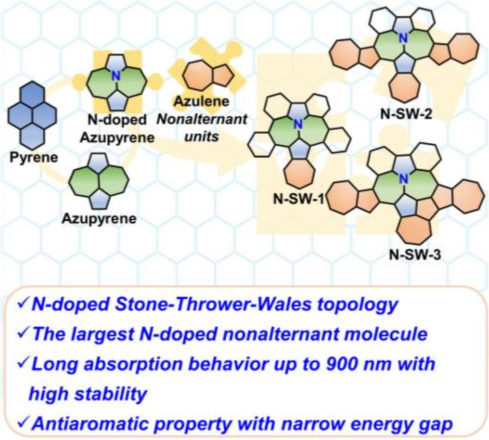
Chang Wang,[1] Ziqi Deng,[1] David Lee Phillips,[1] Junzhi Liu[1,]*

[1]State Key Laboratory of Synthetic Chemistry, HKU-CAS Joint Laboratory on New Materials and Department of Chemistry, The University of Hong Kong, Hong Kong, China

E-mail: juliu@hku.hk

Abstract

Nonalternant topologies have attracted considerable attention due to their unique physiochemical characteristics in recent years.[1-3] Here, three novel topological nanographenes molecular models of N-doped Stone-Thrower-Wales (S-T-W) defect were achieved through intramolecular direct arylation. Among them, threefold intramolecular direct arylation compound (**N-SW-3**) is the largest nanographene bearing a N-doped nonalternant topology to date, in which the non-benzenoid rings account for 83% of the total molecular skeleton, with a long tail up to 900 nm, yet is stable under ambient conditions. Our work demonstrates that the nonalternant topology could significantly influence the electronic configurations of nanocarbons, where the introduction of a nonalternanting topology may be an effective way to narrow the energy gap without extending the molecular π-conjugation.



References

Reference:

1. Fei, Y.; Liu, J. *Adv. Sci.* **2022**, *9*, 2201000.

2. Luo, H.; Liu, J. *Angew. Chem. Int. Ed.* **2023**, *62*, e202302761.

3. Wang, C.; Deng, Z.; Phillips, D. L.; Liu, J. *Angew. Chem. Int. Ed.* **2023**, *62*, e202306890.

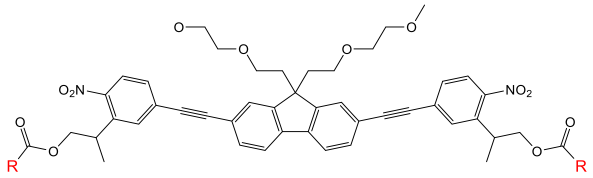
Design, and Synthesis of Functionalized Two-Photon Caging Platforms

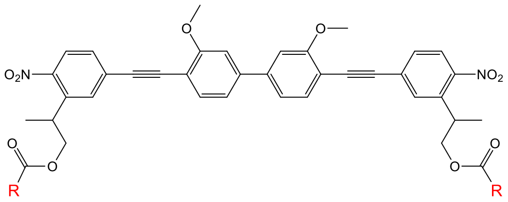
CHANG Tristan Juin Han, LIU Ling Sum and LO Pik Kwan*

Department of Chemistry, City University of Hong Kong
Email: tjhchang2-c@my.cityu.edu.hk

Abstract

Two-photon absorption (TPA) has become popular for biological applications, owing to its advantageous property of being able to achieve photophysical reactivities at long wavelengths in the near infrared region, it minimizes photodamage to materials and biological samples. Furthermore, deep tissue penetration and lower scattering can be achieved with long wavelengths. TPA photocleavable molecules are able to act as protecting groups for biological systems, creating caged compounds. An example of these types of biological cages in the literature are caged neurotransmitters, glutamate. Molecules that exhibit good TPA cross section are BNSF-Glu and BNSMB-Glu.[1] This experiment aims to replace the double bond linking the chromophore with the photolabile units in BNSF and BNSMB with a triple bond through Sonogashira coupling to discern the effect of this change to their photocleavage properties. This modification was made in hopes of increasing the photocleavage properties of BNSF and BNSMB by increasing the number of electrons in the conjugated system and increasing the rigidity and planarity of the conjugate system. We report the synthesis and photophysical properties of triple bond versions of BNSMB and BNSF, serving as cages for R = phenylalanine, glutamic acid or γ-aminobutyric acid.





Triple bond BNSF

Triple bond BNSMB

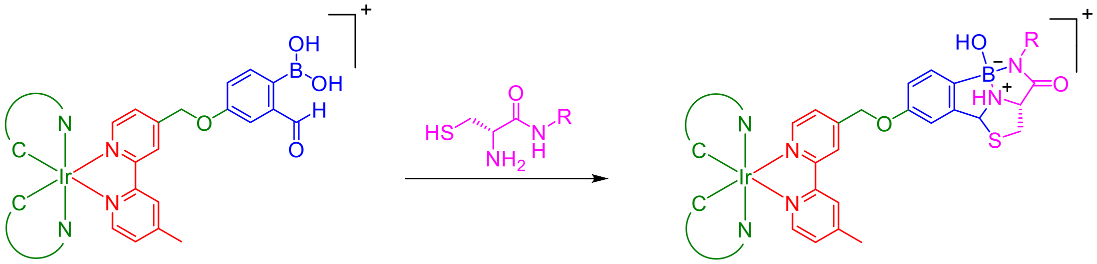
Reference:

1. Gug, S., Bolze, F., Specht, A., Bourgogne, C., Goeldner, M., & Nicoud, J. *Angewandte Chemie International Edition*, **2008**, 47(49), 9525-9529.

Construction of Photofunctional Peptide Conjugates through Selective Modification of N-Terminal Cysteine with Cyclometalated Iridium(III) 2-Formylphenylboronic Acid Complexes for Organelle-Specific Imaging, Enzyme Activity Sensing, and Photodynamic Therapy

Lili Huang, Lawrence Cho-Cheung Lee, Justin Shum, Guang-Xi Xu, and Kenneth Kam-Wing Lo*
Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China (Email: bhkenlo@cityu.edu.hk)

2-Formylphenylboronic acid (2-FPBA) can react selectively and rapidly with N-terminal cysteine (N-Cys) to form a highly stable thiazolidino boronate derivative. In this study, three luminescent iridium(III) complexes bearing a 2-FPBA moiety were designed and synthesized. Upon photoexcitation, all the complexes displayed intense and long-lived greenish-yellow to red emission in solutions. One of the complexes was utilized to modify N-Cys-containing organelle-targeting peptides to afford conjugates with different intracellular localization properties. Also, a peptide conjugate containing a furin-cleavable peptide sequence between the complex and the emission quencher QSY7 was prepared to examine furin activity; the conjugate exhibited phosphorogenic response toward furin in live cells, enabling the specific targeting of cancer cells based on the activity of this enzyme.



We thank the Hong Kong Research Grants Council (Project No. CityU 11301121, CityU 11317022, CityU 11309423, C6014-20W, and C7075-21GF) and the Hong Kong Research Grants Council, National Natural Science Foundation of China (Project No. N_CityU104/21) for financial support.

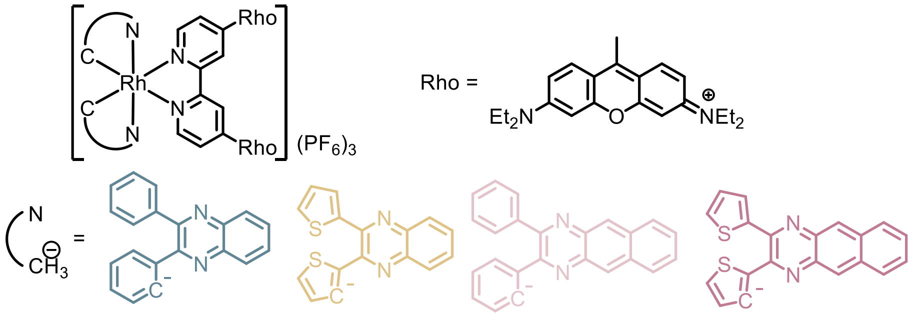
Reference

Huang, L.; Lee, L. C.-C.; Shum, J.; Xu, G.-X.; Lo, K. K.-W. *Chem. Commun.* **2024**, *60*, 6186 – 6189.

Cyclometalated Rhodium(III) Complexes Appended with Two Rhodamine Units as Type I Photosensitizers for Inducing Pyroptosis

Katherine Gui-Min Jiang,[a,b] Keith Man-Chung Wong,[b,]* and Kenneth Kam-Wing Lo[a,]*
[a] Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China; bhkenlo@cityu.edu.hk
[b] Department of Chemistry, Southern University of Science and Technology, 1088 Xueyuan Blvd., Shenzhen, P. R. China; keithwongmc@sustech.edu.cn

In this study, a series of rhodium(III) complexes containing two rhodamine moieties was developed. These complexes exhibited strong absorption in the visible region and demonstrated moderate to intense rhodamine luminescence in solutions upon light irradiation. Time-resolved transient absorption spectroscopy revealed a long-lived and non-emissive rhodamine triplet state as the lowest-lying excited state in this hybrid system. The efficient population of this state is attributed to the presence of the rhodium(III) center. Although these complexes showed weak singlet oxygen photosensitization, they efficiently generated superoxide anion and hydroxyl radicals via a Type I pathway upon photoirradiation. The effective production of these reactive oxygen species in cells led to mitochondrial dysfunction and subsequent cell death through pyroptosis. This novel rhodium(III)–rhodamine system represents a promising candidate for theranostic applications.



We thank the Hong Kong RGC (CityU 11301121, CityU 11317022, CityU 11309423, and C7075-21GF), the Hong Kong RGC and NSFC (N_CityU104/21), and "Laboratory for Synthetic Chemistry and Chemical Biology" under the Health@InnoHK Program launched by Innovation and Technology Commission, the Government of Hong Kong SAR, P. R. China.

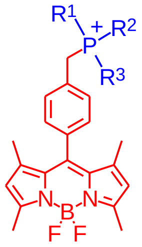
Mitochondria-Targeting Biocompatible Fluorescent BODIPY Probes

Lawrence Cho-Cheung Lee,[‡,a] Edward R. H. Walter,[‡,b] Peter Kam-Keung Leung,[a] Kenneth Kam-Wing Lo,*[,a] and Nicholas J. Long*[,b]

[a] Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China; Email: bhkenlo@cityu.edu.hk

[b] Department of Chemistry, Imperial College London, Molecular Sciences Research Hub, W12 0BZ, UK.

Mitochondria are important subcellular organelles that play a key role in energy production and cellular metabolism. An increase in the mitochondrial membrane potential (MMP) is a characteristic feature of cancer and cardiovascular disease. In this study, we designed and synthesized a series of BODIPY dyes (**BODIPY-Mito-*n***) for mitochondria-targeted imaging. These BODIPY dyes displayed high fluorescence quantum yields in biologically relevant media, and showed high MMP-sensitive mitochondrial localization. Notably, the incorporation of poly(ethylene glycol) chains to the phosphonium cation unit significantly improved the biocompatibility of the probes. The high MMP sensitivity and enhanced biocompatibility of the probes make them potential candidates for reporting on changes in mitochondrial function in cancer and cardiovascular disease.



$R^1 = R^2 = R^3$ = Cy (**BODIPY-Mito-1**)
$R^1 = R^2$ = Cy, R^3 = Ph (**BODIPY-Mito-2**)
R^1 = Cy, $R^2 = R^3$ = Ph (**BODIPY-Mito-3**)
$R^1 = R^2 = R^3$ = Ph (**BODIPY-Mito-4**)
$R^1 = R^2 = R^3 = C_6H_4\text{-}O(CH_2CH_2O)_2CH_3$ (**BODIPY-Mito-5**)
$R^1 = R^2 = R^3 = C_6H_4\text{-}O(CH_2CH_2O)_7CH_3$ (**BODIPY-Mito-6**)

We thank "Laboratory for Synthetic Chemistry and Chemical Biology" under the Health@InnoHK Program launched by Innovation and Technology Commission, The Government of HKSAR, P. R. China for financial support.

References

1. Walter, E. R. H.; Lee, L. C.-C.; Leung, P. K.-K.; Lo, K. K.-W.; Long, N. J. *Chem. Sci.* **2024**, *15*, 4846 – 4852.
2. Walter, E. R. H.; Leung, P. K.-K.; Lee, L. C.-C.; Lo, K. K.-W.; Long, N. J. *J. Mater. Chem. B* **2024**, *12*, 10409 – 10415.

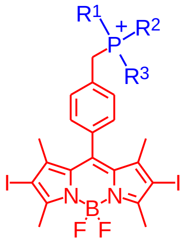
Potent BODIPY-Based Photosensitizers for Selective Mitochondrial Dysfunction and Effective Photodynamic Therapy

Peter Kam-Keung Leung,[‡,a] Edward R. H. Walter,[‡,b] Lawrence Cho-Cheung Lee,[a] Kenneth Kam-Wing Lo,*[,a] and Nicholas J. Long*[,b]

[a] Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China; Email: bhkenlo@cityu.edu.hk

[b] Department of Chemistry, Imperial College London, Molecular Sciences Research Hub, W12 0BZ, UK.

The development of new and effective mitochondria-targeting photosensitizers (PSs) is important to improving photodynamic therapy (PDT). In this study, we designed and synthesized a series of di-iodinated BODIPY-based PSs (**BODIPY-Mito-I-*n***) for mitochondria-targeted PDT. All the BODIPY PSs exhibited very high photocytotoxicity toward HeLa cells ($IC_{50,light}$ = 1.30 – 6.93 nM) with photocytotoxicity indices of up to 2,120. Mechanistic studies revealed that **BODIPY-Mito-I-6** induced reactive oxygen species overproduction and mitochondrial dysfunction in cells upon irradiation, resulting in cancer cell apoptosis and necrosis. It is anticipated that our design will contribute to the development of more effective mitochondria-targeting PSs for cancer therapy.



$R^1 = R^2 = R^3$ = Cy (**BODIPY-Mito-I-1**)
$R^1 = R^2$ = Cy, R^3 = Ph (**BODIPY-Mito-I-2**)
R^1 = Cy, $R^2 = R^3$ = Ph (**BODIPY-Mito-I-3**)
$R^1 = R^2 = R^3$ = Ph (**BODIPY-Mito-I-4**)
$R^1 = R^2 = R^3 = C_6H_4\text{-}O(CH_2CH_2O)_2CH_3$ (**BODIPY-Mito-I-5**)
$R^1 = R^2 = R^3 = C_6H_4\text{-}O(CH_2CH_2O)_7CH_3$ (**BODIPY-Mito-I-6**)

We thank “Laboratory for Synthetic Chemistry and Chemical Biology” under the Health@InnoHK Program launched by Innovation and Technology Commission, The Government of HKSAR, P. R. China for financial support.

References

1. Walter, E. R. H.; Leung, P. K.-K.; Lee, L. C.-C.; Lo, K. K.-W.; Long, N. J. *J. Mater. Chem. B* **2024**, *12*, 10409 – 10415.
2. Walter, E. R. H.; Lee, L. C.-C.; Leung, P. K.-K.; Lo, K. K.-W.; Long, N. J. *Chem. Sci.* **2024**, *15*, 4846 – 4852.

TNA-Mediated Antisense Strategy to Knockdown Akt Genes for Triple-Negative Breast Cancer Therapy

Pan Li, Shixue Zheng, Hoi Man Leung, Ling Sum Liu, Tristan Juin Han Chang, Alishba Maryam, Fei Wang, Y. Rebecca Chin, Pik Kwan Lo
Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong
Email: panli8-c@my.cityu.edu.hk

Abstract

Triple-negative breast cancer (TNBC) remains a significant challenge in terms of treatment, with limited efficacy of chemotherapy due to side effects and acquired drug resistance.[1,2] In this study, we employed a threose nucleic acid (TNA)-mediated antisense approach to target therapeutic Akt genes for TNBC therapy.[3] Specifically, we designed and synthesized two new TNA strands (anti-Akt2 and anti-Akt3) targeting Akt2 and Akt3 mRNAs. These TNAs exhibited exceptional enzymatic resistance, high specificity, enhanced binding affinity with their target RNA molecules, and improved cellular uptake efficiency compared to natural nucleic acids. In both 2D and 3D TNBC cell models, the TNAs effectively inhibited the expression of their target mRNA and protein, surpassing the effects of scrambled TNAs. Moreover, when administered to TNBC-bearing animals with lipid nanoparticles, the targeted anti-Akt TNAs led to reduced tumor sizes and decreased target protein expression compared to control groups. Silencing the corresponding Akt genes also promoted apoptotic responses in TNBC and suppressed tumor cell proliferation in vivo. This study introduces a novel approach to TNBC therapy utilizing TNA polymers as antisense materials and holds promise as a cost-effective platform for TNBC treatment.

References

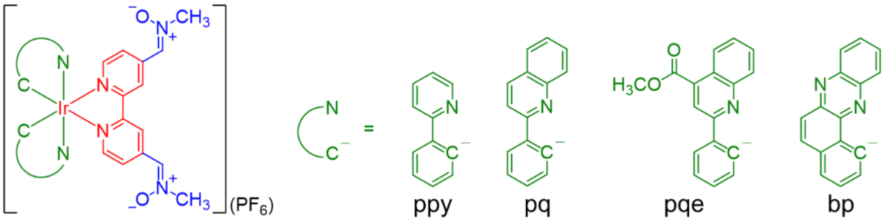
1. O. Beiki, P. Hall, A. Ekbom, T. Moradi, Breast Cancer Research 2012, 14, R5.
2. C. Garbino, Journal of the Senologic International Society 2012, 1, 2427.
3. P. Li, S. Zheng, H. M. Leung, L. S. Liu, T. Juin, H. Chang, et al, Small Methods 2024, 8, 240091.

Exploiting the Potential of Iridium(III) *bis*-Nitrone Complexes as Phosphorogenic Bifunctional Reagents for Phototheranostics

Eunice Chiu-Lam Mak,[a] Ziyong Chen,[b] Vivian Wing-Wah Yam,*[,b] and Kenneth Kam-Wing Lo*[,a]

[a] Department of Chemistry, City University of Hong Kong, Kowloon, Hong Kong, P. R. China; bhkenlo@cityu.edu.hk.
[b] Institute of Molecular Functional Materials and Department of Chemistry, The University of Hong Kong, Hong Kong, P. R. China.

Nitrone is remarkably versatile and applicable in bioorthogonal labeling due to its high reactivity with strained alkynes. In this study, iridium(III) complexes incorporating two nitrone units were designed as novel phosphorogenic bioorthogonal reagents for bioimaging and phototherapeutics. These complexes exhibited efficient emission quenching through a nonradiative decay pathway via the low-lying T_1/S_0 minimum energy crossing point. However, they showed significant emission enhancement and rapid reaction kinetics when interacting with a *bis*-cyclooctyne derivative (*bis*-BCN). The complexes demonstrated higher photocytotoxicity in *bis*-BCN-pretreated cells due to enhanced singlet oxygen ($^1O_2$) photosensitization, which results from the elimination of the nitrone-associated quenching pathway. The cross-linking properties and high reactivity of these complexes make them promising candidates for the development of photofunctional hydrogels and stapled or cyclized peptides.



We thank the Hong Kong RGC (C7075-21GF, CityU 11309423, HKU 17309220), the Hong Kong RGC and NSFC (N_CityU104/21), and "Laboratory for Synthetic Chemistry and Chemical Biology" under the Health@InnoHK Program launched by Innovation and Technology Commission, The Government of HKSAR, P. R. China.

Reference

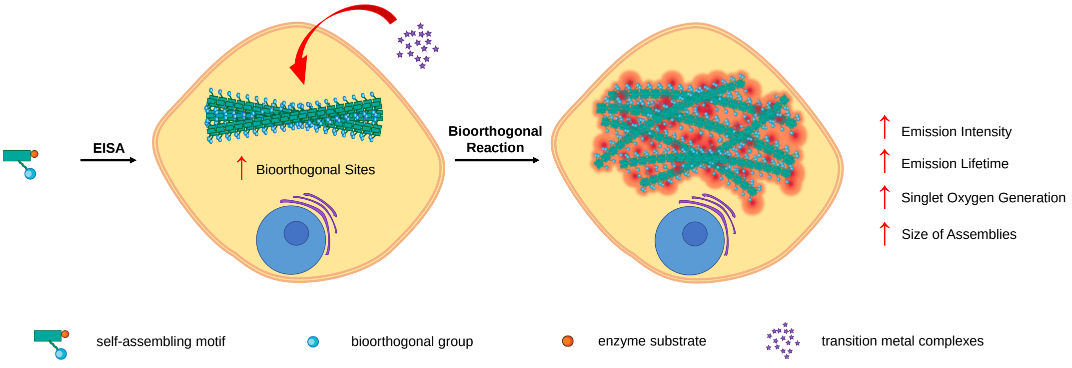
Mak, E. C.-L.; Chen, Z.; Lee, L. C.-C.; Leung, P. K.-K.; Yip, A. M.-H.; Shum, J.; Yiu, S.-M.; Yam, V. W.-W.; Lo, K. K.-W. *J. Am. Chem. Soc.* **2024**, *146*, 25589 − 25599.

A Concerted Enzymatic and Bioorthogonal Approach for Extra- and Intracellular Activation of Environment-Sensitive Ruthenium(II)-Based Imaging Probes and Photosensitizers

Justin Shum,[a] Lawrence Cho-Cheung Lee,[a] Michael Wai-Lun Chiang,[a] Yun-Wah Lam,[a] and Kenneth Kam-Wing Lo[a]*

[a]*Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China; Email: bhkenlo@cityu.edu.hk*

We report a novel targeting strategy involving the combination of an enzyme-instructed self-assembly (EISA) moiety and a strained cycloalkyne to generate a large accumulation of bioorthogonal sites in cancer cells. These bioorthogonal sites can serve as activation triggers in different regions for transition metal-based probes, which are new ruthenium(II) complexes carrying a tetrazine unit for controllable phosphorescence and singlet oxygen generation. Importantly, the environment-sensitive emission of the complexes can be further enhanced in the hydrophobic regions offered by the large supramolecular assemblies, which is highly advantageous to biological imaging. Additionally, the (photo)cytotoxicity of the large supramolecular assemblies containing the complexes was investigated, and the results illustrate that cellular localization (extracellular and intracellular) imposes a profound impact on the efficiencies of photosensitizers.



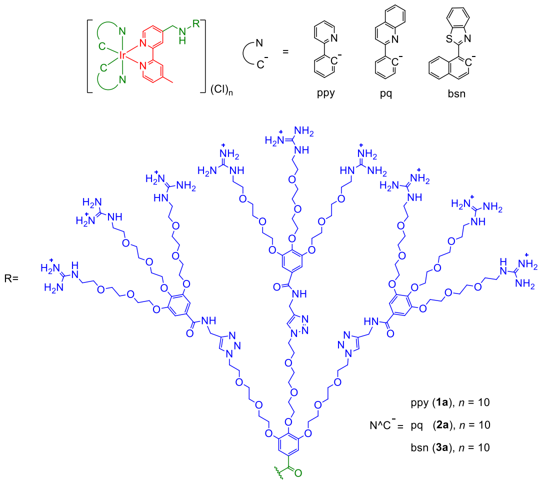
Reference

Shum, J.; Lee, L. C.-C.; Chiang, M. W.-L.; Lam, Y.-W.; Lo, K. K.-W. *Angew. Chem. Int. Ed.* **2023**, *62*, e202303931.

Luminescent Iridium(III) Polypyridine Complexes Modified with a Molecular Glue as Photofunctional Cellular Reagents

Jiahao Wang,[a] Kou Okuro, *[,b] and Kenneth Kam-Wing Lo*[,a]
[a] Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China; bhkenlo@cityu.edu.hk.
[b] State Key Laboratory of Synthetic Chemistry and Department of Chemistry, The University of Hong Kong, Hong Kong, P. R. China

Over the past decade, transition metal complexes have garnered significant attention due to their excellent photophysical and photochemical properties. In this study, we designed three novel cyclometalated iridium(III) complexes, each tethered to multiple guanidinium moieties to serve as molecular glues. Protein-binding studies demonstrated that these complexes exhibit a high binding affinity toward bovine serum albumin (BSA). One of these complexes was used to modify glutathione (GSH)-responsive, doxorubicin (DOX)-loaded BSA nanoparticles (DOX/^{SS}BNPs). Notably, the functionalization of DOX/^{SS}BNPs with the complex reversed the surface charge from negative to positive. Cleavage studies showed a significant decrease in the size of Ir-DOX/^{SS}BNPs, accompanied by efficient DOX release upon incubation with GSH. The positively charged Ir-DOX/^{SS}BNPs exhibited increased cellular uptake in HeLa cells, which was shown to be crucial for their performance in combined chemo-photodynamic therapy. The results indicate that these iridium(III)-based molecular glues can be utilized for intracellular drug delivery and combined chemo-photodynamic therapy.



We thank the Hong Kong RGC (CityU 11301121, CityU 11317022, CityU 11309423, and C7075-21GF) and the Hong Kong RGC and NSFC (N_CityU104/21) and "Laboratory for Synthetic Chemistry and Chemical Biology" under the Health@InnoHK Program launched by Innovation and Technology Commission, The Government of HKSAR, P. R. China.

References

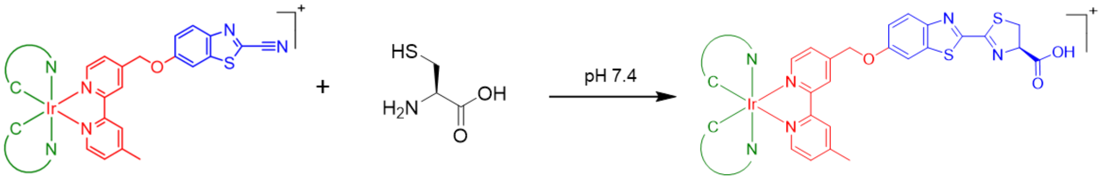
1. Lo, K. K.-W. *Acc. Chem. Res.* **2020**, *53*, 32 – 44.
2. Mogaki, R.; Hashim, P.K.; Okuro, K. *Chem. Soc. Rev.* **2017**, *46*, 6480 – 6491.

Luminescent Iridium(III) 2-Cyanobenzothiazole Complexes as Site-specific Labels to Afford Peptide-based Phosphorogenic Probes and Hydrogels for Enzyme Activity Sensing, Cancer Imaging and Photodynamic Therapy

Jun-Wen Xu,[a] Lawrence Cho-Cheung Lee,[a] Alex Man-Hei Yip,[a,b] Guang-Xi Xu,[a] Peter Kam-Keung Leung,[a,c] and Kenneth Kam-Wing Lo*[a,c]

[a] Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China; bhkenlo@cityu.edu.hk
[b] Laboratory for Synthetic Chemistry and Chemical Biology Limited, Units 1503–1511, 15/F, Building 17 W, Hong Kong Science Park, New Territories, Hong Kong, P. R. China.
[c] State Key Laboratory of Terahertz and Millimeter Waves, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China

In this study, we designed and synthesized three luminescent iridium(III) 2-cyanobenzothiazole (CBT) complexes featuring a moiety that acts as a site-specific label for N-terminal cysteine (NCys). These complexes exhibited high reactivity and selectivity toward NCys, facilitating facile peptide conjugation through the CBT–NCys condensation reaction. Complex **2** was employed to develop a peptide-based phosphorogenic probe, **2-MMP-QSY7**, for sensing the activity of matrix metalloproteinase-2/9 (MMP-2/9). Additionally, the complex was used to create two types of hydrogels: a non-biodegradable hydrogel, **Gel-1**, which serves as a cell culture scaffold for examining MMP-2/9 activity in 3D cell cultures; and a biodegradable hydrogel, **Gel-2**, designed as an MMP-2/9-sensitive carrier for the selective delivery of luminescent iridium(III) complexes into cancer cells for imaging and photocytotoxic applications..



We thank the Hong Kong Research Grants Council (Project Nos. CityU 11301121, CityU 11317022, CityU 11309423, and C7075-21GF) and the Hong Kong Research Grants Council and National Natural Science Foundation of China (Project No. N_CityU104/21). We also thank the funding support from "Laboratory for Synthetic Chemistry and Chemical Biology" under the Health@InnoHK Programme launched by Innovation and Technology Commission, The Government of Hong Kong SAR, P. R. China.

Reference

Xu, J.-W.; Lee, L. C.-C.; Yip, A. M.-H.; Xu, G.-X.; Leung, P. K.-K.; Lo, K. K.-W. *Inorg. Chem. Front.* **2025**, DOI: .10.1039/d4qi03276d.

Bioorthogonally Dissociative Rhenium(I) Polypyridine-based Photosensitizers for the Controlled Induction of Immunogenic Cell Death

Alex Man-Hei Yip,[a,b] Guang-Xi Xu,[b] and Kenneth Kam-Wing Lo*[b]

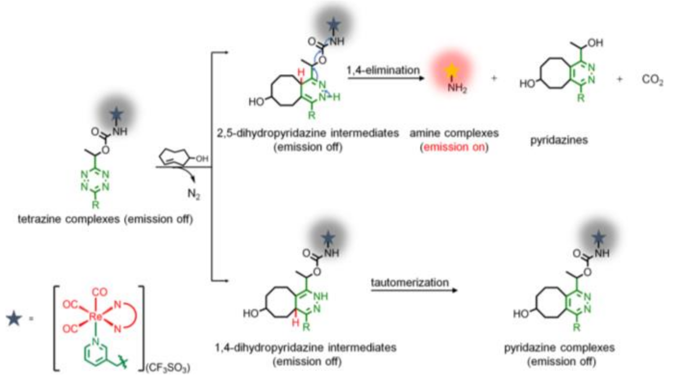
[a] *Laboratory for Synthetic Chemistry and Chemical Biology Limited, Units 1503-1511, 15/F, Building 17 W, Hong Kong Science Park, New Territories, Hong Kong, P. R. China*

[b] *Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, P. R. China*

Email: bhkenlo@cityu.edu.hk

Abstract

Cancer immunotherapy offers a promising approach for tumor eradication and prevention of recurrence by enhancing the host immune response. However, challenges such as tumor immunosuppression and off-target toxicity hinder its clinical application. In this study, we designed and synthesized rhenium(I) polypyridine complexes modified with a tetrazine-functionalized carbamate linker as bioorthogonally dissociative photosensitizers for the controlled induction of immunogenic cell death (ICD). These complexes remained inactive under normal conditions, exhibiting low emission intensities and singlet oxygen ($^1O_2$) generation efficiencies. However, they were activated upon bioorthogonal dissociation with *trans*-cyclooct-4-enol (TCO-OH), releasing highly (photo)cytotoxic rhenium(I) aminomethylpyridine derivatives. Notably, the poly(ethylene glycol)-modified complex was specifically localized in the lysosomes and displayed substantially enhanced emission and $^1O_2$ generation upon bioorthogonal activation. Light irradiation of the activated complex induced lysosomal dysfunction, autophagy suppression, and robust ICD, effectively promoting tumor cell death and immune stimulation. This approach highlights the potential of bioorthogonally activatable rhenium(I) polypyridine complexes as innovative photoimmunotherapeutic agents, enabling tumor-specific activation with minimal side effects and potent anticancer immunity.



We thank the Hong Kong Research Grants Council (CityU 11302820, CityU 11301121, CityU 11317022, C6014-20W, and C7075-21GF) and the Hong Kong Research Grants Council, National Natural Science Foundation of China (Project no. N_CityU104/21) for financial support. We also thank the funding support from "Laboratory for Synthetic Chemistry and Chemical Biology" under the Health@innoHK Program launched by Innovation and Technology Commission, The Government of Hong Kong S.A.R, P. R. China.

Reference

G.-X. Xu, E. C.-L. Mak, L. C.-C. Lee, J. Shum, P. K.-K. Leung, K. Y. Zhang, Q. Zhao, K. K.-W. Lo, *Chem. Sci.* **2023**, *14*, 13508.

Biomimetic Modification of TNA-mediated ASO Nanoparticles for Targeted Therapy in Breast Cancer

Wei Zheng, Pan Li, Hoi Man Leung, Miu Shan Chan, Pik Kwan Lo*
Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong
Email: wzheng42-c@my.cityu.edu.hk

Abstract

Tumor development and progression are characterized by complex biological processes. Triple-negative breast cancer (TNBC) remains one of the most aggressive cancers, with an urgent need for effective treatments. Gene therapy has emerged as a promising novel approach to complement conventional chemotherapy; however, enhancing the efficiency of drug delivery remains a significant challenge. The use of cationic polymers for complexing gene drugs, such as siRNA, holds great potential for improving the efficacy of tumor therapy[1,2]. In this study, we designed biomimetic membrane-encapsulated nanocomplexes composed of polylysine-compressed threose nucleic acid (TNA)-mediated antisense molecules to facilitate cellular uptake and lysosomal escape. We designed and synthesized novel TNA chains (anti-Akt2) to target and degrade Akt2, a protein positively associated with cancer progression. Through electrostatic and amphiphilic interactions between positively charged polylysine and negatively charged TNA, we successfully prepared homogeneous nanoparticles. These nanoparticles, modified with MDA-MB-468 cell membranes, demonstrated excellent cellular uptake efficiency and enhanced transfection efficacy. They effectively reduced the expression of the target protein in vitro, while promoting apoptosis and inhibiting tumor cell proliferation in vivo. This study introduces a novel strategy for treating TNBC using membrane-mimetic TNA nanoparticles as antisense materials, which is expected to significantly improve the therapeutic outcomes for TNBC patients.

References

1. Xu J.et al, *ACS Appl Mater Interfaces*. **2024**,16(44):59765-59776.

2. Chen T. et al, *ACS Appl Mater Interfaces*. **2023,** 15(50):58067-58078.

Theoretical study on the effects of atmospheric water on •OH-initiated oxidation of Guaiacol

Sheng Yiqi

yqsheng3-c@my.cityu.edu.hk

Abstract

Guaiacol is important methoxyphenol derived from lignin pyrolysis and also a significant part of biomass burning emissions, which can be caused by natural fires, human-initiated fires, or even residential wood combustion. Methoxyphenols could react with the oxidants in the atmosphere, including •OH, which is the major oxidant in the atmosphere with an extremely reactive oxidant. The reaction of methoxyphenols and •OH can produce secondary organic aerosols, which is an important atmospheric degradation process. In addition, water vapor is ubiquitous in the atmosphere. Water molecules can have effects on the reaction mechanisms involved in the atmospheric reactions between •OH and volatile organic compounds. Recent experimental researches have studied that guaiacol has high reactive with •OH to leading to formation of secondary organic aerosols and calculate reaction mechanism and rate constant with •OH. In this study, this project is to calculate reaction mechanisms of guaiacol with •OH under different water molecules in the atmosphere by theoretical study.

References

[1] Liu C, Chen D, Chen X. *Environ Sci Technol*., **2022**, *56*, 2897-2916.

[2] An Z, Sun J, Han D, et al. *Sci Total Environ*. **2019**, *685*, 729-740.

[3] Li F, Zhou S, Du L, Zhao J, Hang J, Wang X. *Sci Total Environ*. **2023**, *856*, 158895.

Controlling Chemoselectivity in Ruthenium(II)-Induced Cyclization of Aniline-Functionalized Alkynes

Kai-Wa Io, Hau-Lam Shek, Tsun-Yin Li, Ka-Kit Li, Daniel Shiu-Hin Chan, Shek-Man Yiu, and Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong SAR

E-mail: acywong@cityu.edu.hk

Abstract

The cyclization of heteroatom-functionalized alkynes induced by d^6-transition-metal centers has traditionally been associated with the vinylidene pathway. However, recent evidence suggests that d^6-transition-metal centers can also activate alkynes through non-vinylidene pathways. In this study, we conducted a comprehensive experimental and theoretical investigation into the reactions between the Ru(II) complex $[Ru([9]aneS3)(bpy)(OH_2)]^{2+}$ and 2-alkynylanilines. Our study revealed that the selectivity between the vinylidene and non-vinylidene pathways can be tuned by reaction temperature, substrate, and solvent polarity. This strategic control allows for the preferential formation of either *C2*- or *C3*-metalated indole zwitterion complexes. Additionally, we identified a rare decyclization mechanism that enables the conversion of *C2*-metalated indoles to *C3*-metalated indoles, underscoring the significance of product stability in these pathways. Overall, this work demonstrates practical approaches to control the preference between vinylidene and non-vinylidene pathways, which is crucial for the design of new catalysts and metalated heterocyclic complexes.

Cyclization, Decyclization, and Metallacyclization of Pyridine-Substituted Homopropargylic Alcohols on Ruthenium(II) and Osmium(II) Centers

Tsun-Yin Li, Hau-Lam Shek, Chi-Fung Yeung, Lai-Hon Chung, Man-Kit Tse, Shek-Man Yiu, and Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong SAR

E-mail: acywong@cityu.edu.hk

Abstract

Systematic investigations on the reactions between *cis*-[M(dppm)$_2$Cl$_2$] (M=Ru/Os; dppm=1,1-bis(diphenylphosphino)methane) and pyridine/quinoline substituted homopropargylic alcohols uncovered the diverse Ru(II)/Os(II)-induced alkyne activation pathways. The alkynes underwent cyclization on M via a "non-vinylidene" pathway at lower temperatures, resulting in alkenyl intermediates which might further metallacyclize to give metallapyrroloindolizines. Conversely, reactions at higher temperatures induced alkyne cyclization on M via a "vinylidene" pathway, affording cyclic oxacarbene complexes. Additionally, a rare decyclization mechanism was observed during the transformation of a metallacyclization-resistant alkenyl complex into a cyclic oxacarbene complex. DFT calculations were employed to validate the experimental findings. Overall, these results not only provide insights into controlling alkyne activation pathways, but also offer new strategies for preparing metalated heterocyclic and metallacyclic complexes.

Cyclic Ruthenium(II)−Halocarbon Complexes Derived from Ru(II)-Induced Cyclization of Homopropargylic Halopyridines: Mechanism, Bonding and Reactivity

Chi-Fung Yeung, Sik-Him Tang, Hau-Lam Shek, Shek-Man Yiu, and Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong SAR

E-mail: acywong@cityu.edu.hk

Abstract

The activation of various homopropargylic pyridines by *cis*-[$Ru^{II}/Os^{II}(dppm)_2Cl_2$] (dppm=1,1-bis(diphenylphosphino)methane) has previously been shown to generate a diverse array of metallacycles and metalated heterocyclic complexes. However, a minor structural modification of introducing a halide onto the pyridyl group of the alkyne substrate resulted in the formation of unprecedented Ru(II)/Os(II)−haloquinolizine complexes. These complexes display (1) $\kappa^2(X,C)$-haloquinolizine chelates arising from the cycloisomerization of $HC{\equiv}CC(OH)(CH_2(6\text{-}X\text{-}2\text{-}py))(Ph)$ on [$Ru^{II}/Os^{II}(dppm)_2]^{2+}$ moieties via a vinylidene pathway, (2) five-membered Ru/Os−X−C−N−C rings (X=F, Cl, Br) *ortho*- and *peri*-fused to quinolizinium skeletons, and (3) uncommon M−X−R bonding interactions that are atypical in coordination complexes. Despite being divalent and integrated into a five-membered Ru−X−C−N−C ring system, the X atoms in the Ru(II) complexes are susceptible to substitution by O in the presence of ^{-}OH, resulting in the formation of quinolizinium-fused ruthenaoxazole complexes. Overall, this work highlights the importance of considering metal−halocarbon bonding interactions in catalytic or coordination designs.

Facile Aromatic Carbon-Nitrogen Bond-forming Reaction Enabled by Parts per Million Level of Pd-Indolylphosphine Catalyst System

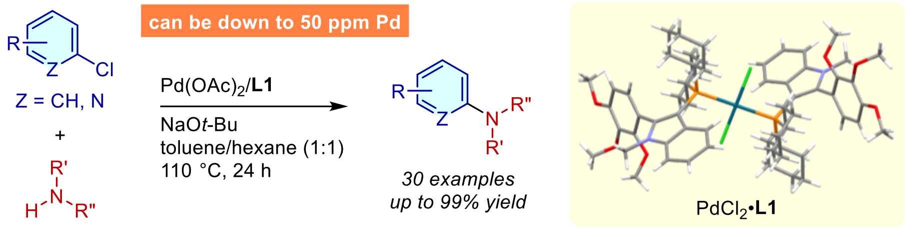
Cheuk Long LI,[a,b] Man Ho TSE,[a] Pui Ying CHOY,[a,b*] Fuk Yee KWONG[a,b*]

[a]Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

[b]Shenzhen Center of Novel Functional Molecules, Shenzhen Municipal Key Laboratory of Chemical Synthesis of Medicinal Organic Molecules, CUHK Shenzhen Research Institute, Shenzhen, China

Email: pychoy@cuhk.edu.hk; fykwong@cuhk.edu.hk

Abstract



A Pd/**L1** catalyst system has been devised for Buchwald-Hartwig amination, featuring a tailor-made, highly electron-rich indolylphosphine ligand (**L1** = *3-(dicyclohexylphosphino)-1-methyl-2-(2,3,4-trimethoxyphenyl)-1H-indole*). The system exhibited excellent performance in the C–N bond formation under ppm level of the palladium catalyst. An extensive range of aryl chlorides and amines were coupled smoothly in good-to-excellent yields. Remarkably, the coupling of extremely sterically congested amine (i.e. 2,6-diisopropylaniline) with aryl chloride was also made possible with the new catalyst system.

References

1. Li, C. L.; Tse, M. H.; Choy, P. Y.; Kwong, F. Y. Application of indole-based monophosphine in ppm level Pd-catalyzed C–N bond formation. *J. Organomet. Chem.* **2024**, *1011*, 123124 (in honor to Prof. W. T. WONG's 60th birthday).
2. Tse, M. H.; Choy, P. Y.; Kwong, F. Y. Facile Assembly of Modular-Type Phosphines for Tackling Modern Arylation Processes. *Acc. Chem. Res.* **2022**, *55*, 3688–3705.

Alternating Current-Promoted Palladium-Catalyzed C(sp^2)-H Alkynylation

Junya Wang,[a,b,+] Xiaozhou Wang,[a,c,+] Pui Ying Choy,[a,b] Gui-Juan Cheng[c,*] and Fuk Yee Kwong[a,b,*]

[a]*Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China*

[b]*Shenzhen Center of Novel Functional Molecules, Shenzhen Municipal Key Laboratory of Chemical Synthesis of Medicinal Organic Molecules, CUHK Shenzhen Research Institute, No. 10. Second Yuexing Road, Shenzhen 518172, China*

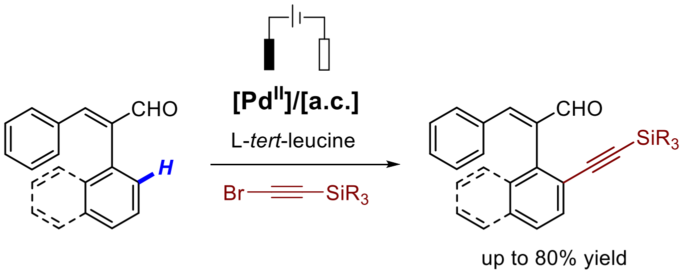
[c]*Warshel Institute for Computational Biology and School of Life and Health Sciences, School of Medicine, The Chinese University of Hong Kong, Shenzhen, Shenzhen 518172, China*

Email: chengguijuan@cuhk.edu.cn; fykwong@cuhk.edu.hk

[+]These authors contributed equally to this work.

Abstract

Alkynes are versatile molecules that can be widely applied for transformations in organic synthesis.[1] Using electro-redox instead of chemical redox pathway,[2] an electrochemical palladium-catalyzed alkynylation of cinnamaldehyde derivatives promoted by alternating current has been developed.



References

1. Choy, P. Y.; Gan, K. B.; Kwong, F. Y. *Chin. J. Chem.* **2023**, *41*, 1099−1118.
2. Li, C.; Kawamata, Y.; Nakamura, H.; Vantourout, J. C.; Liu, Z.; Hou, Q.; Bao, D.; Starr, J. T.; Chen, J.; Yan, M.; Baran, P. S. *Angew. Chem. Int. Ed.* **2017**, *56*, 13088–13093.

Using a Sterically Bulky Guanidinate Ligand for Stabilization of Group 14 and Divalent Lanthanide Metal Complexes

Chak Him Chung and Hung Kay Lee*
Department of chemistry, The Chinese University of Hong Kong, Shatin, New Territories,
Hong Kong SAR, P. R. China
hklee@cuhk.edu.hk

Abstract

Guanidinate anions of the formula $[(R'_2N)C(NR)_2]^-$ (R, R' = alkyl, aryl or silyl substituents) exhibit rich coordination chemistry.[1] The tunable steric and electronic properties of guanidinates can be achieved by introducing appropriate substituents at the nitrogen atoms.[2] The NCN backbone of guanidinate ligands enables delocalization of anionic charge for stabilization of different metal complexes.[3]

In the present study, group 14 metal complexes supported by guanidinate ligand $[(2,6\text{–}\mathrm{Pr}^{i}{}_2\mathrm{C_6H_3N})_2\mathrm{C}\{\mathrm{NH}(2,6\text{–}\mathrm{Pr}^{i}{}_2\mathrm{C_6H_3})\}]^-$ $(\mathbf{HL}^1)^-$ were synthesized by salt metathesis reactions of the corresponding group 14 metal chloride ($SiCl_4$, $GeCl_2$·(dioxane) and $SnCl_2$) with one equivalent of lithium guanidinate complex $[\mathrm{Li}(\mathbf{HL}^1)(\mathrm{Et_2O})]$ (**1**) in Et_2O. The reactions led to isolation of monosubstituted $[\mathrm{Si}(\mathbf{HL}^1)\mathrm{Cl_3}]$ (**3**), $[\mathrm{Ge}(\mathbf{HL}^1)\mathrm{Cl}]$ (**4**) and $[\mathrm{Sn}(\mathbf{HL}^1)\mathrm{Cl}]$ (**5**) guanidinate complexes, respectively. Meanwhile, salt metathesis reactions of $\mathrm{LnI_2(THF)_2}$ (Ln = $\mathrm{Sm^{II}}$, $\mathrm{Eu^{II}}$) with two equivalents of potassium guanidinate complex $[\mathrm{K}(\mathbf{HL}^1)(\mathrm{THF})_2]$ (**2**) in THF led to successful isolation of mono- and disubstituted guanidinate complexes, $[\mathrm{Sm}(\mathbf{HL}^1)\mathrm{I}]_2$ (**6**) and $[\mathrm{Eu}(\mathbf{HL}^1)_2(\mathrm{THF})_2]$ (**7**), respectively.

Acknowledgements. This work was supported by the Research Grants Council of Hong Kong in the form of a GRF Grant (Ref. No.: CUHK 14300020).

References:

1) Constable, E. C.; Parkin, G.; Que, L., Jr. Ed. *Comprehensive Coordination Chemistry III*, Oxford, Elsevier, **2021**.; (b) Edelmann, F. T. *Coord. Chem. Rev.* **1994**, *137*, 403-481; (c) Junk, P. C.; Cole, M. L. *Chem. Commun*. **2007**, *16*, 1579-1590.
2) Johnson, A. L.; Willcocks, A. M.; Richards, S. P. *Inorg. Chem.* **2009**, *48*, 8613-8622.
3) Brazeau, A. L.; Hänninen, M. M.; Tuononen, H. M.; Jones, N. D. *J. Am. Chem. Soc.* **2012**, *134*, 5398-5414.

Stereoselective Unsymmetrical 1,1-Diborylation of Alkynes with a Neutral sp^2 - sp^3 Diboron Reagent

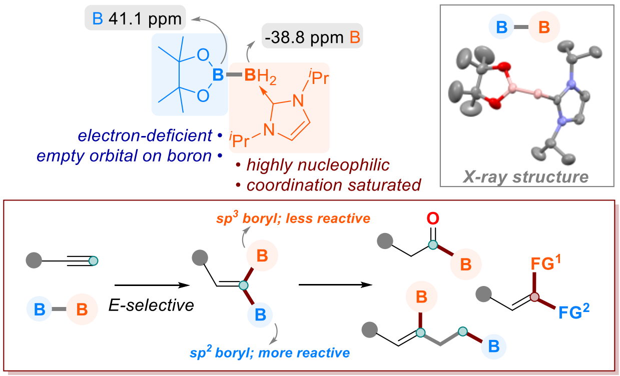
Xiangyu Lou⁺, Jiaxin Lin⁺, Chun Yin Kwok, and Hairong Lyu*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories,
Hong Kong

Email: hrlyu@cuhk.edu.hk.

Abstract:

The incorporation of boron into organic molecules has received growing research focus. Given the versatility of the carbon-boron bond, borylated compounds can readily undergo derivatization, enabling the facile introduction of various functional groups. 1,1-Diborylalkene is a class of diboryl species. It can serve as a precursor of multisubstituted olefins, which are prevalent building blocks in natural products and drug molecules. Diboron reagents such as B_2pin_2 and Bpin-Bdan, has been used in synthesizing 1,1-diborylalkenes. However, two boryl groups with similar chemical properties making them difficult to distinguish during the late-stage functionalization. Here we report a method to access unsymmetrical 1,1- diborylalkene (UDBA) stereoselectively via the reaction of readily available alkynes with a neutral sp^2-sp^3 diboron reagent.[1] Attributing to the chemically easily distinguishable nature of the sp^2 and sp^3 boryl moieties, controllable stepwise derivatization of the resultant UDBAs is realized. This process leads to various multifunctionalized olefins and organoborons, such as acylboranes, which are difficult to prepare by other methods.



References:

1. X. Lou, J. Lin, C. Y. Kwok, H. Lyu, *Angew. Chem. Int. Ed.* **2023**, 62, e202312633.

Functionalization of boranes through thiol/oxygen catalysis

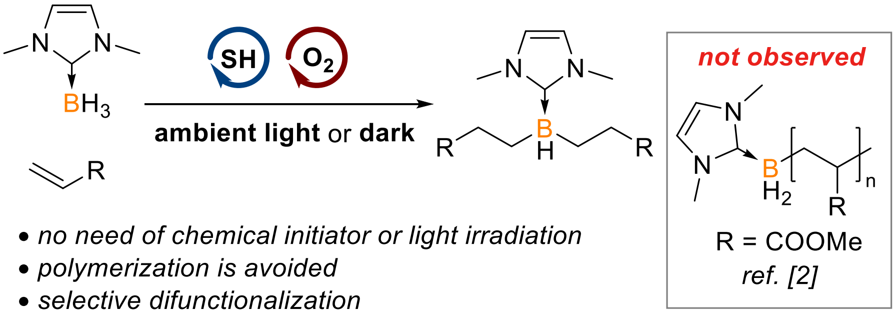
Hongyi Tao and Hairong Lyu*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories,
Hong Kong

Email: hrlyu@cuhk.edu.hk.

Abstract:

Thiyl radical has been recognized as a powerful hydrogen atom transfer (HAT) catalyst, which competently abstracts hydrogen atoms from carbon-hydrogen or element-hydrogen functionalities to deliver the corresponding carbon- or element-centered radical suitable for subsequent transformations. Here we proposed a greener and more convenient methods for the generation of thiyl radical as HAT catalyst, using molecular oxygen to oxidize thiol without the need for chemical initiators or light irradiation, successfully achieving selective di-alkylated or mono-alkaylated functionalizations of NHC borane. [1] A thorough mechanistic investigation underscores the pivotal role of oxygen in directly generating thiyl radical from thiol in an efficient manner. The potential of this thiol/oxygen catalysis extends beyond borane functionalization, as demonstrated by the successful functionalization of silane, suggesting wider applicability in various other chemical transformations.



References:

1. H. Tao, H. Lyu, *Chin. J. Chem.* **2024**, 42, 2804–2810.

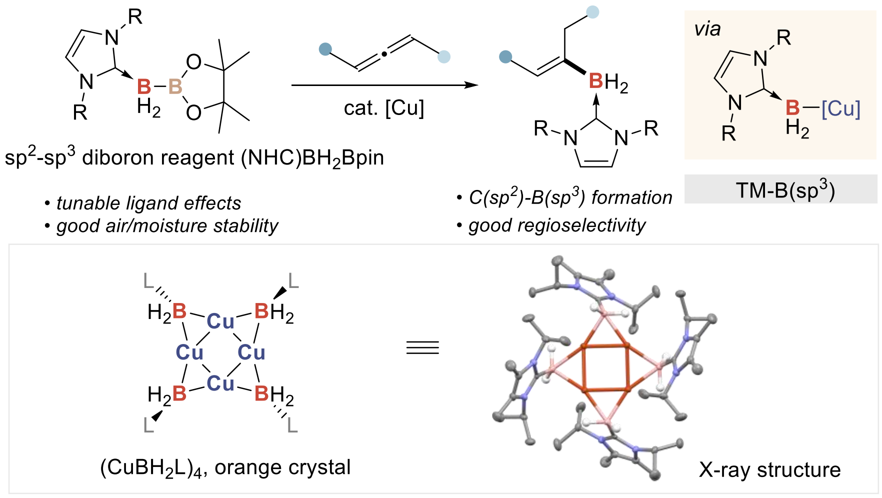
2. M.-A. Tehfe, M. Makhlouf Brahmi, J.-P. Fouassier, D. P. Curran, M. Malacria, L. Fensterbank, E. Lacôte, J. Lalevée, *Macromol.* **2010**, *43*, 2261-2267.

Copper catalyzed C−B (sp^3) bond formation through the intermediacy of Cu−B(sp^3) complex

Zhanqiang Ye,[1] Chun Yin Kwok,[1] Lam Sze Lam,[1] Linlin Wu[2],* and Hairong Lyu[1],*
1 Department of Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong SAR, China
2 Hunan Provincial Key Laboratory of Micro &Nano Materials Interfaces Science, College of Chemistry and Chemical Engi-neering, Central South University, Changsha 410083, P. R. China

Abstract:

The majority of research on transition metal (TM)-catalyzed borylative transformations has primarily focused on TM−B(sp^2) complexes. In contrast, the chemistry of TM−B(sp^3) species and their potential applications in catalytic borylation remain significantly underexplored, largely due to the limited availability of suitable boron(sp^3) reagents. In this study, we address this gap using our recently developed sp^2–sp^3 diboron reagent[1] to enable a copper-catalyzed hydroboration of allenes, resulting in the formation of C−B(sp^3) bonds. A detailed mechanistic investigation, including the isolation and structural characterization of a Cu−B(sp^3) complex, provides direct evidence for the involvement of a Cu−B(sp^3) intermediate in the catalytic cycle.



References:

1. Lou, X.; Lin, J.; Kwok, C. Y.; Lyu, H.* ***Angew. Chem. Int. Ed.*** 2023, *62*, e202312633.

Synthesis and properties of Dipolar Polycyclic Aromatic Hydrocarbons (Dipolar PAHs)

Zipeng Liu, Qian Miao *

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories,
Hong Kong, China; chmjonathanliu@link.cuhk.edu.hk; miaoqian@cuhk.edu.hk

Abstract

Non-alternant Polycyclic Aromatic Hydrocarbons have attracted people's attention in recent years. Due to their special molecular structure and great potential in various applications such as NIR(Near-infrared) dyes and OFET[1], large amount works on this area were reported in the past decades. Caused by the tendency of intramolecular charge transfer of fused five and seven-member rings, this work based on the key idea of introducing of five and seven-member-rings as replacement for six-member ring at two terminals of PAH framework may lead to great dipole moment. And to fulfill the requirements in application area like electric controlled liquid crystal.

References

[1] Fu, L.; Liu, P.; Xue, R.; Tang, X.; Cao, J.; Yao, Z.; Liu, Y.; Yan, S.; Wang, X. *Angewandte Chemie International Edition* **2023**, *62* (36). https://doi.org/10.1002/anie.202306509.

Organic Electronic Materials based on Trioxotriangulene Stable Neutral π-Radicals

Huishu Ma

Department of Chemistry, the Chinese University of Hong Kong, Shatin, New Territories, Hong Kong; 1155184288@cuhk.edu.hk

Abstract

The synthesis of trioxotriangulene neutral radical was repeated[1] and vapor deposition was employed to prepare its thin film. This film showed the field effect and semiconductor properties. The poor morphologies of vapor deposited films were observed by Atomic Force Microscope. The solubility of this radical is too poor to use solution based fabrication method, which is a common strategy to improve morphologies of thin films. Chemical modification is in progress in order to improve the solubility of neutral radicals.

Reference

1. Morita, Y.; Murata, T.; Ueda, A.; Yamada, C.; Kanzaki, Y.; Shiomi, D,; Sato, K.; Takui, T. *Bull. Chem. Soc. Jpn.* **2018**, *91*, 922 ‒ 931.

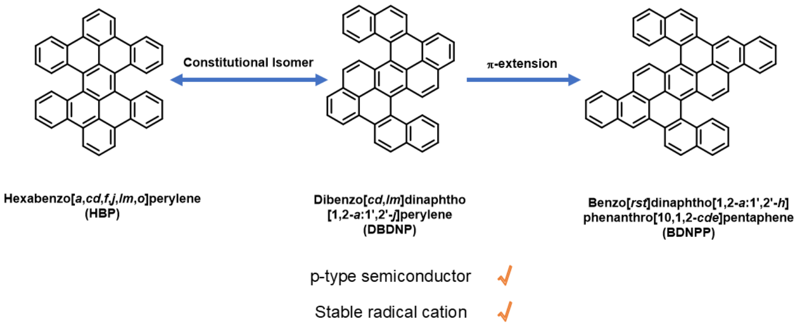
Synthesis, properties, and π-extension of a double helicene isomeric to Hexabenzo[a,cd,f,j,lm,o]perylene (HBP)

Shilong Su, Qian Miao *

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories,
Hong Kong, China; miaoqian@cuhk.edu.hk

Abstract

Hexabenzo[a,cd,f,j,lm,o]perylene (HBP) has proven to be an effective channel material in organic field effect transistors (OFETs)[1], and can form robust radical cation via both photooxidation and chemical oxidation[2]. In this study, we synthesized dibenzo[cd,lm]dinaphtho[1,2-a:1',2'-j]perylene (DBDNP), a constitutional isomer of HBP, through regioselective Scholl Reaction involving 4-alkoxy-1-naphthyl group. The radical cation of DBDNP can be formed via chemical oxidation and remains stable under ambient conditions. DBDNP functions as a p-type semiconductor with a field effect mobility of 1.98×10^{-3} cm^{2}V^{-1}s^{-1}. Additionally, we synthesized a π-extended version of DBDNP, benzo[rst]dinaphtho[1,2-a:1',2'-h]phenanthro[10,1,2-cde]pentaphene(BDNPP), using a similar approach.



References

[1] Shan, L.; Liu, D.; Li, H.; Xu, X.; Shan, B.; Xu, J. B.; Miao, Q. *Adv. Mater.* **2015**, 27, 3418-3423.

[2] Wang, Y.; Gong, Q.; Pun, S. H.; Lee, H. K.; Zhou, Y.; Xu, J.; Miao, Q. *J. Am. Chem. Soc.* **2022**, 144, 16612-16619.

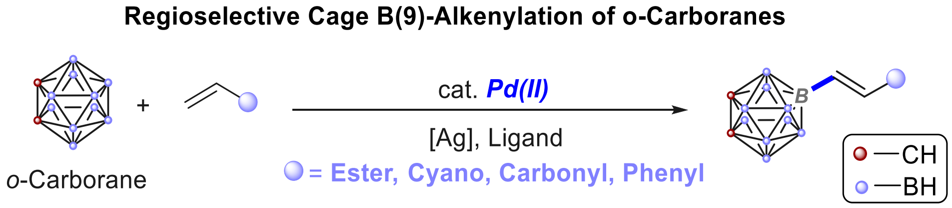
Ligand-Assisted Regioselective Cage B(9)-Alkenylation of *o*-Carboranes

Chen HUANG[a], Jie ZHANG*[a] and Zuowei XIE*[a,b]

[a] Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Hong Kong, China. [b] Shenzhen Grubbs Institute and Department of Chemistry, Southern University of Science and Technology, Shenzhen 518055, China. Email: jiezhang@cuhk.edu.hk; zwxie@cuhk.edu.hk.

Abstract

Carboranes are a class of polyhedral boron-carbon molecular clusters with unique properties including three-dimensional aromaticity conjugated by σ-bonds, icosahedral geometry and inherent robustness.[1] These clusters are finding many applications in luminescent materials, electron sinks, pharmaceuticals, polymers, coordination chemistry, and catalysis.[2] In recent decade, transition metal-catalyzed selective cage B-H activation has been accomplished to realize numerous functionalization of *o*-carboranes.[3] However, regioselective cage B(9)-H or B(8)-H activation still remains a research gap. We describe here a ligand-assisted Pd-catalyzed selective cage B(9)-H activation, and the corresponding alkenylation products were obtained in moderate to good yields with the selectivity of B(9)/B(8) > 20. The ligand may not only stabilize the Pd(II) intermediate, but also act as an internal base to promote the CMD process. In addition, the binding of L1 results a bulky coordination environment of Pd center, which may lead to regioselective functionalization of B(9)-H bond.[4] This strategy represents a new way to regioselectively functionalize cage B(9)-H bond in o-carboranes.



References

1. *Carboranes*, 3rd ed.; Grimes, R. N., Ed.; Elsevier: Oxford, U.K., 2016.

2. Xie, Z. *Coord. Chem. Rev.* **2002**, 231, 23-46.

3. Qiu, Z.; Xie, Z. *Acc. Chem. Res*. **2021**, *54*, 4065-4079.

4. Wang, P.; Verma, P.; Xia, G.; Shi, J.; Qiao, J. X.; Tao, S.; Cheng, P. T. W.; Poss, M. A.; Farmer, M. E.; Yeung, K.-S.; Yu, J.-Q. *Nature*. **2017**, *551*, 489-493.

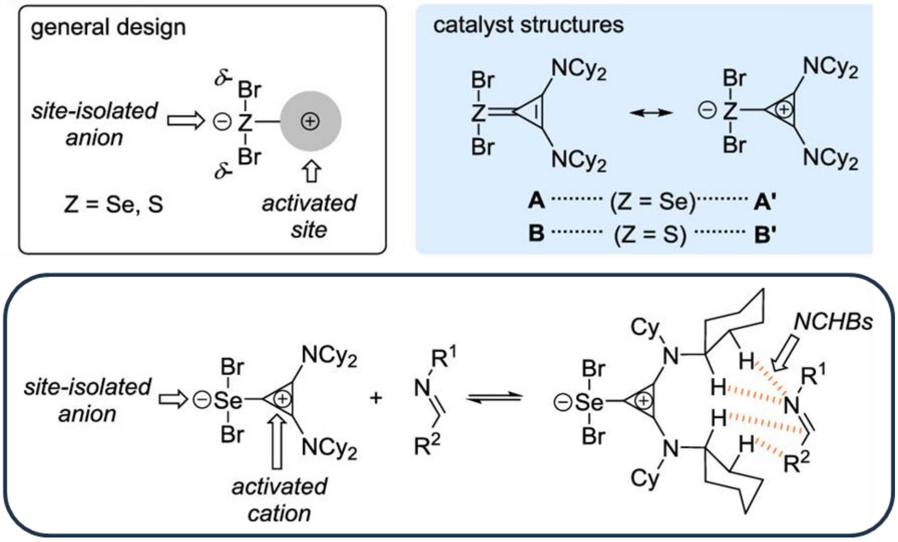
Design and Applications of Cyclopropenium Chalcogen Dihalides in Catalysis via C(sp3)−H···X Interactions

Junjie Yang,† Yabin Zhang,† Hong-Chai Fabio Wong, Jingxian Huang, Ying-Lung Steve Tse,*
and Ying-Yeung Yeung*
Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories,
Hong Kong

Keywords: chalcogen, cyclopropenium, noncovalent interactions, nonclassical hydrogen bond, organocatalysis

Abstract:

In many areas such as crystal engineering, protein binding, and supramolecular chemistry, noncovalent interactions originated from $C(sp^3)-H\cdots X$ hydrogen bonds frequently appear in recent years. However, employing this class of $C(sp^3)-H\cdots X$ interactions in catalysis is less common due to their insufficient catalytic performance. $C(sp^3)-H\cdots X$ hydrogen bonds are relatively weak , however, incorporation of electron-withdrawing substituents in close proximity to the $C(sp^3)-H$s can enhance their noncovalent attractive interactions to electron donors. Herein, we report the use of cyclopropenium chalcogen dihalides as catalysts, in which effective site isolation of the counteranion significantly enhances the availability of the noncovalent interaction donor. The catalytic performance is comparable to those of some typical Lewis acids and much better than those of many common catalysts based on noncovalent interactions. Our mechanistic study suggests that the catalysts activate substrates via multiple $C(sp^3)-H\cdots X$ hydrogen bonds.



References:

1. Czernek, J.; Brus, J.; Czerneková, V.; Kobera, L. *Molecules.* 2023, 28, 4478.
2. Xue, X. S.; Li, X.; Yu, A.; Yang, C.; Song, C.; Cheng, J. P. *J. Am. Chem. Soc.* 2013, 135, 7462.
3. Yang, J., Zhang, Y., Wong, H. C. F., Huang, J., Tse, Y. L. S., & Yeung, Y. Y. *ACS Catalysis.* 2024, 14: 3018-3027.

Synthesis, Structure and Potential Application of $[Rh^{III}(bda)X_2]^-$

Lulu Liu, and Wai-Lun Man*

Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, HKSAR, P. R.
China. Email: wlman118@hkbu.edu.hk

Abstract

Inspired by the d^6 complexes, $Ru^{II}(bda)(L)_2$ (bda = 2,2'-bipyridine-6,6'-dicaboxylate dianion; L = N-bond heterocycles) which exhibits promising activities in the oxidation of water and ammonia,[1,2] we have synthesized two similar d^6 rhodium complexes, $[Rh^{III}(bda)X_2]^-$ [X = Cl (**1**) and N_3 (**2**)] (Figure 1). Complex **1** exhibits similar reactivity towards NH_3 and forms another octahedral complex $[Rh^{III}(\kappa^3\text{-bda})(NH_3)Cl_2]^-$, indicating that one of the Rh–O bonds is fragile for small molecule coordination. However, both complexes **1** and **2** show almost no activity in water and ammonia oxidation with a wide range of external oxidants. In this work, we will present the potential applications of complexes **1** and **2** as nitrene and carbene transfer catalysts.

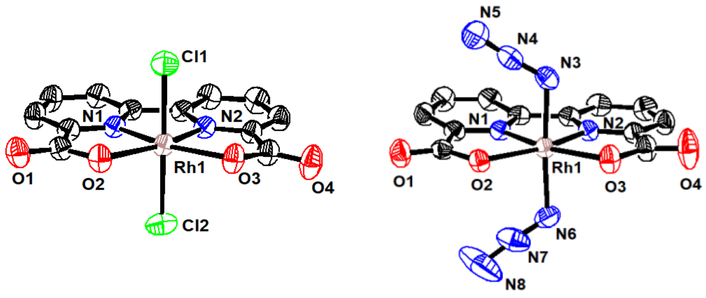


Figure 1. X-ray structures of **1** and **2**.

Reference

1. Duan, L.; Bozoglian, F.; Mandal, S.; Stewart, B.; Privalov, T.; Llobet, A.; Sun, L. *Nat. Chem.* **2012**, *4*, 418–423.
2. Nakajima, K.; Toda, H.; Sakata, K.; Nishibayashi, Y. *Nat. Chem.* **2019**, *11*, 702−709.

Ir-Catalyzed Facile Ammonia Oxidation to Nitrate in Water

Daniel Nnaemaka Tritton,[a] Tai-Chu Lau,[b] Yingying Liu,[c] and Wai-Lun Man[a,*]

[a]Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, HKSAR, P. R. China. [b]Department of Chemistry, City University of Hong Kong, Kowloon Tong, HKSAR, P. R. China. [c]Institute of Intelligent Machines, Hefei Institutes of Physical Science, Chinese Academy of Sciences, Hefei, P. R. China.

Email: wlman118@hkbu.edu.hk

Abstract

The increasing demand for sustainable energy solutions is driving the development of efficient molecular catalysts for the oxidation of ammonia (NH_3). Understanding the underlying mechanisms of this oxidation process is essential. While the 6e^- oxidation process that converts NH_3 to dinitrogen (N_2) has been extensively studied, reports on the analogous 8e^- oxidation process that converts NH_3 to nitrate (NO_3^-) are sparse.[1]

Herein we report the synthesis and characterization of an iridium complex, $[Ir^{III}(bda)Cl_2]^-$ (bda = 2,2'-bipyridine-6,6'-dicarboxylate dianion) (**Figure 1**). $[Ir^{III}(bda)Cl_2]^-$ functions as a homogeneous catalyst for the efficient oxidation of NH_3 to NO_3^- in water, using sodium periodate ($NaIO_4$) as the terminal oxidant. The proposed mechanism, which mimics the biological nitrification process, will be discussed based on experimental evidence from isolating key intermediates, combined with density functional theory (DFT) calculations.

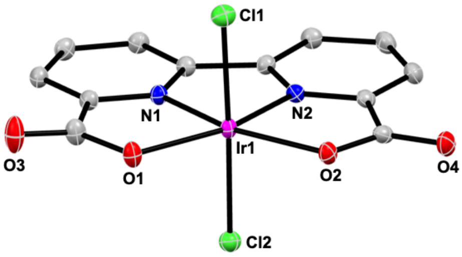


Figure 1. X-ray structure of $[Ir^{III}(bda)Cl_2]^-$.

References

1. Jacob, S. I.; Chakraborty, A.; Chamas, A.; Bock, R.; Sepunaru, L.; Ménard, G., Rapid Aqueous Ammonia Oxidation to N_2 Using a Molecular Ru Electrocatalyst. *ACS Energy Lett.* **2023,** *8* (9), 3760–3766.

Mechanism of Action and Evaluation of Ratiometric Probes for Uric Acid Using Lanthanide Complexes with Tetraazatriphenylene Sensitisers

Xinyi WEN, David Parker.

Department of Chemistry, Hong Kong Baptist University, Hong Kong SAR, P. R. China

Email: davidparker@hkbu.edu.hk

Abstract

A series of new ligands has been synthesised that incorporate electron-poor aromatic moieties (dpqMe$_2$ and dpqPh$_2$ chromophores) into tetraazacyclododecane or triazacyclononane based complex structures. Lanthanide coordination complexes have been made and their photophysical properties studied. Each complex exhibits millisecond lifetimes, and photoluminescence quantum yields in water are 10 to 50 %. Their suitability for the selective and rapid analysis of urate has been examined. The highest sensitivity to urate quenching was observed with a mono-cationic complex $[LnL^3]^+$ (Ln = Eu/Tb) which was used for urate analysis in diluted human serum. Mechanistic studies were conducted to probe the nature of the intermediate exciplex and excited state dynamics were studied using picosecond and nanosecond absorption spectroscopy.

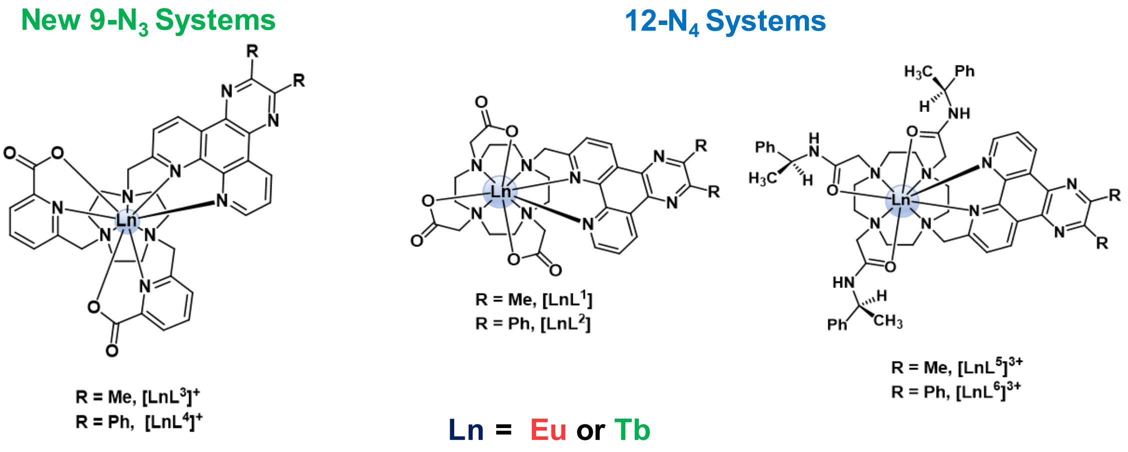


Figure 1. Lanthanide complexes with a tetraazatriphenylene sensitiser. (Ln = Eu/Tb)

References

1. Wen, X. Y.; Li, H. S.; Ju, Z. J.; Deng, R.; Parker, D. *Chem. Sci.*, **2024**,*15*, 19944-19951.

Three/four-Coordinated [2]Rotaxane Cu(I) Catalyst for Cross Dehydrogenative C-O Coupling

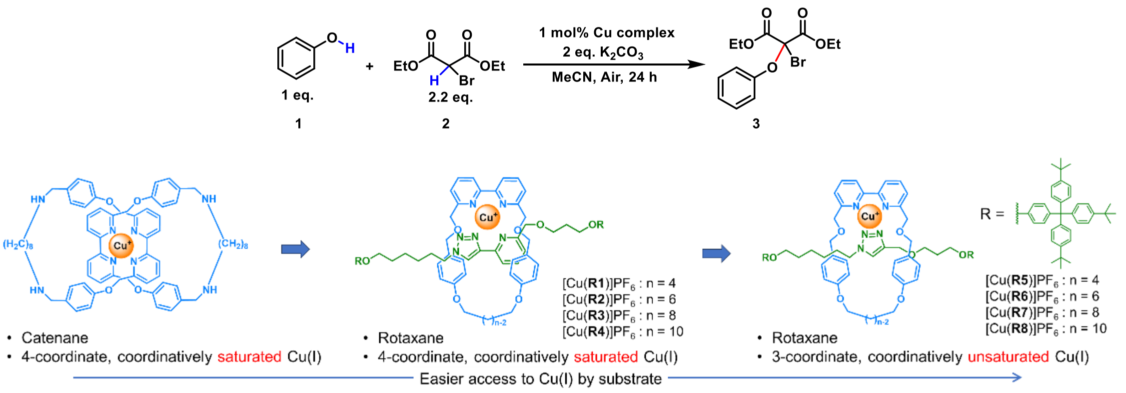
Yan Zhang,[a] Lihui Zhu,[a] and Ho Yu Au-Yeung[a]*

[a]*Department of Chemistry, The University of Hong Kong, Hong Kong, P. R. China*

Email: *hoyuay@hku.hk*

Abstract

Catalytic activity of copper(I) complexes supported by rotaxane ligands towards a dehydrogenative C–O cross coupling is reported. By comparing the catalytic efficiency of 3/4-coordinated [2]rotaxanes obtained from active templated synthesis and our previously reported 4-coordinated [2]catenane, we found that unsaturated 3-coordinated [2]rotaxanes could catalyze the C–O cross coupling more efficiently at room temperature, but more susceptible to side reaction at higher temperature. Effects of the size of macrocycle and the distance of the stopper groups to the Cu(I) center in the 3/4-coordinated [2]rotaxanes were also investigated.



Reference

1. L. Zhu, J. Li, J. Yang and H. Y. Au-Yeung, Chem. Sci., **2020**, *11*, 13008–13014.

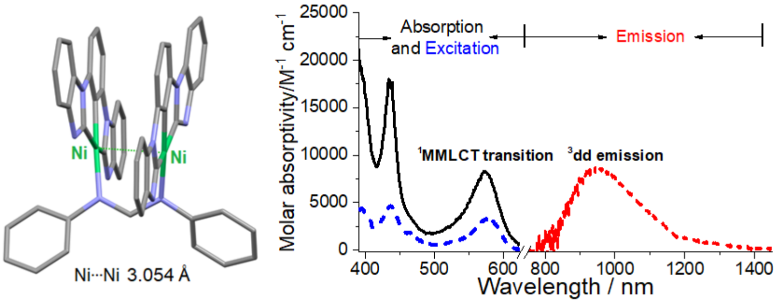
Dinuclear Cyclometalated Pincer Nickel(II) Complexes with Metal-Metal-to-ligand Charge Transfer Excited States and Near-Infrared Emission

Mengyue Gao, Wai-Pong To, Glenna So Ming Tong, Lili Du, Kam-Hung Low, Zhou Tang, Wei Lu, and Chi-Ming Che

Postal address; cmche@hku.hk

Abstract

Facile non-radiative decay of low-lying metal-centered (MC) d-d excited states has been well documented to pose a significant obstacle to the development of phosphorescent $\mathrm{Ni^{II}}$ complexes due to substantial structural distortions between the dd excited state and the ground state.[1, 2] Herein, dinuclear pincer-type Ni(II) complexes bridged by formamidinate/α-carbolinato ligands and the dinuclear Pt(II) and Pd(II) analogues were studied. These Ni(II) complexes exhibit short Ni-Ni distances of 2.947-3.054 Å and singlet metal-metal-to-ligand charge transfer transitions at 500-550 nm. At 77 K, these Ni(II) complexes display phosphorescence (τ=2.6-8.6 μs) in the NIR (800-1400 nm) spectral region in 2-MeTHF and in the solid state, which originates from the ^{3}dd excited state as supported by DFT calculations. One example is presented below.



References

1. Ogawa, T.; Ogawa,; Sinha, N.; Pfund, B.; Prescimone, A.; Wenger, O. S.; *J. Am. Chem. Soc.* **2022**, *144*, 21948-21960.
2. Dorn, M.; East, N. R.; Förster, C.; Kitzmann, W. R.; Moll, J.; Reichenauer, F.; Reuter , T.; Stein, L.; Heinze, K. *Comprehensive Inorganic Chemistry III. Elsevier*, **2023**, *8*, 707-788.

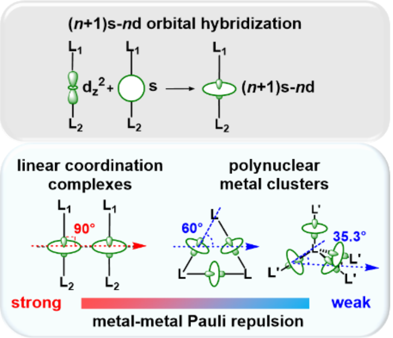
Anisotropic Metal−Metal Pauli Repulsion in Polynuclear d^{10} Metal Clusters

Authors' Names: Shuo Xu, Qingyun Wan*, Jun Yang, Chi-Ming Che*

Postal addresses: cmche@hku.hk, wendyqyw@hku.hk

Abstract

Metallophilicity has been widely considered to be the driving force for self-assembly of closed-shell d^{10} metal complexes, but this view has been challenged by our recent studies showing that metallophilicity in linear d^{10}-d^{10} dimers is repulsive. This is due to strong metal-metal (M-M′) Pauli repulsion.[1] Here, we study M-M′ Pauli repulsion in d^{10} metal clusters. Our results show that M-M′ Pauli repulsion in d^{10} polynuclear clusters is weaker than in similar linear d^{10} complexes due to the anisotropic shape of (n+1)s-nd hybridized orbitals. The overall M-M′ interactions in closed-shell d^{10} polynuclear metal clusters remain repulsive. The effects of coordination geometry, relativistic effects, and the ligand's electronegativity on M-M′ Pauli repulsion in polynuclear d^{10} clusters have been explored. These findings provide valuable guidance for the design and development of ligands and coordination geometries that alleviate M-M′ Pauli repulsion in d^{10} metal cluster systems.[2]



Scheme 1. Metal-metal Pauli repulsion in d^{10} metal clusters.

References

1. Wan, Q.*; Yang, J.*; To, W.-P.; Che, C.-M.* *Proc. Natl. Acad. Sci. U. S. A.* **2020**, *118*, e2019265118.

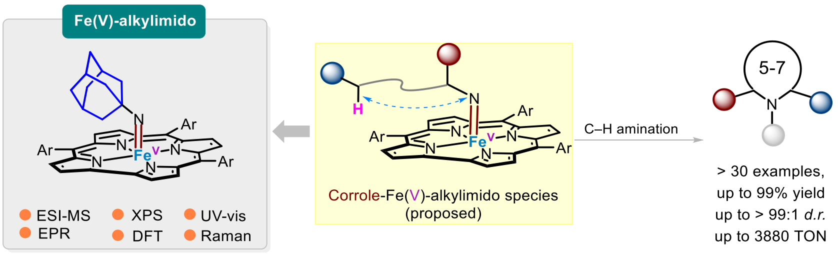
2. Xu, S.; Wan, Q.*; Yang, J.; Che, C.-M.* *J. Phys. Chem. Lett.* **2024**, *15*, 2193-2201.

Iron Corrole-Catalyzed Intramolecular Amination Reactions of Alkyl Azides. Spectroscopic Characterization and Reactivity of [Fe^{V}(Cor)(NAd)]

Tingjie You, Ka-Pan Shing, Liangliang Wu, Kai Wu, Hua-Hua Wang, Yungen Liu, Lili Du,
Runhui Liang, David Lee Phillips, Xiao-Yong Chang, Jie-Sheng Huang, Chi-Ming Che*
State Key Laboratory of Synthetic Chemistry, Department of Chemistry, The University of
Hong Kong, Pokfulam Road, Hong Kong 000000, P. R. China
cmche@hku.hk

Abstract

Iron-catalyzed intramolecular C(sp^3)–H amination of alkyl azides (N$_3$R)[1] via iron-alkylimido/alkylimidyl (Fe(NR), R = alkyl) intermediates is an appealing strategy to access N-heterocycles. As nitrogen analogues of iron-oxo species, high-valent iron-imido species have attracted great interest in the past decades. However, Fe^{V}(NR) species capable of reacting with C(sp^3)–H bonds or serving as active intermediates for the catalytic functionalization of C(sp^3)–H bonds remain unexplored. Here we present our recent work on iron-corrole (Cor) catalyzed intramolecular C–H amination reactions of alkyl azides to afford a variety of N-heterocyclic compounds, possibly via high-valent Fe^{V}-alkylimido species. We independently prepared the [Fe^{V}(Cor)(NAd)] (Ad = adamantyl) complex and characterized it by various spectroscopic methods, and its hydrogen atom abstraction (HAA) reactivity towards C(sp^3)–H bonds was studied.[2]



References

1. Hennessy, E. T.; Betley, T. A.* *Science*, **2013**, *340*, 591 – 595.
2. You, T.; Shing, K.-P.; Wu, L.; Wu, K.; Wang, H.-H.; Liu, Y.; Du, L.; Liang, R.; Phillips, D. L.; Chang, X.-Y.; Huang, J.-S.; Che, C.-M.* *Adv. Sci.*, **2024**, *11*, 2401420.

Dearomative Intramolecular (4+3) Cycloadditions of Epoxy Enolsilanes with Benzene Derivatives

CHAN LONG YING, PAULINE CHIU*

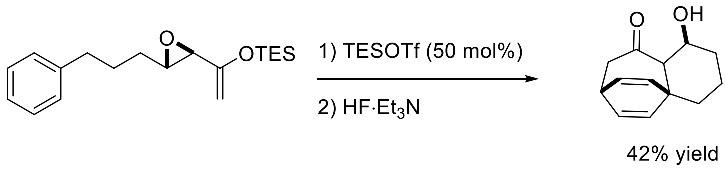
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong

pchiu@hku.hk

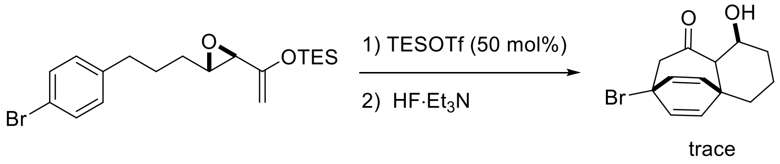
Abstract

Benzene is a readily available building block; however, owing to its high aromaticity, many of its reactions generate aromatic products. On the other hand, dearomative reactions of benzenes under mild conditions to produce alkenes are more challenging.

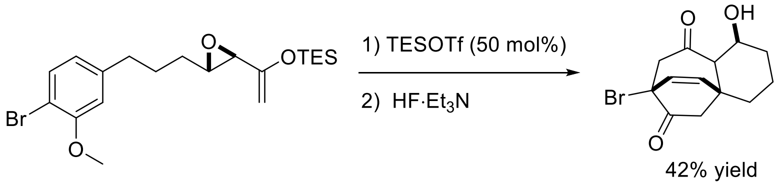
Our previous research reported an intramolecular (4+3) dearomative cycloaddition of epoxy enolsilanes with arenes, in which a reactive diene in the context of a [6,7]-fused ring system is produced under mild conditions (Eq. 1).[1] Here, an in-depth study focusing on the substituent effects in this dearomatizing cycloaddition of various benzene derivatives is presented. Benzenes substituted with bulky or even electron-withdrawing groups have been found to undergo this transformation in moderate to good yields.



(Eq. 1)[1]



(Eq. 2)



(Eq. 3)

Reference

1. Ling, J.; Lam, S.; Lo, K-H.; Chiu. P. *Angew. Chem. Int. Ed.*, **2017**, *56*, 8879 – 8882.

[13]-Graphanyl-X: Expanding the 3D Saturate Chemical Space

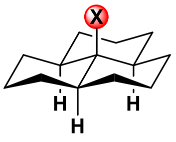
Alex K.H.Chu, Antonio Rizzo*, Pauline Chiu*

Department of Chemistry, Chong Yuet Ming Chemistry Building, The University of Hong Kong, Pokfulam Road, Hong Kong

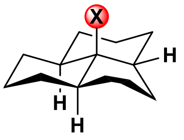
u3009245@connect.hku.hk

Abstract

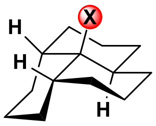
[13]Graphanyl-X is a hydrocarbon scaffold consisting of three fused cyclohexane rings with functionalization on the central carbon. There are four possible stereoisomers depending on the relationship between the central C-X bond and the three vicinal C-H bonds (*trans-trans-trans*, *cis-trans-trans*, *cis-cis-trans* and *cis-cis-cis*). They feature hydrophobicity, conformational rigidity, and the all-*trans* isomer has C_3 symmetry, negative electron affinity and a hydrogen terminated surface. Possible applications of this class of saturated hydrocarbon include drug discovery,[1] metal organic frameworks[2] and nanoelectronics.[3] We envisage a new scalable synthetic route that would enable us to access these isomers of [13]-graphanyl-OH. Using modern radical catalysis pioneered by Macmillan,[4] we aim to derivatize the central carbon in order to access functional groups as handles for further derivatization or as an add-on to existing molecules.



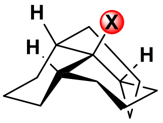
TTT



CTT



CCT



CCC

References

1. F. Lovering, J. Bikker and C. Humblet, *J. Med. Chem.*, **2009**, 52, 6752–6756.
2. Slyusarchuk, V. D.; Kruger, P. E.; Hawes, C. S. *Chempluschem*, **2020**, *85*, 845-854.
3. Vanderweide, J.; Zhang, Z.; Baumann, P. K.; Wensell, M. G.; Bernholc, J.; Nemanich, R. J. *Physical Review B*, **1994**, *50*, 5803-5806.
4. Chan, A. Y.; Perry, I. B.; Bissonnette, N. B.; Buksh, B. F.; Edwards, G. A.; Frye, L. I.; Garry, O. L.; Lavagnino, M. N.; Li, B. X.; Liang, Y. F.; et al. *Chemical Reviews*, **2022**, *122*, 1485-1542.

Inter- and intramolecular (4+3) cycloadditions with epoxy allylsilanes as dienophiles

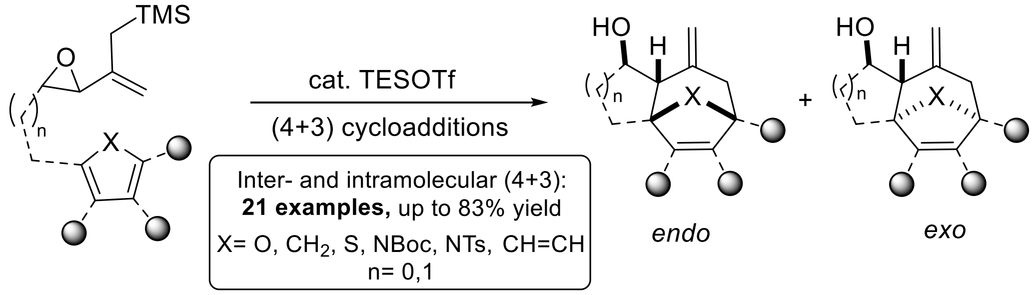
Qin Han Teo and Pauline Chiu*

Department of Chemistry, The University of Hong Kong

pchiu@hku.hk

Abstract

The formation of methylenated bicyclic adducts was achieved by formal (4+3) cycloadditions of epoxy allylsilanes with different dienes. The epoxy allylsilane functions as a dienophile in the (4+3) cycloaddition reaction. The oxirane in the epoxy allylsilane, once activated by a Lewis acid, serves as a good dienophile while the allylsilane moiety completes the construction of the cycloadducts by desilylation of the (trimethylsilyl)methyl group. Epoxy allylsilane reacts with simple dienes in the presence of a catalytic amount of TESOTf results in the formation of intermolecular (4+3) cycloadducts with moderate yields. The epoxy allylsilane tethered to different dienes with TESOTf constructs cycloadducts with 6,7- and 5,7-fused bicyclic systems in moderate to good yields. Both *endo* and *exo* cycloadducts are formed in the cycloaddition reaction. The synthesis of the dienophile precursor and the inter- and intramolecular (4+3) cycloadditions of epoxy allylsilanes with different dienes to provide methylenated cycloheptanes are presented.



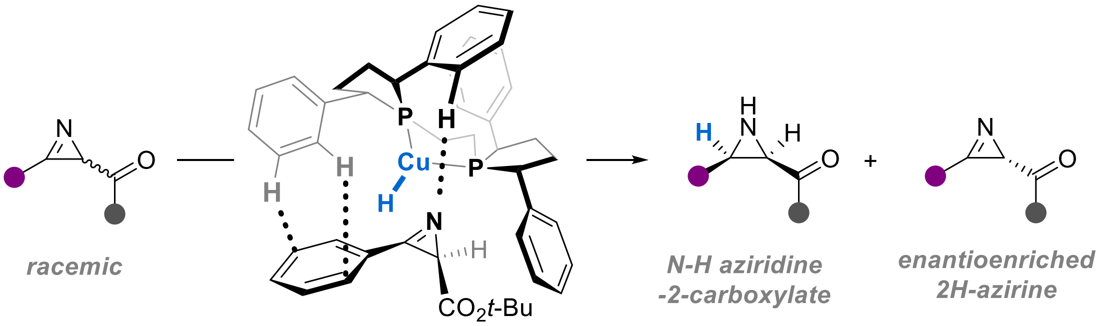
Enantiomerically-enriched Aziridine-2-carboxylates via Copper-catalyzed Reductive Kinetic Resolution of 2*H*-Azirines

Yinuo Zheng, Elvis Wang Hei Ng, Antonio Rizzo,* and Pauline Chiu*

E-mail: anrich@hku.hk, pchiu@hku.hk

Abstract

We present the first reductive kinetic resolution of racemic 2*H*-azirines for securing optically enriched *N*-H aziridine-2-carboxylates, a bench stable and easily diversifiable building block, concomitantly with the corresponding enantiomerically enriched 2*H*-azirines. The *N*-H aziridines were obtained with excellent diastereoselectivity (>20:1) and high enantioselectivity (up to 94%). A Hammett study revealed a linear free energy relationship between the $\Delta\Delta G^{\ddagger}$ of the diastereomeric transition states and the σ_p^- values. DFT calculations and non-covalent interaction analysis suggested that a non-classical H-bonding interaction and edge-to-face aromatic interactions between the substrate and the ligand are responsible for the stereoselectivity and also for the substrate electronic effects observed in the Hammett study.



- *First CuH-catalyzed reduction of an alkyl imine*
- *Diastereoselectivity up to >20:1*
- *Enantioselectivity up to 94% ee*
- *IGMH analysis supports two non-covalent interactions in favored transition state*

Reference

Preprint: Zheng Y, Rizzo A, Chiu P. **2024,** Asymmetric Syntheses of Aziridine-2-carboxylates via Reductive Kinetic Resolution of 2*H*-Azirines. DOI: 10.26434/chemrxiv-2024-7dxzq.

Research Article: submitted.

Utilizing Mechanically Interlocked Catenane for Selective Alkali Metal Cation Binding and Extraction

Mingda Hu, Hang Zhou, and Ho Yu Au-Yeung*

Department of Chemistry, HKU-CAS Joint Laboratory of New Materials, University of Hong Kong, Hong Kong SAR, China

Emile: *hoyuay@hku.hk

Abstract

Catenane ion-hosts enable conformational tuning to achieve size and shape complementarity upon guest binding due to their rotatory motions.[1] To recognize and to separate alkali metal cations, catenanes possessing the varied chain length (**C8**/**C10**/**C12**) have been synthesized based on our previous work.[2] ^{1}H NMR binding studies of three catenanes revealed a preference for binding Li^+ over Na^+/K^+. Importantly, the observed preference for Li^+ binding allows exclusive extraction of Li^+ which is demonstrated by solid–liquid extraction studies. In addition, this series of catenanes will be tested as a potential active carrier to separate alkali metal cations through selective binding and transport across aqueous/organic phases.

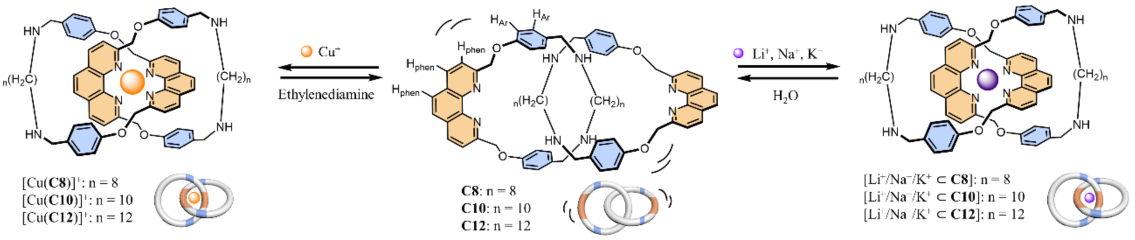


Fig 1. Co-conformational changes of catenane upon binding metal ions.

Reference

1. Y. Yao, Y. Deng, L. Kong and H. Y. Au-Yeung, *Eur. J. Inorg. Chem.*, **2022**, *22*, e202200271.

2. Y. Yao, Y. C. Tse, S. K.-M. Lai, Y. Shi, K.-H. Low, H. Y. Au-Yeung, *Nat. Commun.*, **2024**, *15*, 1952.\

O-to-O Acyl Transfer for Epimerization-free Peptide C-terminal Salicylaldehyde Ester Synthesis

Zhixiang Zhong, Wang Xia, Bing-Wen Li, Han Liu, Zhi-Xiang Yu, and Xuechen Li*
Department of Chemistry, The University of Hong Kong, Hong Kong, China;
xuechenl@hku.hk

Abstract

As the requisite reacting partner of serine/threonine ligation which was developed in 2010 by Li et al., peptide salicylaldehyde esters have been reported to be prepared through different methods towards protein chemical synthesis. Due to the intrinsic epimerization pathway, it is very difficult to achieve direct C-terminal derivatization using side chain protected peptide acids after Fmoc-solid phase peptide synthesis which generally is cost-effective and efficient. In this work, we developed a reagent 2-(dichloromethyl)phenol (DCP) which can directly form peptide salicylaldehyde esters in an epimerization-free manner. The DCP reagent served as the source of highly reactive quinone methide species, which could be trapped by the peptide C-terminal carboxylate to give α-chloroesters, followed by an unprecedented O_{benzylic}-to-O_{phenolic} acyl transfer and Cl^- extrusion. The scope of this method was demonstrated with syntheses of peptide SAL esters of various lengths ranging from 5 to 49 amino acids. The resulting peptide SAL esters were free of epimerization and were successfully applied for the convergent total chemical synthesis of 212-residue linker histone H1.2 protein using serine/threonine ligations.

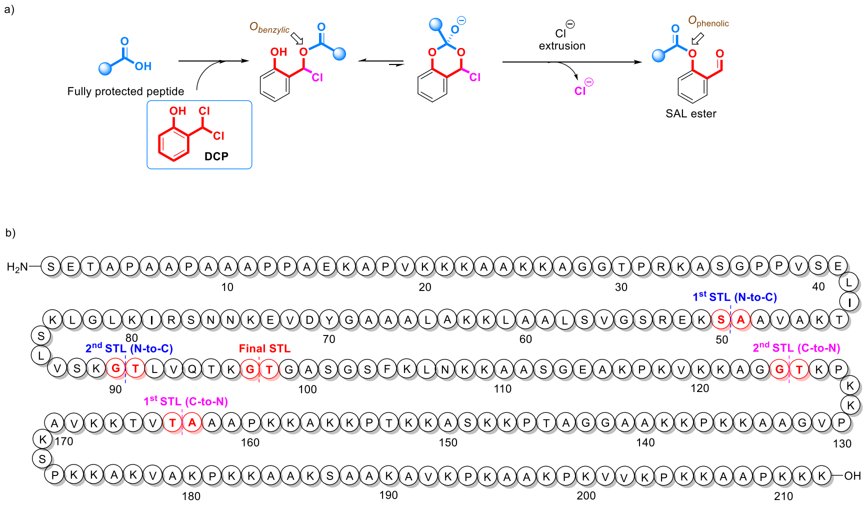


Figure. a) Design of the 2-(dichloromethyl)phenol (DCP) facilitated the salicylaldehyde ester formation. b) Convergent synthesis of Histone H1.2 via serine/threonine ligations.

Reference: X. Li, H. Y. Lam, Y. Zhang, C. K. Chan, Organic Letters 2010, 12, 1724-1727.

Figure-Eight Typed Macrocycle Based Exciplex Complexes with Full-color-tuned Thermally Activated Delayed Fluorescence

Fei Liu, Junzhi Liu
Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The University of Hong Kong Pokfulam Road, Hong Kong (China); E-mail: juliu@hku.hk

Abstract

Thermally activated delayed fluorescence (TADF) materials, as 3rd-generation emitter for organic light-emitting diodes (OLEDs), have rapidly gathering more and more attention in recent years owing to their high internal quantum efficiency (IQE) and low costs (noble metal-free) in comparison with the conventional fluorescent and phosphorescent OLED devices.[1] Among them, supramolecular-based exciplex complexes, relying on the intermolecular charge transfer from host to guest, plays a stronger advantage on the modulation of the superstructures and properties of the materials by taking advantage of dynamic and reversible noncovalent interactions.[2] Herein, we designed and synthesized an unlocked figure-eight typed macrocycle with dynamic assemble behavior and a locked figure-eight typed macrocycle with stable multi-dimensional channel structure as donors to build exciplex complexes with a series of guests with different number of benzene rings and cyano groups. Those complexes achieved full-color-tuned fluorescence emission and the control of TADF.

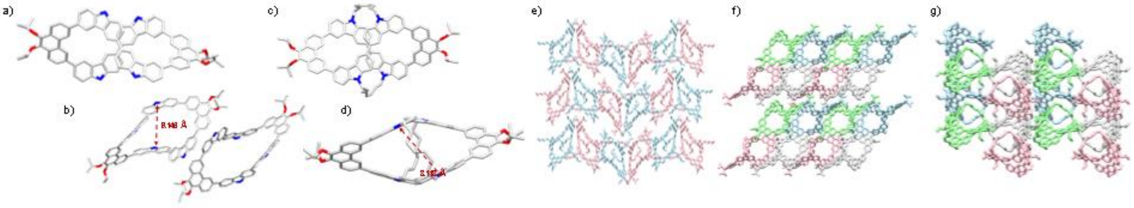
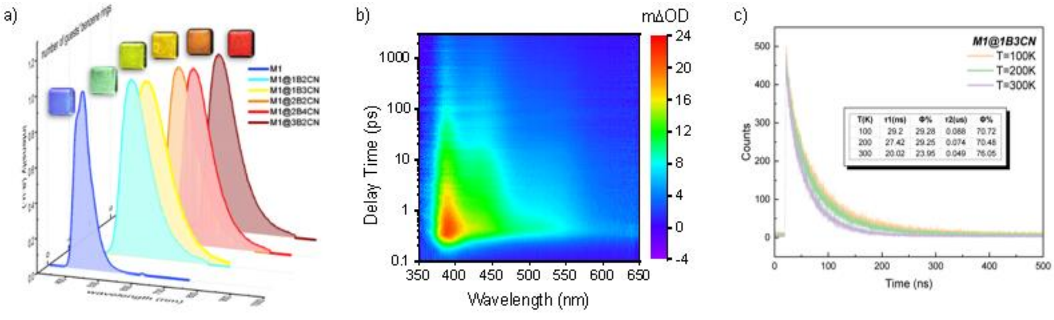


Figure 1. the structure analysis for unlocked/locked figure-eight typed macrocycles



T(K)	τ1(ns)	Φ%	τ2(us)	Φ%
100	29.2	29.28	0.088	70.72
200	27.42	29.25	0.074	70.48
300	20.02	23.95	0.049	76.05

Figure 2. a) the FL spectrum for complexes containing unlocked figure-eight typed macrocycle and different guests, b) transient absorption and c) variable-temperature PL spectrums of a crystalline films containing unlocked figure-eight typed macrocycle and benzene-1,3,5-tricarbonitrile

References

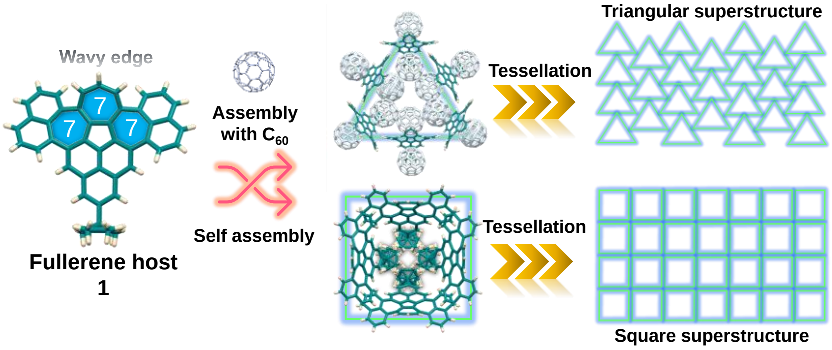
1. Feng, Quanyou, et al. *Advanced Functional Materials* 34.14 (2024): 2312622.
2. Xue, Nan, et al. *Nature Communications* 15.1 (2024): 1425.

Exploring Diverse Supramolecular Tessellation through Hierarchical Assemblies of Non-alternant Nanographene Containing Three Consecutive Heptagons

Jian Sun, Junzhi Liu*
Key Laboratory of Synthetic Chemistry, HKU-CAS Joint Laboratory on New Materials and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong.
juliu@hku.hk

Abstract

Tessellation, as an ancient and captivating mathematical pursuit, has not only captivated mathematicians but has attracted more attention at molecular level[1] in recent years. Exploring tessellation at molecular scale is pivotal for gaining profound insights into the effects of tessellation on materials and elucidating the essential design principles for molecular tessellation as well. In this study, we develop a novel "Janus" type fullerene host (**1**) through rational molecular design, employing three consecutive heptagons to induce distortions[2-3] in the edge. The hierarchical assembled molecular superstructure via co-crystallization of **1** with C_{60} exhibits highly ordered triangular tessellation pattern, which is the first layered tessellated framework in supramolecular chemistry of fullerene. This work not only enriches the development of in-solution supramolecular tessellation but also paves a new way for rational design of tessellated 2D layered molecular materials.



References

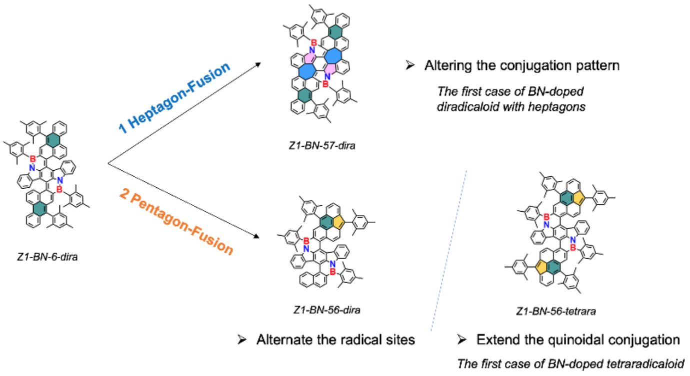
1.Yassine Beldjoudi, J. Fraser Stoddart, *et al. J. Am. Chem. Soc.* 2019, **141**(44) : 17783-17795;
2.Junting Wang, Junzhi Liu, *et al*. *Angew. Chem. Int. Ed.* 2023, **135**(10): e202217124;
3.Chang Wang, Junzhi Liu, *et al*. *Angew. Chem. Int. Ed.* 2023, **62**(35): e202306890;

BN-doped Polyradicaloids toward Photothermal Therapy

Peiyun Zeng[1], Junzhi Liu[1,*]
[1]State Key Laboratory of Synthetic Chemistry, HKU-CAS Joint Laboratory on New Materials and Department of Chemistry, The University of Hong Kong, Hong Kong, China
E-mail: juliu@hku.hk

Abstract

Boron, nitrogen (BN)-doped diradicals represent a unique class of organic compounds, characterized by their open-shell[1] electronic structure and fascinating optoelectronic properties. The incorporation of boron atoms within the molecular framework imparts peculiar characteristics to these compounds[2], allowing them to have numerous potential applications. Here, we synthesized BN-doped diradicaloids and tetraradicaloids, also changed their conjugation system by fusing heptagons to form another diradicaloids, thereby enhancing the near-infrared absorbing. Experimental and theoretical results show that BN-doped diradicals have extremely narrow energy gaps and have dramatically strong absorption in the near-infrared region. These open-shell compounds can coordinate with water-soluble polymer to form nanoparticles with excellent photothermal conversion efficiency, which can be used to ablate tumor cells.



References

1. Fei, Y.; Liu, J. *Adv. Sci.* **2022**, 9: 2201000.
2. Luo H.; Wan, Q.; Choi, W.; Tsutsui, Y.; Dmitrieva, E.; Du L.; D.; Phillips, D. L.; Seki S.; Liu, J. *Small*. **2023**, 2301769.

Triplet-Ground-Stated Nonalternant Nanographene with Exceptional Stability and Long Spin Lifetimes

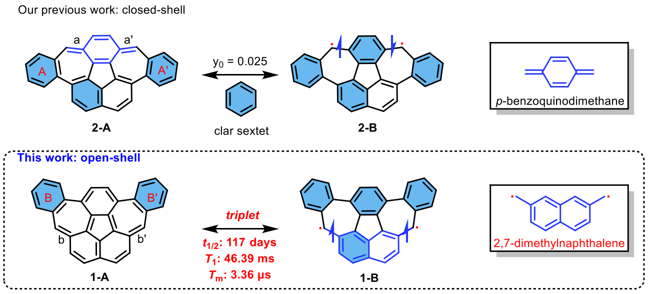
Weixiang Zhou[1], Yiyang Fei[1], Yu-Shuang Zhang[2], Xiaohe Miao[3], Shang-Da Jiang[2] and Junzhi Liu[1,4]

[1]Key Laboratory of Synthetic Chemistry, HKU-CAS Joint Laboratory on New Materials and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, China [2]Spin-X Institute, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou, China [3]Instrumentation and Service Center for Physical Sciences, Westlake University, Hangzhou, China

[4]Lead contact

Corresponding Author E-mail: juliu@hku.hk

Abstract: Carbon-based polyradicals with high-spin states hold promise for applications in quantum information storage and sensing. However, their practical use is limited by structural diversity and chemical instability. Here, we present a facile synthetic method for preparing a nonalternant nanographene (**1**) with a triplet ground state. Departing from the conventional m-xylylene scaffold, we introduce seven-five-seven (7–5–7)-membered rings combining with 2,7-dimethylnaphthalene subunit to create novel and remarkably stable high-spin diradicals with half-lives ($t_{1/2}$) of up to 117 days. Compound **1** exhibits long spin relaxation, with a spin–lattice relaxation time (T_1) of 46.39 ms and a coherence time (T_m) of 3.36 μs at 10 K, indicating its potential for spin-based information retention and quantum computing applications.



References

1. Fei Y, Fu Y, Bai X, Du L, Li Z, Komber H, *et al. J. Am. Chem. Soc.* 2021, **143**(5)**:** 2353-2360.

Bi(III) complexes as antibiotics adjuvants against *P. aeruginosa*

Chun Lung Chan[1], YuShan Xia [1], XueYing Wei [1], Hongyan Li[1], Hongzhe Sun[1,*]
Department of Chemistry, The University of Hong Kong
Email: u3532614@connect.hku.hk

Abstract

P. aeruginosa was listed as top priority in WHO list of "priority pathogens" for R&D of new antibiotics[1]. Due to its intrinsic resistance to many antibiotics and strong acquired resistance, it nearly resistance to all antibiotics[2].

Fortunately, our group previously found out that existing FDA approved Bi(III) drug do have good synergy to many antibiotics against. *P. aeruginosa* which can improve MICs of macrolides by 64 times[3], this Bi(III) adjuvants was also effective under the influences if biofilm[4].

However, the best structure for such purpose was still unknown. We then synthesized more than 70 Bi(III) complexes with various binding motifs. We found that Bi-thiolate, Bi-carboxylate and Bi-pyridine have a FIC <0.25 for the fluoroquinolones, macrolides and tetracyclines in PAO1 with $Bi(bpy)_2(OTf)_3$ showed the lowest FICs which can improve the MICs of tetracyclines and macrolides by 256-1024 times with just 8μM of Bi(III) complexes required, as a result, macrolides which originally resisted by *P. aeruginosa* can be potent antibiotics with Bi(III) as adjuvants.

To find out the molecular targets of Bi(III) drugs, a biotin based probe consist of a biotin, a photo-crosslinker and a nitriloacetic acid act as Bi(III) chelator as then designed, synthesized and characterized. With the use of such probe, 26 proteins was identified as Bi(III) target in *P. aeruginosa*, which provided cues that how Bi(III) can assist antibiotics entry, against biofilm formation so as slow down the resistance development of antibiotics.

References

1. WHO (27 February 2017). WHO "priority pathogens" for R&D of new antibiotics.
2. CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019
3. Xia, Y., Wei, X., Gao, P., Wang, C., Sun, H. *et al.* Bismuth-based drugs sensitize Pseudomonas aeruginosa to multiple antibiotics by disrupting iron homeostasis. *Nat Microbiol* **9**, 2600-2613 (2024).
4. Wang, C., Xia, Y., Wang, R., Li, J., Kao, RYT., Ho, P., Toy, PH., Sun, H. *et al.* Metallo-sideromycin as a dual functional complex for combating antimicrobial resistance. *Nat Commun* **14**, 5311 (2023)

Bi(III) disrupts glycolysis to "turn off" the regulator of virulence of *Streptococcus pyogenes*

Jingru LI, Peng GAO, Hongyan LI and Hongzhe SUN
The University of Hong Kong, Pokfulam Road, Hong Kong, P.R.China;
jingru97@connect.hku.hk

Abstract

Streptococcus pyogenes (*S. pyogenes*) as one of the major human-specific bacterial pathogens, causing common infective diseases such as pharyngitis to severe infections including necrotizing fasciitis[1]. Bi(III) drug, well-known for anti- *Helicobacter pylori* (*H. pylori*) activity with extremely low toxicity to human body, were found to be effective in eradicating *S. pyogene*. with the lowest MIC value of 0.5 μM (BiBen), comparable to its first-line antibiotic. Apart from antibacterial activity, Bi(III) (BiBen) also demonstrated excellent anti-virulence ability against *S. pyogenes*, inhibiting 77.57% of leucotoxicity and 38.99% of hemolysis at very low concentration (0.0625 μM), being indicative of good potential to serve as virulence inhibitor. Through employing RNA-seq, several key genes, e.g. *ptsG, scrK* and *fruK,* were differentially regulated by Bi(III). Metabolites related to these genes, i.e. FBP and G6P, and glucose were supplemented with Bi(III) and successfully rescued *S. pyogenes* from the inhibitory concentration of Bi(III), confirming the important roles of carbohydrate in mode of action of Bi(III). Besides, low levels of F6P and G6P and the inhibited enzymatic activity of 1-PFK led to low level of FBP induced drastic down-regulation in expression of global regulator, *rgg3,* indicating that Bi(III)-induced low level of carbohydrate can significantly "turn off" the expression of this regulator to inhibit virulence.

Reference

1.Tyrrell, G. J.; Bell, C.; Bill, L.; Fathima, S. *Emerg Infect Dis,* **2021,** *27,* 443-451.

Designing Chelators and Complexes for Bismuth

Jamie Guan-Tai Lok[1], Abhisek Bhattarai[2], Varut Vardhanabhuti[2], Hongzhe Sun[1]
[1]Department of Chemistry and [2]Department of Diagnostic Radiology, The University of Hong Kong, Pokfulam, Hong Kong. Email: jamielok@connect.hku.hk

Abstract

Bismuth (Bi) is considered an intermediate (borderline) metal in HSAB theory[1]. As such, ligands and chelators can be tailored to tune the hardness/softness of the coordinating atoms so desired medicinal properties can be optimised. For example, bismuth has high X-ray attenuation, low toxicity, high abundance, and low cost, making it a great candidate for CT contrast agents, in particular for difficult targets such as in cases of osteoarthritis (OA)[2]. Thus, modifying functional groups on chelators to design bismuth-specific X-ray CT contrast agents with favourable safety profiles, biodistribution and targeting properties for fast, deep cartilage imaging in OA will improve the diagnostic efficacy[3]. Herein, ligands and chelators were designed for bismuth coordination and applied to X-ray CT cartilage imaging as well as antibacterial screening. Initial bismuth complexes displayed effective CT imaging ability and low toxicity, but limited water solubility and stability, with newer iterations overcoming these drawbacks.

References

[1] D. M. Griffith, H. Li, M. V. Werrett, P. C. Andrews and H. Sun, *Chem Soc Rev* **2021**, *50*, 12037-12069.

[2] A. Bhattarai, J. G. Lok, H. Sun and V. Vardhanabhuti, *Ann Biomed Eng* **2023**, *51*, 977-986.

[3] B. M. Yeh, P. F. FitzGerald, P. M. Edic, J. W. Lambert, R. E. Colborn, M. E. Marino, P. M. Evans, J. C. Roberts, Z. J. Wang, M. J. Wong and P. J. Bonitatibus, Jr., *Adv Drug Deliv Rev* **2017**, *113*, 201-222.

Construction of Holomycin Conjugates as Hybrid Dual-acting Antibiotics to Overcome Bacterial Intrinsic Resistance

Liang Zhong, Hongzhe Sun*
Department of Chemistry, The University of Hong Kong; hsun@hku.hk

With the emergence of multidrug-resistant bacteria, antibiotics that target a single site are no longer effective in combating rapidly mutating bacterial strains. Compared to traditional antimicrobial agents, holomycin exhibits potent broad-spectrum, multi-target inhibitory activity against bacteria[1,2]. Furthermore, holomycin containing dithiolopyrrolone is a potential vector for elevating the payload accumulation in the bacterial cells through thiol-mediated uptake[3]. Despite its excellent antibacterial activity and drug delivery potency, the application of holomycin has been hindered by attendant toxicity[2]. In this talk, based on previous attempts with aim of improving selectivity between batciera and mammalian cells by means of conjugating mono/bis-catecholate siderophore [4], Our focus will be placed on the conjugation of known antibiotics, such as sulfonamides, with holomycin as a dual-acting antibacterial agents to overcome antimicrobial resistance.

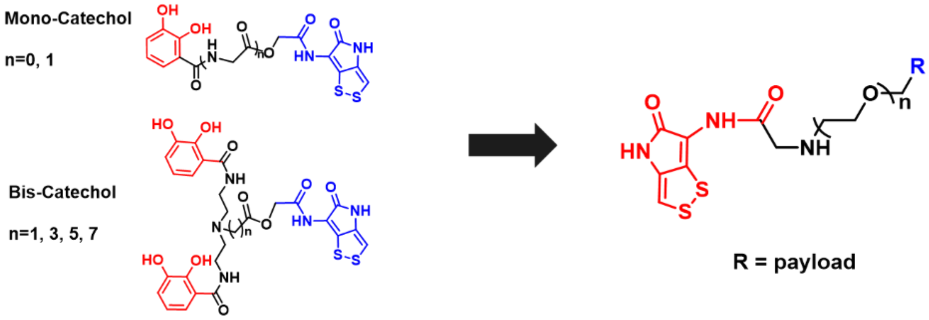


Fig 1. Generalized sideromycins (*left*) and new designs of dual-acting antibiotics (*right*)

We thank the Research Grants Council (R7070-18, 17308921, 17318322, 2122-7S04) and the University of Hong Kong financial support.

References

1. Li, B.; Wever, W. J.; Walsh, C. T.; Bowers, A. A. *Nat Prod Rep*, **2014**, *31*, 905-923.
2. Chan, A. N.; Shiver, A. L.; Wever, W. J.; Razvi, S. Z.; Traxler, M. F.; Li, B. *Proc Natl Acad Sci*, **2017**, 114, 2717-2722.
3. Johnson, R. M.; Li, K.; Chen, X.; Morgan, G. L.; Aubé, J.; Li, B. *ACS Infect Dis*, **2024**, 10, 582–593.
4. Miller, M. J.; Liu, R. *Acc Chem Res*, **2021**, *54*, 1646–1661.

Protonic Nanoenvironment Engineering for Tuning the Electrocatalytic Efficiency and Product Selectivity of O_2 Reduction

Yau Hei Tung

htyau@connect.hku.hk

Abstract

Precise control over oxygen reduction reaction (ORR) catalysts is essential in proton-exchange membrane (PEM) fuel cells. This study introduces a hybrid bilayer membrane (HBM) featuring a self-assembled monolayer (SAM) with a custom tridentate ligand, 2,2’:6’,2’’-terpyridine-4’-oxy-hexane-1-thiol (TPY), which hosts Cu(II), Ni(II), and Mn(II), forming M-TPY SAMs.[1] Integrating a lipid monolayer and proton carriers (PC) onto M-TPY SAM regulates proton transfer kinetics, which alters both ORR activity and selectivity. Additionally, the variations in ORR performance between M-TPY SAM are attributed to the formation of distinct M–O intermediates. These insights into proton-coupled electron transfer (PCET) pathways offer potential improvements for electrocatalysts in renewable energy applications.

References

Yau, H. T.; Yu, Z. H.; Tse, E. C. M. *Inorg. Chem. Front.*, **2023**, *10*, 7308 – 7318

Thermo-Responsive Platinum(II) Complexes with Unusual Aggregation Behavior upon Heating

Tracy Ho-Ying Chan, Ziyong Chen, Ming-Yi Leung, Michael Ho-Yeung Chan, Eric Ka-Ho Wong, Wai Kit Tang, Vivian Wing-Wah Yam*
Institute of Molecular Functional Materials and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China
E-mail: wwyam@hku.hk

Abstract

A series of alkynylplatinum(II) complexes with tridentate *N*-donor ligand has been synthesized and characterized by ^{1}H NMR spectroscopy, HR-ESI mass spectrometry, elemental analysis and X-ray crystallography, and their photophysical properties have also been investigated. Interestingly, the complexes have been found to exhibit drastic color changes with absorption maxima extended to the longer-wavelength region upon increasing temperature. Transmission electron microscopy (TEM) and variable-temperature ^{1}H NMR spectroscopy suggest the association of such color change with a thermo-responsive morphological transformation behavior from rods at room temperature to ring-like aggregates at high temperature. Such ring-like aggregates, which are not observed in the reference control complexes, are formed via the preferential formation of □□□□and Pt···Pt interactions at high temperature, as supported by spectroscopic and computational studies. This unusual optical and morphological transformations are rarely observed, as it represents a stark contrast to the deaggregation behavior upon increasing temperature typical of the control and commonly found platinum(II) complexes and organic compounds.

Two-Component Co-Assembly of Platinum(II) Complexes and Block Copolymers

Priscilla Lok-Yi Chiu, Kaka Zhang, Michael Ho-Yeung Chan and Vivian Wing-Wah Yam*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China
Email: wwyam@hku.hk

Abstract

The co-assembly of anionic alkynylplatinum(II) terpyridine (tpy) or bis(benzimidazol-2-yl)pyridine (bzimpy) complexes with poly(ethylene glycol)-*b*-poly(2-(dimethylamino)ethyl methracrylate) (PEG-*b*-PDMAEMA) diblock copolymers in aqueous solution has been studied. The electrostatic interaction between platinum(II) complexes and the PDMAEMA block of PEG-*b*-PDMAEMA brings the platinum(II) complexes into close proximity. The Pt···Pt and/or π–π stacking interactions favour directional stacking and growth of the platinum(II) complexes in the aggregates, resulting in anisotropic supramolecular nanostructures, together with observable changes in the spectroscopic and luminescence properties. The morphology of the nanostructures can be modulated by varying the composition and incubation condition of the system, such as structural parameters of polymers and complexes, as well as complex/polymer feed ratios. This work demonstrates the potential of multi-component co-assembly as a plausible strategy for the preparation of programmable supramolecular nanostructures.

Supramolecular Co-Assembly of Luminescent Platinum(II) Complexes and Block Copolymers

Ki Ip, Zhen Geng, Eric Ka-Ho Wong, and Vivian Wing-Wah Yam*
Institute of Molecular Functional Materials, State Key Laboratory of Synthetic Chemistry and
Department of Chemistry, The University of Hong Kong,
Pokfulam Road, Hong Kong, P. R. China
*E-mail: *wwyam@hku.hk*

Abstract

Platinum(II) complexes have been known for their rich photophysical properties and intriguing supramolecular assembly. In recent years, two-component supramolecular co-assembly of cationic platinum(II) complexes and anionic polyelectrolyte-containing block copolymers has been studied. Cationic platinum(II) polypyridine complexes have been found to interact with the anionic poly(acrylic acid) (PAA) block of the diblock copolymers via electrostatic interaction to form water-soluble and crystalline core-shell nanofibers, which consist of a core with hexagonally packed columns of platinum(II) complexes and PAA blocks and a solvated shell of poly(ethylene glycol) (PEG) blocks. Herein, a series of isocyano platinum(II) complexes has been synthesized and their supramolecular co-assembly with PEG-*b*-PAA has been investigated. Drastic spectroscopic changes have been observed upon the supramolecular co-assembly of platinum(II) complexes and block copolymers, directed by non-covalent metal–metal and/or π–π interactions. Results from electron microscopy revealed the formation of nanofibers and nanoribbons.

Thermally Activated Delayed Fluorescence and Thermally Stimulated Delayed Phosphorescence Gold(III) Complexes for Organic Light-Emitting Devices

Wing-Kei Kwok,[a] Cathay Chai Au-Yeung,[a] Chin-Ho Lee,[a] Ming-Yi Leung,[a] Shiu-Lun Lai,[a] Man-Chung Tang,[a] Shun-Cheung Cheng,[b] Wai-Lung Cheung,[a] Chi-Chiu Ko,*[b] Mei-Yee Chan,[a] Vivian Wing-Wah Yam*[a]

[a] *Institute of Molecular Functional Materials, Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong (P. R. China); Email: wwyam@hku.hk*

[b] *Department of Chemistry, City University of Hong Kong, Kowloon, Hong Kong (P. R. China) Email: vinccko@cityu.edu.hk*

Abstract

Several new classes of tetradentate C^C^N^N and tridentate C^N^C ligand-containing gold(III) complexes have been designed and synthesized. Manipulation of the nature and energy of the excited states has empowered the complexes with thermally activated delayed fluorescence (TADF) and/or thermally stimulated delayed phosphorescence (TSDP) properties. High photoluminescence quantum yields of up to 0.83 and large radiative decay rate constants in the orders of 10^5 s^{-1} in solid-state thin film have been achieved. The TADF and/or TSDP properties are probed by transient absorption spectroscopy, time-resolved, and temperature-dependent emission spectroscopy. In particular, the direct observation of the reverse intersystem crossing and reverse internal conversion processes and the determination of the activation barriers are achieved in the variable-temperature fs-transient absorption spectroscopic studies. High external quantum efficiencies of >15% have been achieved in both solution-processed and vacuum-deposited organic light-emitting devices.

References

1. Kwok, W.-K.; Li, L.-K.; Lai, S.-L.; Leung, M.-Y.; Tang, W. K.; Cheng, S.-C.; Tang, M.-C.; Cheung, W.-L.; Ko, C.-C.; Chan, M.-Y.; Yam, V. W.-W., *J. Am. Chem. Soc.* **2023**, *145*, 9584.
2. Au-Yeung, C. C.; Leung, M.-Y.; Lai, S.-L.; Cheng, S.-C.; Li, L.-K.; Tang, M.-C.; Kwok, W.-K.; Ko, C.-C.; Chan, M.-Y.; Yam, V. W.-W., *Mater. Horiz.* **2024**, *11*, 151.
3. Lee, C.-H.; Tang, M.-C.; Leung, M.-Y.; Cheng, S.-C.; Wong, G. Y.-P.; Cheung, W.-L; Lai, S.-L.; Ko, C.-C.; Chan, M.-Y.; Yam, V. W.-W., *Adv. Opt. Mater.* **2024**, 2401841.

Supramolecular Assembly of Amphiphilic Platinum(II) Schiff Base Complexes: Diverse Spectroscopic Changes and Nanostructures Through Rational Molecular Design and Solvent Control

Huilan Zhang,[ab] Michael Ho-Yeung Chan,[b] Jonathan Lam,[b] Ziyong Chen,[b] Ming-Yi Leung,[b]
Eric Ka-Ho Wong,[b] Lixin Wu[a] and Vivian Wing-Wah Yam[ab]

a. State Key Laboratory of Supramolecular Structure and Materials, College of
Chemistry, Jilin University, Changchun 130012, P. R. China.
E-mail: wwyam@hku.hk, wulx@jlu.edu.cn

b. Institute of Molecular Functional Materials, Department of Chemistry, The
University of Hong Kong, Pokfulam Road, Hong Kong SAR, P. R. China.
E-mail: wwyam@hku.hk

Abstract

A new class of amphiphilic tetradentate platinum(II) Schiff base complexes has been designed and synthesized. The self-assembly properties by exploiting the potential Pt···Pt interactions of amphiphilic platinum(II) Schiff base complexes in the solution state have been systematically investigated. The presence of Pt···Pt interactions has further been supported by computational studies and non-covalent interaction (NCI) analysis of the dimer of the complex. The extent of the non-covalent Pt···Pt and π–π interactions could be regulated by a variation of the solvent compositions and the hydrophobicity of the complexes, which is accompanied by attractive spectroscopic and luminescence changes and leads to diverse morphological transformations. The present work represents a rare example of demonstration of directed cooperative assembly of amphiphilic platinum(II) Schiff base complexes by intermolecular Pt···Pt interactions in solution with an in-depth mechanistic investigation, providing guiding principles for the construction of supramolecular structures with desirable properties using platinum(II) Schiff base building blocks.

References

Zhang, H.; Chan, M. H.-Y.; Lam, J.; Chen, Z.; Leung, M.-Y.; Wong, E. K.-H.; Wu, L.; Yam, V. W.-W. *Chem. Sci.*, **2024**, *15*, 8545−8556.

Design and Synthesis of Luminescent Gold(III) C^N^C Complexes

Pamela Audrey Lie, Wing-Kei Kwok, Vivian Wing-Wah Yam*

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China

E-mail: wwyam@hku.hk

Abstract

The locked conformation of cyclometalated C^N^C arylgold(III) complexes arising from the inherent steric effects helps to suppress excimeric emission, as well as inhibit non-radiative decay pathways. In this study, a series of arylgold(III) complexes has been designed and synthesized, focusing on the effects of structural modifications to the aryl auxiliary ligand. Rigidification of the molecular structure is achieved by modification of the aryl ligands to increase the photoluminescence quantum yield (PLQY). The photophysical properties, as revealed from the UV-vis and emission spectroscopy, have been studied. In addition, the electrochemical properties have been investigated by means of cyclic voltammetry. Green-emitting arylgold(III) complexes with high PLQYs doped in mCP thin films have been achieved. It is envisaged that this class of arylgold(III) complexes are suitable candidates for various photofunctional applications.

Ensembles of PFP-NMe_3^+ and Anionic Platinum(II) Complexes: From FRET Properties to Application Studies in Pathogen Imaging and Photodynamic Therapy

Angela Lok-Yin So[a], Jungu Guo[a], Huanxiang Yuan[b], Qi Shen[b], Eric Ka-Ho Wong[a], Shu Wang[b]* and Vivian Wing-Wah Yam[a]*

[a]Institute of Molecular Functional Materials and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, PR China.

[b]Beijing National Laboratory for Molecular Sciences, Key Laboratory of Organic Solids, Institute of Chemistry, Chinese Academy of Sciences, Beijing, PR China.

E-mail: wwyam@hku.hk; wangshu@iccas.ac.cn

Abstract

A series of anionic platinum(II) complexes has been synthesized and characterized. The complexes are found to form ensembles with a cationic poly(fluorene-*co*-phenylene) derivative (PFP-NMe_3^+) through electrostatic, Pt(II)···Pt(II) and π–π stacking interactions. Förster resonance energy transfer (FRET) has been found to take place and consequently gave rise to fluorescence quenching of the polymer donor and a growth of low-energy emission from the platinum(II) complex assemblies. The spectroscopic and FRET properties of the two-component systems have been investigated by UV–vis absorption, emission and Stern–Volmer quenching studies. Pathogen imaging and photodynamic therapy (PDT) studies by the polymer–platinum(II) complex ensembles with better performance compared to PFP-NMe_3^+ have been demonstrated in this work, which highlights the potential of this class of ensembles in achieving various biological applications.

Acknowledgements

This work was supported by CAS-Croucher Funding Scheme for Joint Laboratories on Molecular Functional Materials for Electronics, Switching, and Sensing.

Stimuli-Induced Reversible Transformation between Decanuclear and Pentanuclear Gold(I) Sulfido Complexes

Liang-Liang Yan, Ho Chuen Wan and Vivian Wing-Wah Yam*
Institute of Molecular Functional Materials and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China
E-mail: wwyam@hku.hk

Abstract

Decanuclear gold(I) sulfido clusters of phenanthrene-, dibenzothiophene- and carbazole-based diphosphine ligands were synthesized and characterized. Unprecedented stimuli-induced reversible transformation between decanuclear and pentanuclear gold(I) sulfido complexes was observed, which could be readily monitored by NMR and UV−vis absorption spectroscopy in solution. Remarkably, the decanuclear gold(I) sulfido complex (**Au_{10}-L^{Ph}**) was found to show a highly reversible transformation process, which is stable for over 10 successive cycles in solution. The stimuli-induced reversible transformation behavior of the gold(I) sulfido complexes was found to depend on the P−P bite distance of the bidentate phosphine ligands.[1]

Reference

1. Yan, L.-L.; Yao, L.-Y.; Ng, M.; Tang, W. K.; Leung, M.-Y.; Yam, V. W.-W.; *J. Am. Chem. Soc.*, **2022**, *144*, 19748–19757.

Effects of Length Alteration of OPE-Containing Mono- and Dinuclear Alkynylplatinum(II) Terpyridine Complexes on Photophysical, Structural and Morphological Properties

Jason Koon-Lam Poon, Sammual Yu-Lut Leung, Eric Ka-Ho Wong, and Vivian Wing-Wah Yam*
Institute of Molecular Functional Materials, State Key Laboratory of Synthetic Chemistry and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China
E-mail: wwyam@hku.hk

Abstract

A series of mononuclear complexes and unsymmetric dinuclear alkynylplatinum(II) terpyridine complexes with oligo(*para*-phenylene ethynylene) (OPE)-derived backbone with a variation of the lengths of alkoxy chains and OPE backbones was synthesized. The morphological properties, packing lattice and gelation behaviors of the mononuclear complexes were systematically studied, and the thermodynamic parameters and packing lattices of the dinuclear complexes were also investigated, providing further insights into the roles of the non-covalent interactions and their delicate balance in constructing sophisticated supramolecular architectures. Metallogel and nanotube formation have been observed upon a delicate control of the intermolecular interactions by altering the lengths and structural dimensions of the complexes.[1]

Reference

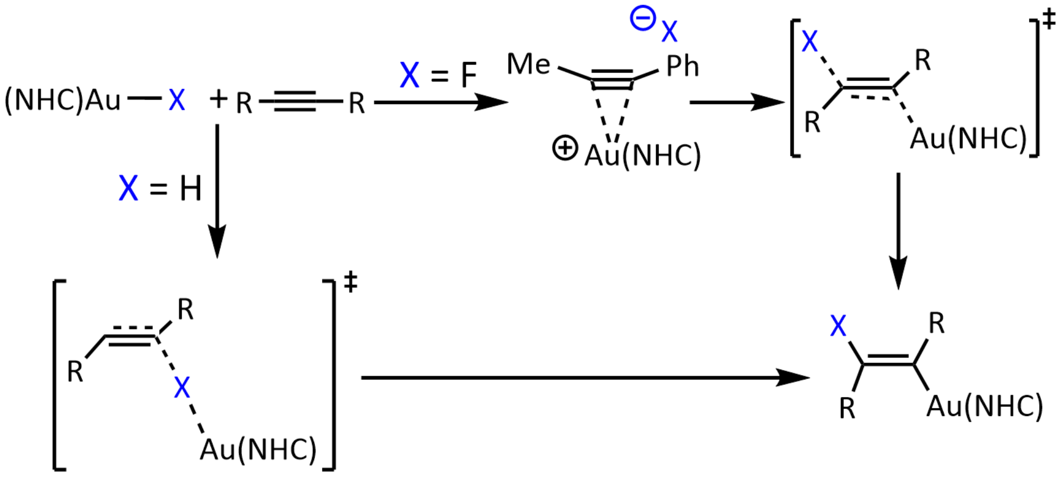
1. Poon, J. K.-L.; Leung, S. Y.-L.; Wong, E. K.-H.; Yam, V. W.-W., *Nano. Res.*, **2024**, *17*, 8893–8903.

Understanding the Reaction Mechanism of *anti*-Addition of (NHC)Au(I)-H and (NHC)Au(I)-F across Alkyne

Wing Chun Chan, and Zhenyang Lin*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, Hong Kong, P. R. China
Email: chzlin@ust.hk

Abstract

The experimentally observed *anti*-addition reactions of (NHC)Au(I)-H with dimethyl acetylenedicarbonxylate (DMAD) MeOOCC≡CCOOMe and (NHC)Au(I)-F with phenylacetylene MeC≡CPh are intriguing and deserve more in-depth study. In this work, with the aid of density functional theory (DFT) calculations and intrinsic bond orbital (IBO) analysis, we systematically investigated the addition reactions of (NHC)Au(I)-X (X = H, Me and halides) with different alkynes. The detailed reaction mechanisms obtained lead to an in-depth understanding of these reactions.



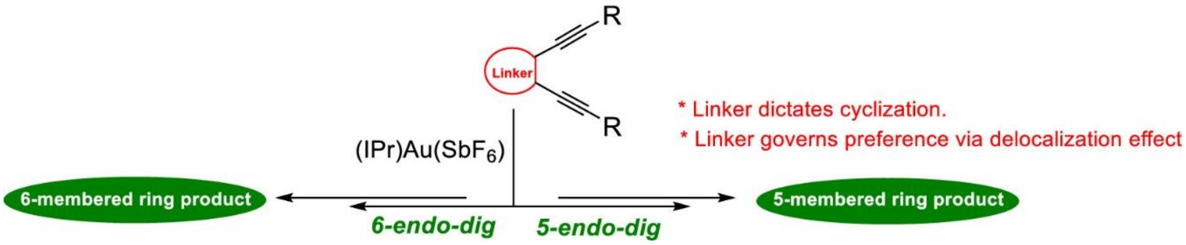
Same stereoselectivity, different mechanism!

Cyclization Reactions of 1,5-Diynes: Mechanisms and the Role of the Central Linker

Farshad Shiri, and Zhenyang Lin*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, Hong Kong, P. R. China
Email: chzlin@ust.hk

Abstract

This study employed computational methods to elucidate the influence of structural features on the cyclization pathways of 1,5-diynes through the 5-endo-dig and 6-endo-dig mechanisms. The results revealed that the nature of the central linker played a significant role in dictating the preferred cyclization pathway. Notably, the capacity of this linker to extend delocalization appears to be the key factor governing the reaction pathway preference.



Investigating Short-Chain Acids as Surface Ligands in Photoinduced Charge Transfer Dynamics of CsPbBr3 Perovskite Nanocrystals

KUMAR Nitish, Prof. Jonathan E. HALPERT*

Department of Chemistry, The Hong Kong University of Science and Technology,

Kowloon, Hong Kong SAR, China

E-mail: jhalpert@ust.hk

Abstract

Perovskite nanocrystals (PNCs) are typically capped with insulating ligands such as oleic acid and oleylamine to improve their stability and optical properties. However, these ligands hinder charge transport across the PNC surface, limiting their utility in device applications. In this study, we explore the effects of post-treating $CsPbBr_3$ PNCs with short-chain ligands, specifically benzoic acid (BA) and ascorbic acid (AA). Both BA- and AA-treated PNCs exhibit enhanced stability and optical properties compared to untreated PNCs. Notably, BA-treated PNCs demonstrate superior charge transport rates due to the conjugated nature of BA, as evidenced by photoelectrochemical measurements showing more efficient electron flow across the PNC surface. Additionally, BA-treated PNCs exhibit longer carrier lifetimes and faster charge transfer kinetics, making them promising candidates for real-world device applications.

References

1. Biswas, S., Akhil, S., Kumar, N., Palabathuni, M., Singh, R., Dutt, V.G.V., Mishra, N., 2023. J. Phys. Chem. Lett. 14, 1910–1917.

2. Ko, P.K., Ge, J., Ding, P., Chen, D., Tsang, H.L.T., Kumar, N., Halpert, J.E., n.d. Adv. Mater. n/a, 2407764.

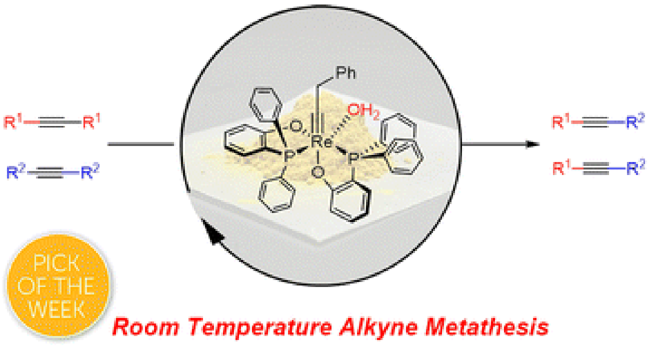
Exploring efficient and air-stable d Re(v) alkylidyne catalysts: toward room temperature alkyne metathesis

Mingxu Cui,[†] Jie Huang,[†] Long Yiu Tsang, Herman H. Y. Sung, Ian D. Williams,* Guochen Jia*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China; Email: chjiag@ust.hk

Abstract

Transition metal-catalyzed alkyne metathesis has become a useful tool in synthetic chemistry. Well-defined alkyne metathesis catalysts comprise alkylidyne complexes of tungsten, molybdenum and rhenium. Non-d^0 Re(V) alkylidyne catalysts exhibit advantages such as remarkable tolerance to air and moisture as well as excellent functional group compatibility. However, the known Re(V) alkylidynes with a pyridine leaving ligand require harsh conditions for activation, resulting in lower catalytic efficiency compared to d^0 Mo(VI) and W(VI) alkylidynes. Herein, we report the first non-d^0 alkylidyne complex capable of mediating alkyne metathesis at room temperature, namely, the Re(V) aqua alkylidyne complex $Re(\equiv CCH_2Ph)(^{Ph}PO)_2(H_2O)$. The aqua complex readily dissociates a water ligand in solution, confirmed by ligand substitution reactions with other σ-donor ligands. The aqua complex can be readily prepared on a large scale, and is stable to air and moisture in the solid state and compatible with a variety of functional groups. The versatile ability of the catalyst has been demonstrated through examples of alkyne cross-metathesis (ACM), ring-closing alkyne metathesis (RCAM), and acyclic diyne metathesis macrocyclization (ADIMAC) reactions.



Room Temperature Alkyne Metathesis

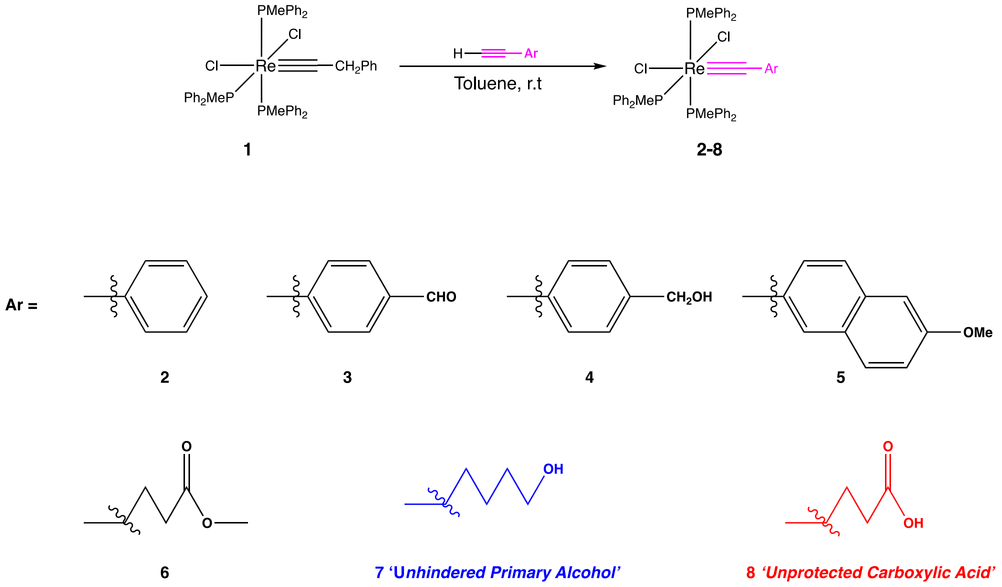
Metathesis Reactions of Re(V) carbyne complex with terminal aryl and aliphatic alkynes

Byeongsoo Park, Wei Bai, Lam Cheung Kong, Herman H. Y. Sung, Ian D. Williams and Guochen Jia*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China. Email: chjiag@ust.hk

Abstract

Alkyne metathesis is finding growing practical applications in areas such as organic synthesis, polymerization as well as dynamic covalent chemistry, typically using internal alkynes as the starting materials. Terminal alkynes are common reagents for organic synthesis¸ and therefore are also attractive substrates for alkyne metathesis reactions. However, their metathesis reactions are rare. To address this limitation, we have studied reactions of low valent (non-d^0) carbyne complexes with terminal alkynes. The d^2 Re (V) carbyne complexes $Re(\equiv CR)Cl_2(PMePh_2)_3$ were found to undergo stoichiometric metathesis reactions with a wide range of terminal aryl and aliphatic alkynes $HC\equiv CR'$ to selectively give substituted carbyne complexes $Re(\equiv CR')Cl_2(PMePh_2)_3$ and $HC\equiv CR$. The metathesis reactions exhibit a wide substrate scope and are compatible with challenging function groups such as aldehyde, alcohol, ester, and even unprotected carboxylic acid groups. Density Functional Theory (DFT) calculations suggest that the formation of substituted carbyne complexes is both thermodynamically and kinetically more favorable than the formation of methylidyne complexes.

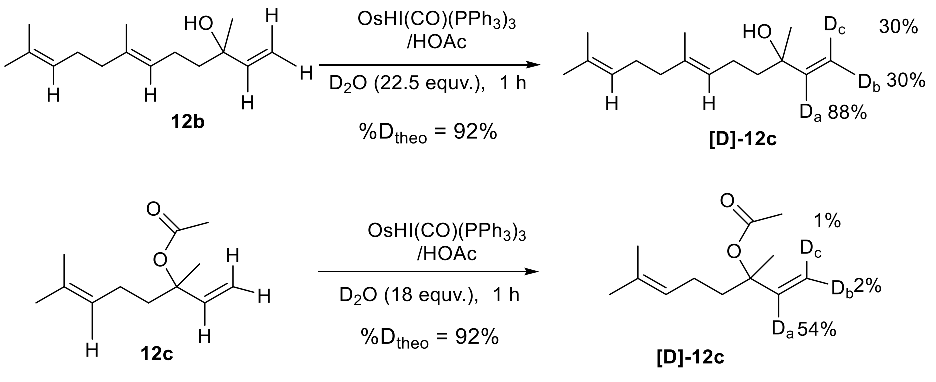


Selective deuteration of terminal olefins with D_2O by catalysis of osmium-hydride complexes

Wenwei Qin, Herman H. H. Sung, Ian D. Williams and Guochen Jia*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, People’s Republic of China

Abstract.

An efficient catalytic system for selective deuteration of terminal olefins using D_2O as the deuterium source has been developed. A series of osmium hydride complexes of the type $OsHX(CO)(PR_3)_2(L)$ (where represents halides) has been evaluated as catalyst precursors for H/D exchange between olefins and D_2O. The catalytic activity of the complexes were found to depend on the ligands present. Among the complexes tested, the complex $OsHI(CO)(PPh_3)_3$ exhibited excellent catalytic activity for the hydrogen-deuterium (H/D) exchange of terminal olefins with D_2O, especially in the presence of acetic acid. The system shows high selectivity for deuteration at terminal double bonds over internal ones. It can catalyze H/D exchange reactions of olefins without causing isomerization, and can induce selective H/D exchange at the methine carbon (=CHR) over the methylylidene carbon (=CH_2) for substrates RCH=CH_2 with a bulky substituent R. Additionally, these reactions can be performed on substrates with various functional groups, making this system useful for the selective labeling of olefins in complex molecules.



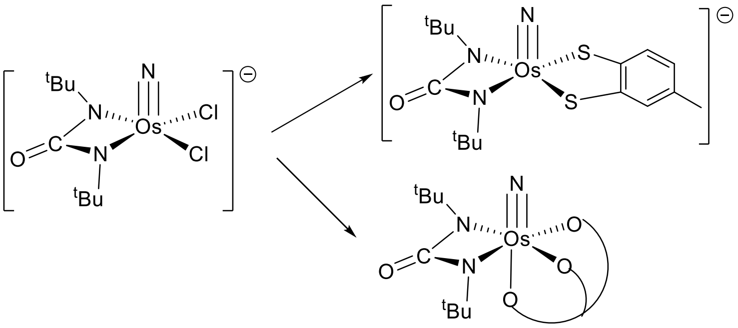
Synthesis and Catalytic Activity of Osmium Complexes with an Ureato Ligand

Chun-Yin Ho, Herman H. Y. Sung, Ian D. Williams,* and Wa-Hung Leung*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, China. E-mail: chwill@ust.hk, chleung@ust.hk

Abstract

Ureato ligands can bind to metal ions in variety of coordination modes, such as κ_1-*N*, κ_2-*N,O*, κ_2-*N*,*N*’ and μ-*N*,*O*. Of special interest are dianionic *N*,*N*’-bonded ureato chelating ligands that are expected to be strong electron donors of high-valent metal ions. In this presentation, we describe the substitution and catalytic activity of the previously reported nitrido-Os(VI) ureato complex $[Ph_4P][Os(N)\{^tBuNC(O)N^tBu\}Cl_2]$ (**1**).[1] Chloride substitution of **1** with NaL_{OEt} and $Na_2(tdt)$ led to formation of $[L_{OEt}Os(N)\{^tBuNC(O)N^tBu\}]$ ($L_{OEt}^- = [CpCo\{P(O)(OEt)_2\}_3]^-$) and $[Ph_4P][Os(N)\{^tBuNC(O)N^tBu\}(tdt)]$ (tdt^{2-} = 3,4-toluenedithiolate(2–)), respectively. Upon chloride abstraction, **1** is an active catalyst for C–H oxidation of hydrocarbons with *tert*-butyl hydroperoxide.



Reference

1. Leung, W.-H.; Wilkinson, G.; Hussain-Bates, B.; Hursthouse, M. B. *J. Chem. Soc., Dalton Trans*. **1991**, 2791-2794.

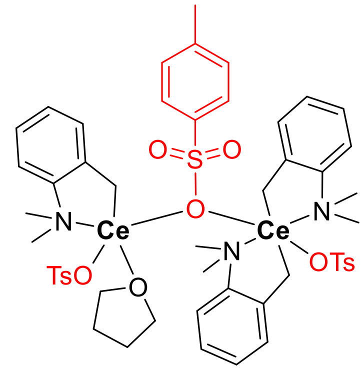
Acknowledgement. This work was supported by the Hong Kong Research Grants Council (project no. 16301120).

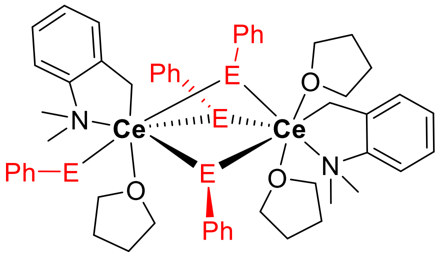
Reactions of Tris(*o*-Dimethylaminobenzyl) Cerium(III) with Oxidizing Agents

Chunteng Wan, Xuyang Yan, Herman H. Y. Sung, Ian D. Williams,* and Wa-Hung Leung*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, China. E-mail: chwill@ust.hk, chleung@ust.hk

Abstract

Lanthanide alkyl complexes have attracted much attention due to their use as precursors to organolanthanide catalysts. Although homoleptic lanthanide *o*-dimethylaminobenzyl complexes are well documented, the organometallic chemistry of the redox-active cerium(III) complex [Ce($CH_2C_6H_4NMe_2$-*o*)$_3$] (**1**) has not been explored. Herein we describe the reactivity of complex **1** toward oxidizing agents, including silver(I) salts and dichalcogenide compounds. The crystal structures of **1**, [Ce_2($CH_2C_6H_4NMe_2$-*o*)$_3$($CH_3C_6H_4SO_3$-*p*)$_3$(THF)] and [Ce_2($CH_2C_6H_4NMe_2$-*o*)$_2$(EPh)$_4$(THF)$_3$] (E = S, Se) will be reported.





E = S, Se

References

1. Harder, S. *Organometallics* **2005**, 24, 373-379.

Acknowledgement. This work was supported by the Hong Kong Research Grants Council (project nos. 16301621 and 16301424)

Metal-Organic Framework Boosts Heterogeneous Electron Donor–Acceptor Catalysis

Jiaxin Lin, Yangjian Quan*

Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon,

Hong Kong SAR, China

E-mail: chyjquan@ust.hk

Abstract:

Metal-organic framework (MOF) is a class of porous materials, providing an excellent platform for engineering heterogeneous catalysis. We herein report the design of MOF Zr-PZDB consisting of Zr_6-clusters and PZDB (PZDB = 4,4'-(phenazine-5,10-diyl)dibenzoate) linkers, which served as the heterogeneous donor catalyst for enhanced electron donor–acceptor (EDA) photoactivation. The high-local concentration of dihydrophenazine active centers in Zr-PZDB can promote the EDA interaction, therefore resulting in superior catalytic performance over homogeneous counterparts. The crowded environment of Zr-PZDB can protect the dihydrophenazine active center from being attacked by radical species. Zr-PZDB efficiently catalyzes the Minisci-type reaction of *N*-heterocycles with a series of C-H coupling partners, including ethers, alcohols, non-activated alkanes, amides, and aldehydes. Zr-PZDB also enables the coupling reaction of aryl sulfonium salts with heterocycles. The catalytic activity of Zr-PZDB extends to late-stage functionalization of bioactive and drug molecules, including Nikethamide, Admiral, and Myristyl Nicotinate. Systematical spectroscopy study and analysis support the EDA interaction between Zr-PZDB and pyridinium salt or aryl sulfonium salt, respectively. Photoactivation of the MOF-based EDA adduct triggers an intra-complex single electron transfer from donor to acceptor, giving open-shell radical species for cross-coupling reactions. This research represents the first example of MOF-enabled heterogeneous EDA photoactivation.[1]

References:

1. Lin, J.; Ouyang, J.; Liu, T.; Li, F.; Sung, H. H.-Y.; Williams, I.; Quan, Y., *Nat. Commun.* **2023**, *14* (1), 7757.,

Synthesis of strained, air-stable boracycles via boron-carbon centered diradicals

Xinmou WANG, Prof. Yangjian QUAN*
Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon, Hong Kong SAR, China
E-mail: chyjquan@ust.hk

Abstract

Boracycles are important functional scaffolds, often exhibiting superior or unique performance compared to their carbon analogs. Five-membered oxaboracycles are key pharmacophores in FDA-approved boron drugs, meanwhile six-membered boron doped polycyclic aromatic hydrocarbons (PAHs) enhance the diversification and functionality of molecular materials. However, boron-containing four-membered rings are less studied due to limited preparative approaches. Their inherent ring strain makes their synthesis thermodynamically unfavorable and hinders the exploration of their properties and applications. Here we report a triplet energy transfer (EnT) catalysis for crafting air-stable benzoboretenes through intramolecular coupling of a boron-carbon-centered diradicals (BCDR). Additionally, by modulating substrate π-conjugation structures and excitation energies, BCDR can undergo formal 1,6- and 1,5-cyclization to deliver dihydroborinine and dihydrocyclopropaborole derivatives, respectively. The metal-free, neutral reaction conditions ensure a broad reaction scope, resulting in structurally diverse boracycles that are stable enough to be purified via column chromatography. Further modification of the boracycles enables the facile synthesis of oxaborabicycles and dihydroborinine-fused PAHs with unique optoelectronic properties.

References

1. Grams, R. J.;Santos, W. L.; Scorei, I. R.; Abad-García, A.; Rosenblum, C. A.; Bita,A.; Cerecetto, H.; Viñas, C. M.; Soriano-Ursua, A. *Chem. Rev.* **2024**, *124*, 2441-2511.
2. Lyu, H., Kevlishvili, I., Yu, X., Liu, P. Dong, G. *Science* **2021**, *372*, 175-182.

Nickel Catalyzed Diastereoselective Hydroboration of Olefins with a Borataallyl Reagent”

Guanwen HU, Prof. Yangjian QUAN*

Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon, Hong Kong SAR, China

E-mail: chyjquan@ust.hk

Abstract

Boron-containing bioisosteres have demonstrated significant potential in enhancing the structural and functional complexity of pharmaceuticals. Nonetheless, the advancement of bioisosteric replacements for boron fragments encounters obstacles, such as the limited diversity of available boron bioisosteres and challenges in their synthesis or incorporation into target functional molecules. In this study, we present a nickel-catalyzed diastereoselective hydroboration of olefins utilizing a newly developed borataallyl reagent. This method facilitates the straightforward introduction of a borataallyl motif, into various drug derivatives. The reaction showed excellent diastereoselectivity and good functional group tolerance. The isolation and structural characterization of a crucial B-H-Ni bonded intermediate, along with control experiments and DFT calculations, highlight a σ-coordination that enables B-H activation. This activation triggers an oxidative metalation, resulting in the simultaneous formation of B-Ni, C-Ni, and C-H bonds. The innovative borataallyl reagent is anticipated to have applications in both synthetic and medicinal chemistry. Furthermore, the unique B-H metalation mechanism revealed through detailed mechanistic studies may offer broader implications for achieving selective B-H functionalization.

References

1. Su, W.; Song, Q., et al.; *Nat. Chem.* **2024**, *16*, 1312-1319.
2. Ghosh, S.; Braunschweig, H., et al.; *Acc. Chem. Res.* **2021**, *54*, 1260-1273.

Modulator Engineering to Bifunctional Metal-Organic Framework for Synergistic Catalysis

Jing Ouyang, Prof. Yangjian QUAN*

Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon, Hong Kong SAR, China

E-mail: chyjquan@ust.hk

Abstract

Pursuing both structural uniformity/crystallinity and functional complexity is a long-term goal in functional materials engineering. Often, efforts to enhance one attribute may compromise the other. Herein, we report an elaborate strategy of "integrating catalytic center into modulator", which enables the one-pot synthesis of a bi-functional metal-organic framework (MOF), Zr-TBAPy-TSA (TBAPy = 1,3,6,8-tetrakis(p-benzoic acid)pyrene; TSA = o-thiosalicylic acid). TSA serves as both a modulator for MOF preparation and a catalytic center. Zr-TBAPy-TSA is distinguished by its highly uniform and crystalline structure, as evidenced by detailed characterizations including single-crystal X-ray diffraction. Additionally, Zr-TBAPy-TSA incorporating both photosensitizer and thiol active centers showcases superior catalytic performance in the activation of element-H bonds (elements include C, B, Si, P). Due to its less defective structure, extra high turnover numbers of up to 14200 and good catalyst recyclability are obtained.

References

1. Guo, J.; Qin, Y. T.; Zhu, Y. F.; Zhang, X. F.; Long, C.; Zhao, M. T.; Tang, Z. Y. *Chem. Soc. Rev.* **2021**, *50 (9)*, 5366-5396.
2. Huang, Y. B.; Liang, J.; Wang, X. S.; Cao, R. *Chem. Soc. Rev.* **2017**, *46 (1)*, 126-157.

Twist-Promoted Photoredox Catalysis in Metal-Organic Framework

Zhiyi YANG, Prof. Yangjian QUAN*

Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon,
Hong Kong SAR, China

E-mail: chyjquan@ust.hk

Abstract

The relatively short excited-state lifetime is one main drawback of organic photosensitizers, resulting in their restricted catalytic capability and high catalyst loadings. We herein report the design of a twisted ligand N9,N9,N10,N10-tetrakis[(1,1'-biphenyl)-4-carboxylic acid]-9,10-anthracene diamine (H4TCPDA). Its twisted geometry significantly elongates the lifetime of charge-separation state as substantiated by detailed ultrafast transient absorption (TA) spectroscopic and electrochemical studies. Moreover, its rigid structure benefits the formation of highly crystalline Y-TCPDA metal-organic frameworks (MOFs) with excellent stability toward F- solutions. Therefore, Y-TCPDA competently catalyzes chemoselective defluorinative modifications, a challenge remained in MOF catalysis, and olefin reductive cross-coupling with high turnover numbers of up to 9000. Control experiments underline the protection of organic photocatalytic centers by the MOF platform, while similar organic catalysts are found to be decomposed in a homogeneous catalytic system.

References

1. Gao, C.; Li, J.; Yin, S.; Sun, J. L.; Wang, C. *J. Am. Chem. Soc*. 2020, 142 (8), 3718-3723.
2. Liang, R.-R.; Fu, Y.; Han, Z.; Yang, Y.; Bakhmutov, V. I.; Liu, Z.; Rushlow, J.; Zhou, H.-C. *Nat. Water* 2024, 2 (12), 1218-1225.

Brenium catalyzed “chain-walking”

Zheng ZHU, Prof. Yangjian QUAN*
Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon,
Hong Kong SAR, China
E-mail: chyjquan@ust.hk

Abstract

Remote functionalization through progressive olefin isomerization enables site-selective modification at a distal position, diversifying synthetic approaches. However, the developed protocols have long relied on transition metal catalysis.[1-2] Transition metal catalyst is deemed irreplaceable, albeit facing challenges in metal residue and catalyst poisoning. In this work, we present a pioneering approach that employs a borenium ion as a catalyst for site-selective, remote borylation, eliminating the need for metal catalysts. As the reaction progresses, borylation isomers at different positions emerge, gradually and ultimately converging into the predominant α-borylation product. This process is akin to a “walking” of boron moiety along a carbon skeleton toward an aryl terminus. Detailed mechanistic studies and DFT calculations substantiate the borenium-catalyzed, stepwise migration via a reversible B-H insertion/elimination sequence. This remote borylation exhibits good functional group compatibility, complementing those methods reliant on transition metals. Furthermore, this metal-free protocol permits the convenient synthesis of silyl-remote-boryl compounds, demonstrating an opposite regioselectivity to that observed in transition metal catalyzed tandem silylation-borylation reactions. This discovery therefore contributes to site-selective, remote di-functionalization via sequential C-B and C-Si derivatizations, exemplified by the synthesis of amino-remote-alcohol bioactive molecules.

References

1. Vasseur, A.; Bruffaerts, J.; Marek, I. *Nat. Chem.* **2016**, *8*, 209-219.
2. Sommer, H.; Juliá-Hernández, F.; Martin, R.; Marek, I. *ACS Cent. Sci.* **2018**, *4*, 153-165.

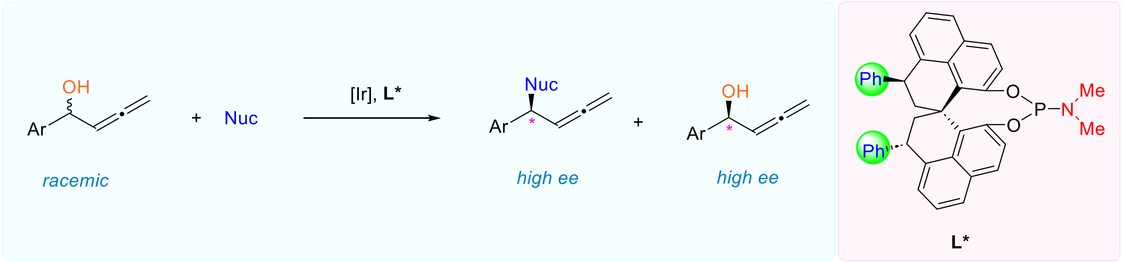
Iridium-Catalyzed Asymmetric Allenylic Substitution via Kinetic Resolution Enabled by New Monodentate Ligands

Youshao Tu, Xiangfeng, Lin, Chaoshen Zhang,* and Jianwei Sun*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China; sunjw@ust.hk

Abstract

Iridium-catalyzed asymmetric allenylic substitution represents a powerful method for the construction of allenes bearing an allenylic central chirality,[1] but current success has uniformly relied on only one specific chiral bidentate ligand. Herein we address the limitation by the design of a new type of monodentate ligands leading to not only excellent enantiocontrol in allenylic substitution, but also efficient kinetic resolution of α-allenylic alcohols, a new phenomenon never observed before in iridium-catalyzed allenylic substitution. This is also a rare demonstration of non-enzymatic kinetic resolution of α-allenylic alcohols. A range of highly enantioenriched allenylic diarylmethanes and α-allenylic alcohols could be accessed under mild conditions. Control experiments and DFT studies indicated that this process proceeds by an S_N1 pathway featuring a rate-determining ionization step followed by ligand-controlled enantiodetermining nucleophilic addition. The newly designed rigid and bulky ligands modified from SPHENOL[2] was believed to assemble the key iridium-bound allenylic carbocation intermediate in a different complexation mode, thus serving as the origin of enantiocontrol and the unprecedented kinetic resolution.



1. Petrone, D. A.; Isomura, M.; Franzoni, I.; Rossler, S. L; Carreira, E. M. *J. Am. Chem. Soc.* **2018**, *140*, 4697 – 4704.
2. Zhang, R.; Ge, S.; Sun, J. *J. Am. Chem. Soc.* **2021**, *143*, 12445 – 12449.

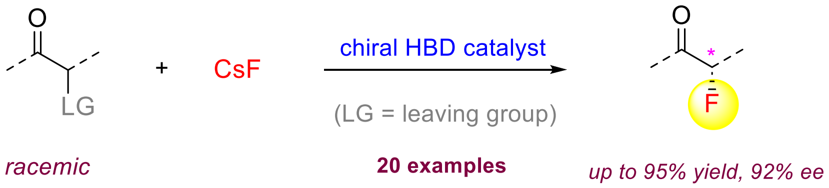
Catalytic Asymmetric α-Fluorination of Ketones with Fluoride

Baocheng Wang, Shuaixin Fan, and Jianwei Sun*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China; sunjw@ust.hk

Abstract

Stereodefined *α*-fluoro carbonyl compounds, such as ketones, have found broad applications as pharmaceuticals and biologically important molecules as well as chiral catalysts in organic synthesis.[1] However, despite their versatile utility, catalytic methods for their synthesis, particularly via enantioselective C−F bond formation at the carbonyl *α*-position, have not been well-developed. Specifically, almost all the current examples have relied on the use of electrophilic fluorination reagents, but rarely nucleophilic fluoride sources. Disclosed here is the first catalytic enantioselective nucleophilic α-fluorination of simple ketones. A new hydrogen bonding donor catalyst was designed to not only overcome the competing catalyst deactivation but also enable efficient enantiocontrol in C−F bond formation between racemic α-keto sulfoniums and CsF. Careful condition optimization resulted in a general and mild protocol applicable for the configurational flexible acyclic α-fluoro ketones bearing a tertiary stereogenic center with high yield and ee values, thus complementary to the previous electrophilic fluorination methods that were only effective to cyclic ketones and/or tetrasubstituted stereogenic centers. Preliminary mechanistic studies support a phase transfer and dynamic kinetic resolution pathway operated by HBD-enabled anion-binding.[2,3]



1. O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308 − 319.
2. Li, Z.; Wang, B.; Zhang, C.; Lo, W. Y.; Yang, L.; Sun, J.* *J. Am. Chem. Soc.* **2024**, *146*, 2779 − 2788.
3. Wang, B.; Fan, S.; Sun, J.* *J. Am. Chem. Soc.* **2025**, *under revision*.

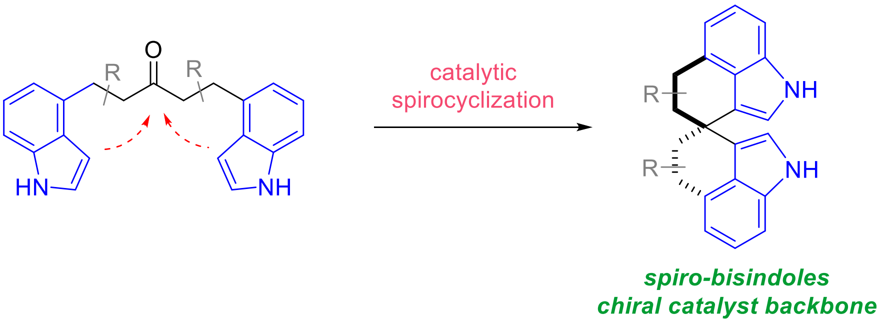
Design, Synthesis and Application of Chiral Spirocyclic Bisindoles

Jing-Yi Wang,[1] Jianwei Sun[1]*

[1]Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon 999077, Hong Kong SAR, China; sunjw@ust.hk

Abstract

Indole-based chiral heterocycles are prevalent in numerous pharmaceuticals, functional materials, and serve as pivotal components in chiral catalysts or ligands. While established chiral catalysts based on BINOL and SPINOL have played significant roles in catalytic asymmetric reactions, there remains a great demand for the design and synthesis of novel privileged catalysts.[1] In recent years, the design and synthesis of axially chiral indole-based frameworks has garnered considerable attention from chemists, resulting in rapid advances. However, the design and synthesis of C_2-symmetric bis(indole) spirocyclic structures remain underexplored.[2] Herein, we present the first example of this type and describe its versatile applications. The chiral catalysts derived from this type of C_2-symmetric spirocyclic bis(indole) structures have shown excellent catalytic performance in asymmetric allylation and cycloaddition reactions.[3] Details will be presented in due course.



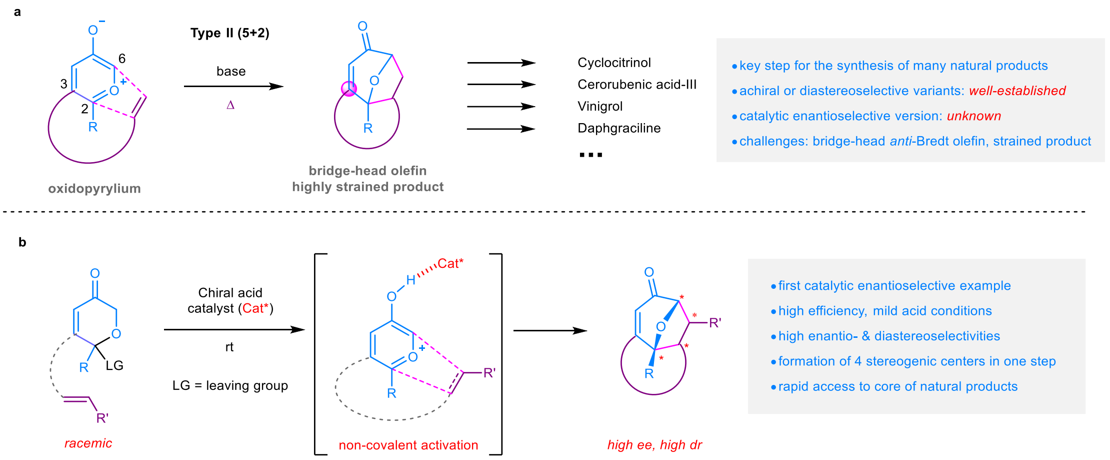
1. Zhang, R.; Ge, S.; Sun, J. *J. Am. Chem. Soc.*, **2021**, *143*, 12445 – 12449.
2. Zhao, H.-W.; Jiang, F.; Chen, S.; Hu, J.; Xiang, S.-H.; Ding, W.-Y.; Lu, W.; Tan, B. *Angew. Chem. Int. Ed.* **2025**, e202422951.
3. Wang, J.-Y.; Sun, J. *Angew. Chem. Int. Ed.* **2025**, e202424773.

Catalytic Enantioselective Type II Intramolecular (5+2) Cycloadditions of Oxidopyrylium Ylides

Liangliang Yang, Ka Lok Chan, Ka Key Cheung, Pauline Chiu,
Zhenyang Lin,* and Jianwei Sun *
*E-mail: chzlin@ust.hk; sunjw@ust.hk

Abstract

Intramolecular (5+2) cycloaddition of oxidopyrylium ylides provide rapids access to the privileged bridged seven-membered polycyclic structures. In particular, the Type II variants permit convenient assembly of the highly strained adducts bearing an anti-Bredt double bond. However, their catalytic enantioselective variants remain unknown. Here we report the first example of catalytic enantioselective enabled by non-covalent activation strategy using chiral acid catalysis. The products generated from this process are not only structurally intriguing, but also represent core structures or advanced intermediates found in natural products. Both mechanistic experiments and DFT calculations indicated that enolization serves as the rate-determining step, whereas the cycloaddition is the enantio-determining step.



References

1. Yang, L.; Chan, K.L.; Cheung, K.K.; Chiu, P.; Lin, Z.*; Sun, J.* *Nat. Synth.* Accepted.

Side-Chain Phenyl Isomerization-Induced Spatial Conjugation for Achieving Efficient Near-Infrared II Phototheranostic Agents

Chunbin Li,[a] Ryan T. K. Kwok,[a] Jacky W. Y. Lam,*[a] Ben Zhong Tang*[a]

[a] The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong
999077, P. R. China. E-mail: chjacky@ust.hk; tangbenz@cuhk.edu.cn

Abstract

The contradiction of near-infrared II (NIR-II) emission and photothermal effects limits the development of phototheranostic agents (PTAs) in many emerging cutting-edge applications. Organic aggregates present a promising opportunity for the balance of competitive relaxation processes through the manipulation of molecular structure and packing. Herein, side chain phenyl isomerization-induced spatial conjugation was proposed for constructing A-D-A type NIR-II PTAs with simultaneous enhancement of fluorescence brightness and photothermal properties. Three pairs of mutually isomeric fluorophores, whose phenyls respectively located at the outside (*o*-series) and inside (*i*-series) of the side chain, were designed and synthesized. The positional isomerization of the phenyl endows the *o*-series crystals with strong spatial conjugation between the phenyl group on the side chain and the backbone, as well as interlocked planar network, which is different to that observed in the *i*-series. Thus, all *o*-series nanoparticles (NPs) exhibit red-shifted absorption, enhanced NIR-II emission, and superior photothermal properties than their *i*-series counterparts. A prominent member of the *o*-series, *o*-ITNP NPs, demonstrated efficacy in facilitating NIR-II angiography and NIR-II imaging-guided tumor photothermal therapy.

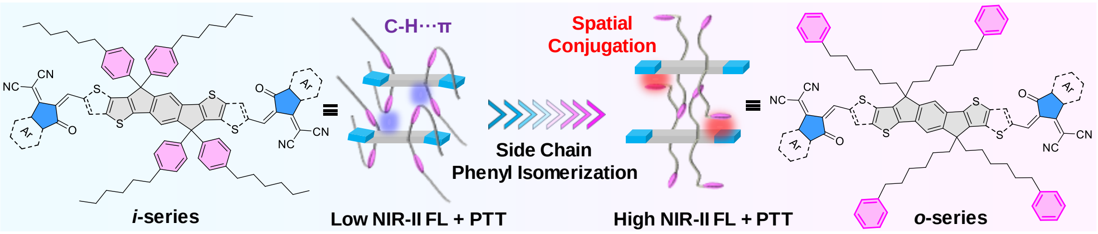


Figure 1. Schematic diagram of side chain phenyl isomerization-induced spatial conjugation for simultaneous enhancement of photothermal properties and NIR-II emission.

References

[1] Li, C., Yao, M., Jiang, G., Feng, L., Wu, Y., Sha, R., Li, Y., Tang, B.Z. & Wang, J. *Angewandte Chemie International Edition*, **2024**, e202419785.

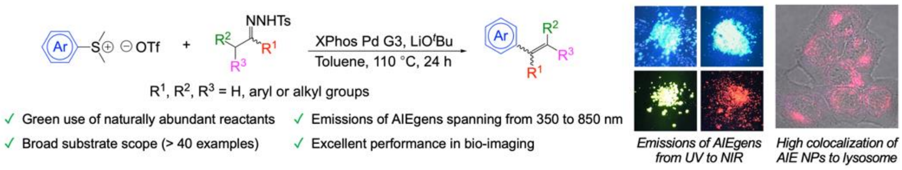
General method to synthesize aggregation-induced emission molecules via carbon-sulfur bond activation

Dr. Bowei Ma, Xinyu Liang, Gu Xu, Guanghao Zhang, Lutang Zhao, Liangzhuo Ma, Dr. Wenbin Xie, Xiang Li, Prof. Dr. Qinqin Shi,* Dr. Kaikai Wen,* Prof. Dr. Hui Huang*

College of Materials Science and Opto-Electronic Technology, University of Chinese Academy of Sciences, Beijing 100049, P. R. China.
E-mail: shiqinqin@ucas.ac.cn, wenkaikai@ucas.ac.cn, huihuang@ucas.ac.cn

Abstract

Poly-substituted olefins are essential aggregation-induced emission luminogens (AIEgens) with broad applications in sensing, bio-imaging, and optoelectronics. However, their synthesis remains challenging due to the limitations of existing methods. Herein, we report an efficient cross-coupling strategy between aryl sulfonium triflates and tosylhydrazones, utilizing readily available thioethers and ketones.[1] This method enables the facile synthesis of over forty AIEgens, with tunable emission properties by structural modifications. Mechanistic studies reveal the critical role of *β*-H elimination in double bond formation. This approach expands the synthetic toolbox for AIEgens and provides a robust platform for advanced luminescent materials.



Scheme 1. Carbon-sulfur bond activation method for the synthesis of AIEgens.

Reference

[1] Ma, B.; Liang, X.; Xu, G.; Zhang, G.; Zhao, L.; Ma, L.; Xie, W.; Li, X.; Shi, Q.; Wen, K.; Huang, H. *Aggregate* **2025**, *6*, e650.

Integration of Motion and Stillness: A Paradigm Shift in Constructing Nearly Planar NIR-II AIEgen with Ultrahigh Molar Absorptivity and Photothermal Effect for Multimodal Phototheranostics

Shiping Yang, Ryan T. K. Kwok, Jianwei Sun, Jacky W. Y. Lam,* and Ben Zhong Tang*
Department of Chemistry, the Hong Kong Branch of Chinese National Engineering Research Center for Tissue Restoration and Reconstruction, Division of Life Science, State Key Laboratory of Molecular Neuroscience, and Department of Chemical & Biological Engineering, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong 999077, China.
Jacky W. Y. Lam: chjacky@ust.hk; Ben Zhong Tang: tangbenz@cuhk.edu.cn

Abstract

The two contradictory entities in nature often follow the principle of unity of opposites, leading to optimal overall performance. Particularly, aggregation-induced emission luminogens (AIEgens) with donor-acceptor (D–A) structures exhibit tunable optical properties and versatile functionalities, offering significant potential to revolutionize cancer treatment.[1,2] However, trapped by low molar absorptivity (ε) owing to the distorted configurations, the ceilings of their photon-harvesting capability and the corresponding phototheranostic performance still fall short.[3,4] Therefore, a research paradigm from twisted configuration to near-planar structure featuring a high ε is urgently needed for AIEgens development. Herein, by introducing the strategy of "motion and stillness" into a highly planar A–D–A skeleton, we successfully developed a near-infrared (NIR)-II AIEgen of Y5-2BO-2BTF, which boasts an impressive ε of 1.06×10^5 M^{-1} cm^{-1} and a photothermal conversion efficiency (PCE) of 77.8%. The modification of steric hindrance on the benzene ring in the acceptor unit of the aggregation-caused quenching counterpart Y5-2BO, to a *meta*-CF_3-substituted naphthyl, leads to reversely staggered packing and various intermolecular noncovalent conformational locks in Y5-2BO-2BTF ("stillness"). Furthermore, the –CF_3 moiety acted as a flexible motion unit with an ultralow energy barrier, significantly facilitating the photothermal process in loose Y5-2BO-2BTF aggregates ("motion"). Accordingly, Y5-2BO-2BTF nanoparticles enabled tumor eradication and pulmonary metastasis

inhibition through NIR-II fluorescence-photoacoustic-photothermal imaging-navigated type I photodynamic-photothermal therapy. This work provides the first evidence that the highly planar conformation with a reversely staggered stacking arrangement could serve as a novel molecular design direction for AIEgens, shedding new light on constructing superior phototheranostic agents for bioimaging and cancer therapy.[5,6]

Reference:

1. Kang, M.; Zhang, Z.; Song, N.; Li, M.; Sun, P.; Chen, X.; Wang, D.; Tang, B. Z. Aggregation-Enhanced Theranostics: AIE Sparkles in Biomedical Field. *Aggregate* **2020**, *1*, 80–106.

2. Zhang, Z.; Kang, M.; Tan, H.; Song, N.; Li, M.; Xiao, P.; Yan, D.; Zhang, L.; Wang, D.; Tang, B. Z. The Fast-Growing Field of Photo-Driven Theranostics Based on Aggregation-Induced Emission. *Chem. Soc. Rev.* **2022**, *51*, 1983–2030.

3. Xu, W.; Wang, D.; Tang, B. Z. NIR-II AIEgens: A Win-Win Integration Towards Bioapplications. *Angew. Chem. Int. Ed.* **2021**, *60*, 7476–7487.

4. Shi, T.; Huang, C.; Li, Y.; Huang, F.; Yin, S. NIR-II Phototherapy Agents with Aggregation-Induced Emission Characteristics for Tumor Imaging and Therapy. *Biomaterials* **2022**, *285*, 121535.

5. Yang, S.; Zhang, J.; Zhang, Z.; Zhang, R.; Ou, X.; Xu, W.; Kang, M.; Li, X.; Yan, D.; Kwok, R. T. K.; Sun, J.; Lam, J. W. Y.; Wang, D.; Tang, B. Z. More Is Better: Dual-Acceptor Engineering for Constructing Second Near-Infrared Aggregation-Induced Emission Luminogens to Boost Multimodal Phototheranostics. *J. Am. Chem. Soc.* **2023**, *145*, 22776–22787.

6. Yang, S.; Jia, Q.; Ou, X.; Sun, F.; Song, C.; Zhao, T.; Kwok, R. T. K.; Sun, J.; Zhao, Z.; Lam, J. W. Y.; Wang, Z.; Tang, B. Z. Integration of Motion and Stillness: A Paradigm Shift in Constructing Nearly Planar NIR-II AIEgen with Ultrahigh Molar Absorptivity and Photothermal Effect for Multimodal Phototheranostics. *J. Am. Chem. Soc.* **2025**, *147*, 3570–3583.

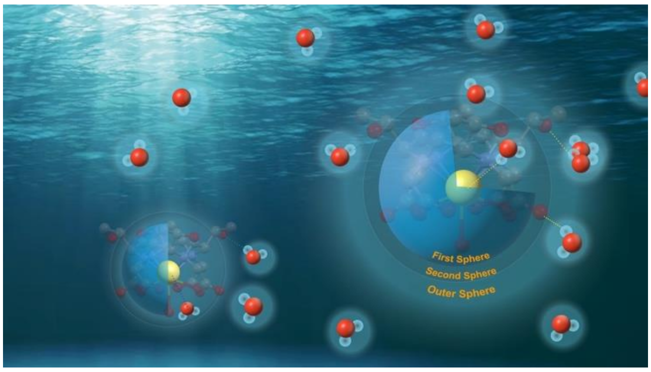
Potential Chiral DOTA-based Gd(III) MRI Contrast agents with Improved T_1 Relaxivities

Li He, Junhui Zhang, Ga-Lai Law*

W710, POLYU, HK ;corresponding author: ga-lai.law@polyu.edu.hk

With one of the highest number of unpaired electrons in its 4*f* obital, Gadolinium trivalent ion has been widely applied in the development of Magnetic resonance imaging (MRI) contrast agents. However, due to the adverse effects of de-metallation in some past concerning FDA-approved Gadolinium-based contrast agents (GBCAs), researchers have been focusing on developing safer and more efficient alternatives that could avoid toxicity caused by free gadolinium ions. Herein, two chiral GBCAs, Gd-LS and Gd-T, are reported as potential contrast agents for magnetic reasonance imaging (MRI) with improved reaxivity compared to the benchmark DOTAREM contrast agent. By adding the chiral sulfonate groups on Gd-LS and chiral hydroxyl groups on Gd-T, the stability and water solubility of these two chiral Gd complexes have been significantly improved and induced secondary-sphere contributions on the overall r_1 relaxivities by these hydrophilic moieties have also been observed.

The locking effects induced by the chiral moieties ensure an irreversible interchange between TSAP and SAP isomers of Gd-LS or Gd-T. After isolating both geometric isomers by HPLC, the r_1 relaxivities of both isomers (TSAP & SAP) for Gd-LS and the SAP isomer of Gd-T measured at 1.4 T and 37°C in water were 7.4 mM^{-1}s^{-1}, 14.5 mM^{-1}s^{-1} and 5.2 mM^{-1}s^{-1}, respectively. These results show that the hydrophilic functional groups introduced to the chiral macrocyclic scaffolds give constructive influences on the second-sphere relaxivity and enhance the overall r_1 value.



Reference:

Zhang, J., Dai, L., He, L.Bhattarai. A., Chan CM., Tai. CS. Vardhanabhuti. V. *Commun Chem* **2023**, 6, 251.

Red Light Controlled Supramolecular Soft Robotics of Indigo Amphiphiles for Macroscopic Photoactuations

CHEN Yanzhi [a], Jerry Chun-Kit Yau [a], Franco King-Chi Leung [a,*]

[a] State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China

Abstract

Amphiphilic molecules with photoresponsive motifs show great potential for advanced biomaterials, particularly in cell-material interfaces and drug delivery. In 2024, our group has demonstrated with a new generation of *N,N*'-diaryl-substituted indigo amphiphiles (IA) exhibiting excellent photoswitchability and photostability under dual red and green light in organic solvent,[1] unlike most reported photoresponsive amphiphiles driven by bioharmful UV-light. IAs and its supramolecular assembled structures in aqueous media respond to red-light, which is less damaging to biological tissues and better tissue penetration. Additionally, IA scaffolds were fabricated via shear-flow methods to show good biocompatibility with human stem cells (h-MSCs). We now report the first instance of red-light-controlled macroscopic actuation of IA scaffolds in aqueous media and compare the photoresponsiveness of IAs with varying hydrophobic chain lengths. These findings highlight the potential for developing next-generation soft functional materials responsive to red-light.

Reference

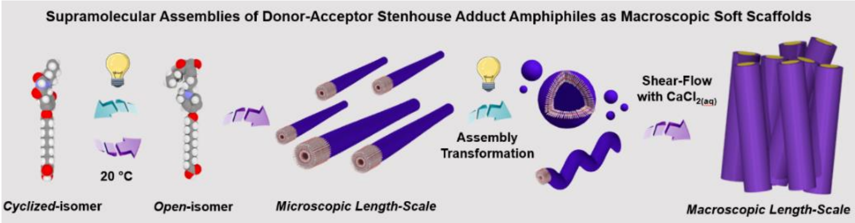
1. Yau, J. C.; Hung, K.; Ren Y.; Kajitani, T.; Stuart, M, C.; Leung, F, K.-C. *Journal of Colloid and Interface Science*, **2024**, 662, 391 – 403.

Supramolecular assemblies of amphiphilic donor–acceptor Stenhouse adducts as macroscopic soft scaffolds

Ka-Lung Hung[1,2], Leong-Hung Cheung[2], Yikun Ren[1,2], Ming-Hin Chau[2], Yan-Yi Lam[2],
Takashi Kajitani[3] and Franco King-Chi Leung*[1,2,4]

1. The Hong Kong Polytechnic University Shenzhen Research Institute, Shenzhen 518057, China.
2. State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China.
3. Open Facility Development Office, Open Facility Center, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8503, Japan.
4. Centre for Eye and Vision Research, 17W Hong Kong Science Park, Hong Kong, China

E-mail: kalung-rick.hung@connect.polyu.hk, kingchifranco.leung@polyu.edu.hk



In the design of photoharvesting and photoresponsive supramolecular systems in aqueous medium, the fabrication of amphiphilic photoswitches enables a noninvasive functional response through photoirradiation. Although most aqueous supramolecular assemblies are driven by high-energy and biodamaging UV light, we have previously reported a design of amphiphilic donor–acceptor Stenhouse adducts (DASAs) controlled by white light. Herein, we present a series of DASA amphiphiles (DAs) with minor structural modifications on the alkyl linker chain length connecting the DASA motif with the hydrophilic moiety. The excellent photoswitchability in organic medium and the photoresponsiveness in aqueous medium, driven by visible light, were investigated by UV–vis absorption spectroscopy. The assembled supramolecular nanostructures were confirmed by electron microscopy, while the supramolecular packing was revealed by X-ray diffraction analysis. Upon visible-light irradiation, significant transformations of the DA geometry enabled transformations of the supramolecular assemblies on a microscopic scale, subsequently disassembling macroscopic soft scaffolds of DAs. The current work shows promising use for the fabrication of visible-light-controlled macroscopic scaffolds, offering the next generation of biomedical materials with visible-light-controlled microenvironments and future soft-robotic systems.

Referencea

[1] Hung, K.-L.; Cheung, L.-H.; Ren, Y.; Chau, M.-H.; Lam, Y.-Y.; Kajitani, T.; Leung, F. K.-C. Beilstein J. Org. Chem. 2024, 20, 1590–1603.

[2] Cheung L.-H., Kajitani T., Leung F.K.-C. (2022) Journal of Colloid and Interface Science, 628 , pp. 984-993.

Supramolecular Interaction Determined Macroscopic Actuation Performances of Azobenzene Amphiphile Derived Supramolecular Soft Robotics

Brian Boyan Liu, Haiqi Zhang, Wai-Ki Wong, Ming-Hin Chau, Leong-Hung Cheung, Takashi Kajitani and Franco King-Chi Leung*
State Key Laboratory of Chemical Biology and Drug Discovery, Research Institute for Future Food, Department of Applied Biology and Chemical Technology, the Hong Kong Polytechnic University Hong Kong, China. E-mail: kingchifranco.leung@polyu.edu.hk

Abstract

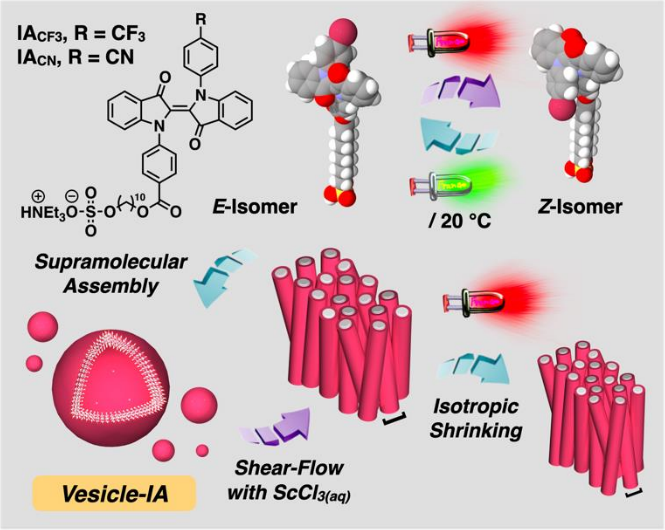
Supramolecular soft robotics with hierarchically assembled architectures can mimic living organisms and respond to external stimulations like light. In development of photoresponsive supramolecular robotics, however, the manipulation of supramolecular interactions to tune the photoactuation abilities has rarely been reported. Here we design photoresponsive azobenzene amphiphiles (AAs) functionalized with different amino acid head groups, which self-assembled into distinct nanostructures in aqueous media. The bulkiness and hydrophobicity of amino acid side chains control the supramolecular interactions between molecules, and control the actuation performance of soft macroscopic scaffolds prepared from the different AA self-assemblies. The scaffold of phenylalanine derivative, from short nanotube assemblies, exhibited rapid actuation at high concentration, but are unstable at low concentrations. Oppositely, the scaffold of valine derivative exhibited slow actuation at high concentration, but high aspect ratio nanoribbon assemblies enable very fast actuation speed at low concentrations (up to 4.36 °/s). This is the first example of supramolecular amplification of molecular properties towards optimization of photoactuators, suggesting an adjustable bottom-up design of future supramolecular smart materials.

Red-light-controlled supramolecular assemblies of indigo amphiphiles at multiple length scales

Jerry Chun-Kit YAU, Ka-Lung HUNG, Yikun REN, Franco King-Chi LEUNG*
State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China.
*Corresponding author. *E-mail address*: kingchifranco.leung@polyu.edu.hk

Abstract

Amphiphilic molecules featured with photoresponsive motif have attractive prospects for applications in smart bio-material owing to the controllable functionality of self-assembled supramolecular structures in aqueous media by light stimulation. However, most of reported photoresponsive amphiphiles are triggered by bio-damaging UV-light, which greatly limits the potential in bio-related applications. Herein, we report red-light controlled *N*,*N'*-diaryl-substituted indigo amphiphiles (**IA**), exhibiting excellent photoswitchablity and photostability in organic media. At macroscopic length-scale, morphological changes of **IA** macroscopic scaffold prepared by a shear-flow method can be fine adjusted upon red-light irradiation. Moreover, the preferential attachment of live h-MSCs to **IA** macroscopic scaffold surface showed a limited cytotoxicity. These results provide the potential for developing the next generation of red-light controlled soft functional materials with good biocompatibility.



Supramolecular Polyelectrolyte Films for Spontaneous Power Generation with Photoresponsive Electronic Signals

Haiqi Zhang, Yiting Feng, Ka-Hei Tang, Shaoyu Chen*
Postal address(es): School of Fashion and Textiles, The Hong Kong Polytechnic University, Hong Kong, China
E-mail address of the corresponding author: shaoyu.chen@polyu.edu.hk

Abstract

Developing supramolecular films from polyelectrolyte amphiphilic building blocks in aqueous media with spontaneous power generation and photoresponsive electronic signals is likely a significant step toward next-generation functional materials for wearable sensors, soft robotics, digital healthcare, and fashion, which remains highly challenging. Herein, we prepared a moisture-powered polyelectrolyte film via supramolecular co-assembly of alkaline solutions of lipoic acid, hyaluronic acid, 1-Ethyl-3-methylimidazolium ethyl sulfate, and amphiphilic azobenzene dopant in a simple and one-pot evaporation-induced polymerization process. Detailed investigations on the photoisomerization of the azobenzene dopant by nuclear magnetic resonance and UV-vis absorption spectroscopy, mechanical properties by tensile testing, assembled layer-by-layer structure by X-ray diffraction, and detecting electronic signals by using a voltage clamp setup were presented. The layer-by-layer structure with water channels and intrinsic hygroscopic features endowed the corresponding polyelectrolyte films with spontaneous electronic generating functions. By absorbing water molecules in the air and inducing diffusion of charged ions in the water channels, a piece of polymer film (0.4 cm × 1.5 cm) could generate a current of up to 11.8 nA in the current loop at 21.6 °C and 69% relative humidity. By incorporating the amphiphilic azobenzene dopant, the current can also be controlled by UV irradiation, which was attributed to variations in molecular geometry and polarity between *trans* and *cis* isomers. Namely, the *cis*-azobenzene amphiphile absorbs more water and increases the volume of the water channels, leading to the increase of electronic signal. This polymer film is easily recycled by redissolving the fragments in water, demonstrating full recyclability and environmental friendliness. This method paves the way for developing recyclable supramolecular films with low-cost, moisture-sensitive, and light-tunable self-powered electric generating functions.

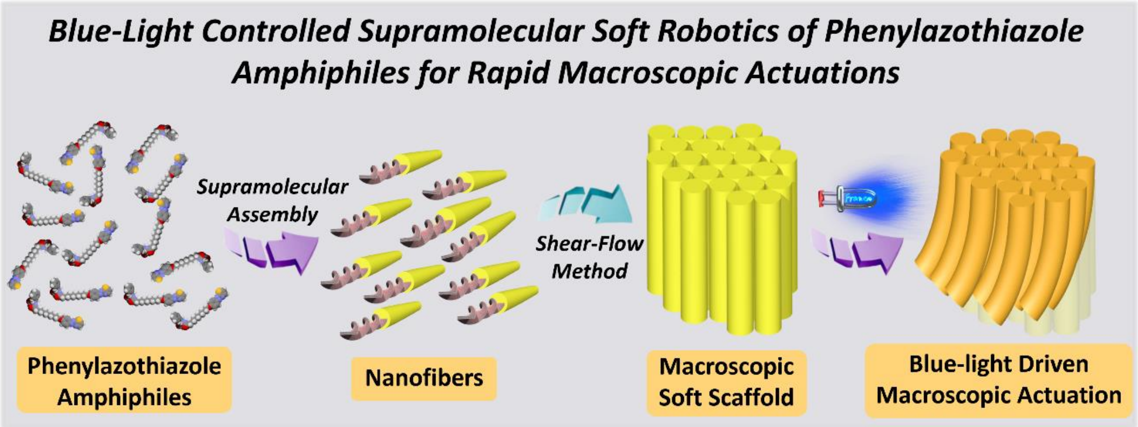
Blue Light Controlled Supramolecular Soft Robotics of Phenylazothiazole Amphiphiles for Rapid Macroscopic Actuations

Ming-Hin Chau, Wai-Ki Wong, Takashi Kajitani, Franco King-Chi Leung*

State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong (China); Email: kingchifranco.leung@polyu.edu.hk

Abstract

Nature preprograms sophisticated processes in operating molecular machines at the nanoscale, amplifying the molecular motion across multiple length-scales, and controlling movements in living organisms. Supramolecular soft robotics serve as a new alternative to hard robotics, are able to transform and amplify collective motions of the supramolecularly assembled molecular machines in attaining macroscopic motions, upon photoirradiation. Unidirectionally aligned nanostructures of the amphiphilic phenylazothiazoles are controlled by non-invasive blue light irradiation and bends toward the light source, demonstrating a fast macroscopic actuation of supramolecular robotic systems (up to 17° s^{-1}) in aqueous media. Through meticulous X-ray diffraction and electron microscopy analyzes, macroscopic actuation mechanism is illustrated in a tight relation to molecular geometric transformations upon photoisomerization. By elucidating the key macroscopic actuation parameters, this paves the way for the next generation design of supramolecular soft robotic systems with enhanced biomimetic actuating functions.



References:

1. M.-H. Chau, W.-K. Wong, T. Kajitani, F. K.-C. Leung*. *Adv. Sci.* 2024, *11 (45)*, 2407130.

Scalable deoxygenative alkynylation of alcohols via flow photochemistry

Pin Xu and Cong Ma

State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong SAR, China

Email: cong.ma@polyu.edu.hk

Abstrcat

Internal alkynes are often contained in bioactive pharmaceuticals and crucial intermediates in material sciences, yet their production methods are often limited and challenging, necessitating the development of more efficient and versatile synthetic routes. Here we report a method of deoxygenative alkynylation of alcohols via flow photochemistry. Formation of N-heterocyclic carbene-alcohol adducts undergoes oxidation by a photocatalyst, generating alkyl radicals. These radicals are subsequently trapped by an alkynylation agent, yielding the desired alkyne. Compared to batch reactions, the strategy using flow photochemistry is practical and efficient to complete the reaction in relatively short time with good yields. A wide range of functional groups were tolerated. The broad application of this method for alkyne synthesis in industry settings is anticipated, supported by the potential in late-stage functionalization of biomolecules and gram-scale synthesis.

Combining Pyrrole Chemistry with Solid-phase Peptide Synthesis: Modular Approaches for Peptide Multifunctionalization

Pak-Lun Lam, Yue Wu*, Ho-Fai Chau, Wing-Sze Tam, Waygen Thor, Yik-Hoi Yeung, Hei-Yui Kai, Ka-Leung Wong*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University,
Hung Hom, Kowloon, Hong Kong SAR
Email: klgwong@polyu.edu.hk

Abstract

Pyrrole chemistries refer to the reactions to synthesize a variety of functional moieties like dipyrrins/BODIPYs, porphyrins, and corroles. Solid-phase peptide synthesis (SPPS) is a modular approach to synthesize peptide derivatives in both laboratories and industries. Previously, to synthesize peptide derivatives that bearing above-mentioned functional moieties, additional synthetic steps is inevitable to prepare the corresponding building blocks, followed by conjugating to peptides. In our studies, by strategically combined the pyrrole chemistries with SPPS, we established a series of synthetic methodologies to modularly construct these functional moieties on peptide. With our approaches, the chemists can obtain these functional peptides more quickly, and the products are easier to diversify in the late stage. Moreover, the products from our synthetic approach also display a wide range of applications as theragnostic agents and biocompatible materials.

Reference

[1] Y. Wu, Y.-T. Wong, Y.-H. Yeung, P.-L. Lam, H.-F. Chau, W.-S. Tam, Q. Zhang, W. C. S. Tai, K.-L. Wong, ***Adv. Sci.***, 2025, Accepted.

[2] Y. Wu, H. F. Chau, H. Y. Kai, W. S. Tam, Y. H. Yeung, W. Thor, T. L. Cheung, C. Xie, J. X. Zhang, K. L. Wong, ***Chem. - A Eur. J.*** 2023, *29*, e202203623.

[3] Y. Wu, H. F. Chau, Y. H. Yeung, W. Thor, H. Y. Kai, W. L. Chan, K. L. Wong, ***Angew. Chem. Int. Ed.*** 2022, *61*, e202207532.

[4] Y. Wu, H. F. Chau, W. Thor, K. H. Y. Chan, X. Ma, W. L. Chan, N. J. Long, K. L. Wong, ***Angew. Chem. Int. Ed.*** 2021, *60*, 20301–20307.

[5] Y. Wu, W. S. Tam, H. F. Chau, S. Kaur, W. Thor, W. S. Aik, W. L. Chan, M. Zweckstetter, K. L. Wong, ***Chem. Sci.*** 2020, *11*, 11266–11273.

Development of Synthetic Approaches in Preparing Luminescent Lanthanide Probes for Biomedical Applications

Yik-Hoi Yeung, Yue Wu, Ho-Fai Chau, Chen Xie, Hei-Yui Kai, Wanqi Zhou, Pak-Lun Lam, Ga-Lai Law*, Ka-Leung Wong*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR
Email: klgwong@polyu.edu.hk

Abstract

Lanthanide ions exhibit distinctive luminescent patterns and specialized photophysical properties which have attracted continuous research interests. Restricted by the f-f forbidden electron transfer, antenna is essential to harvest energy for the characteristic emission patterns of lanthanide ions. The design of targeted luminescent lanthanide probe accommodating antenna and chelator on the targeting motif has hence left great synthetic challenges to accommodate 3 components in one molecule. Herein, by conjugation through strain-promoted azide-alkyne click reaction (SPAAC)[1] and recruiting orthogonally protected amino acid as extension hub[2], we presented 2 strategies to assemble the luminescent lanthanide probe at lower synthetic cost.

This work was supported by RGC Areas of Excellence (AoE) Scheme (AoE/M-401/20)

Reference

1 C. Xie, Y. Wu, H. F. Chau, T. Zhang, C. T. Wong, Y. H. Yeung, P. L. Lam, J. G. Bünzli, L. J. Charbonnière, G. Law and K. L. Wong, *Adv. Opt. Mater.*, 2023, **11**, 2203057.

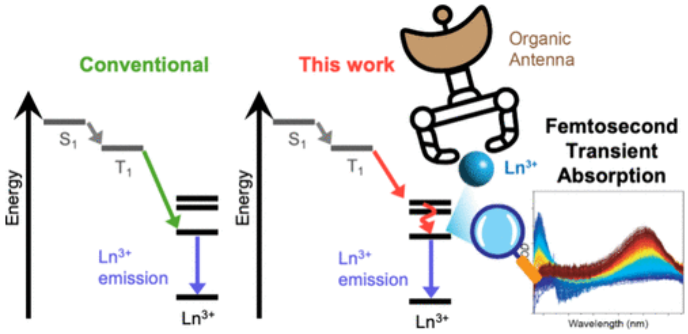
2 Y. H. Yeung, H. F. Chau, H. Y. Kai, W. Zhou, K. H. Y. Chan, W. Thor, L. J. Charbonnière, F. Zhang, Y. Fan, Y. Wu and K. L. Wong, *Adv. Opt. Mater.*, 2024, **12**, 2302070.

Unearthing the Real-Time Excited State Dynamics from Antenna to Rare Earth Ions Using Ultrafast Transient Absorption

Qian Zhang, Peter A. Tanner, and Ka-Leung Wong*

[a] Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University,
Hung Hom, Hong Kong, PR China
(E-mail: klgwong@polyu.edu.hk)

Abstract



The conventional energy transfer pathway in organic lanthanide complexes is purported to be from the excited singlet state of the chromophore to the triplet state and subsequently directly to the emitting state of the trivalent lanthanide ion. With the aid of the antenna effect, luminescence from trivalent lanthanide ions can be harvested despite the weak absorption coefficient of Ln^{3+}.[1,2] To elucidate the excited dynamics in lanthanide complexes, which occur within the ultrafast time scale of picoseconds to nanoseconds, a spectroscopic technique capable of investigating this range is necessary. Femtosecond transient absorption spectroscopy (fs-TAS) can be employed to investigate the excited state properties of organic lanthanide complexes.[3-5]

In this work, we found that the energy transfer occurs from the triplet state to the nearest energy level, instead of directly to the emitting state of the lanthanide ion. The triplet decay rate for different lanthanide ions follows an energy gap law from the triplet level to the receiving level of the lanthanide ion. Three different categories of complexes were synthesized and inspected using different techniques, demonstrating the universality of our findings. This work renews the insights to conventional findings, highlighting the importance of the energy gap between the triplet state and the nearest lanthanide energy level in optimization of light harvesting. The rationale of ligand design of chromophores should be reconsidered, leading to various applications of lanthanide complexes with enhanced quantum yield and brightness.

This work was supported by Innovation and Technology Fund - Partnership Research Programme (ITF-PRP) (PRP/040/23FX)

References

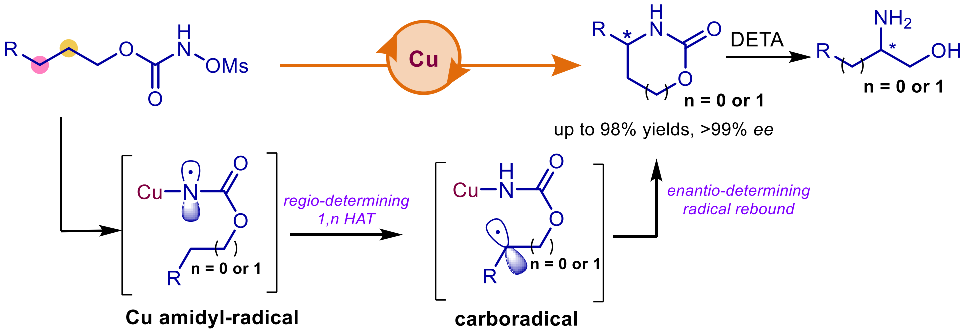
1. Moore, E. G.; Samuel, A. P. S.; Raymond, K. N. From Antenna to Assay: Lessons Learned in Lanthanide Luminescence. Acc. Chem. Res. 2009, 42 (4), 542−552.
2. Bunzli, J.-C. G. Lanthanide Luminescence for Biomedical Analyses and Imaging. Chem. Rev. 2010, 110 (5), 2729−2755.
3. Galán, L. A.; Reid, B. L.; Stagni, S.; Sobolev, A. N.; Skelton, B. W.; Cocchi, M.; Malicka, J. M.; Zysman-Colman, E.; Moore, E. G.; Ogden, M. I.; Massi, M. Visible and Near-Infrared Emission from Lanthanoid β-Triketonate Assemblies Incorporating Cesium Cations. Inorg. Chem. 2017, 56 (15), 8975−8985.
4. Han, S.; Yi, Z.; Zhang, J.; Gu, Q.; Liang, L.; Qin, X.; Xu, J.; Wu, Y.; Xu, H.; Rao, A.; Liu, X. Photon Upconversion Through Triplet Exciton-Mediated Energy Relay. Nat. Commun. 2021, 12 (1), 3704.
5. Zhang, J.-X.; Chan, W.-L.; Xie, C.; Zhou, Y.; Chau, H.-F.; Maity, P.; Harrison, G. T.; Amassian, A.; Mohammed, O. F.; Tanner, P. A.; Wong, W.-K.; Wong, K.-L. Impressive Near-Infrared Brightness and Singlet Oxygen Generation from Strategic Lanthanide−Porphyrin Double-Decker Complexes in Aqueous Solution. Light Sci. Appl. 2019, 8 (1), 46.

Copper-Catalyzed Regio- and Enantioselective C(sp^3)–H Amidation for the Synthesis of β- and γ-Amino Alcohols

Ming-Kit Lin, Hon-Lam Au, Chi-Ming Au and Wing-Yiu Yu*
State Key Laboratory for Chemical Biology and Drug Synthesis, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong
Corresponding e-mail: wing-yiu.yu@polyu.edu.hk

Abstract

Transition metal-catalyzed nitrene transfer reactions constitute a step- and atom-economical strategy for the stereocontrolled aliphatic amines synthesis.[1] While second- and third-row transition metals, such as Rh, Ru, and Ir, are known to stabilize reactive nitrene for regio- and enantiocontrolled nitrene transfer reactions, analogous transformations involving first-row transition metal-mediated acylnitrene transfers are sparse.[2, 3] Recently, Chang and our team reported on the Fe-catalyzed intramolecular acylnitrene insertion into C(sp^3)–H and C(sp^2)–H bonds to synthesize cyclic amides.[4, 5] Herein, we report the copper-catalyzed enantioselective intramolecular C(sp^3)–H amidation to access β- and γ-amino alcohols with high to excellent yields and enantioselectivity (up to 98% yields and >99 %*ee*). The reaction involves hydrogen atom abstraction as the regio-determining step, followed by the enantio-determining radical rebound step. The synthetic utility, such as late-stage functionalization of natural products, will be discussed.



References

1. Ju, M.; Schomaker, J. M. *Nat. Rev. Chem* **2021**.
2. Ye, C.-X.; Dansby, D.R.; Chen, S.; Meggers, E. *Nat. Synth.* **2023**, *2*, 645-652.
3. Lee, J.; Lee, J.; Jung, H.; Kim, D.; Park, J.; Chang, S. *J. Am. Chem. Soc.* **2020**, *142*, 12324-12332.
4. Kweon, J.; Kim, D.; Kang, S.; Chang, S. *J. Am. Chem. Soc.* **2022,** *144,* 1872-1880.
5. Sun, W.; Au, C.-M.; Wong, K.-W.; Chan, K. L.; Ngai, C. K.; Lee, H. K.; Lin, Z.; Yu, W.-Y. *ACS Catal.* **2023**, *13*, 11389-11398.

Ligand Mediated Rh(III)-Catalyzed Regioselective Allylic C–H Alkylation of Unactivated Alkenes with α-Diazomalonates

Sing-Fung Hung,[1] Ka-Wa Wong,[1] Yiu-Wai Yeung,[1] Ka-Chi Chan,[1] Zhenyang Lin,[2] Chun-Ming Chan[1]*, Wing-Yiu Yu[1]*

[1] *State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong*

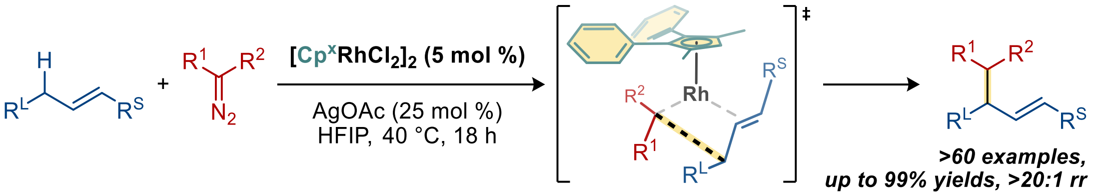
[2] *Department of Chemistry, The Hong Kong University of Science of Technology, Clear Water Bay, Kowloon, Hong Kong*

Corresponding email: wing-yiu.yu@polyu.edu.hk

Abstract

Alkenes are abundant and versatile feedstocks for synthesis of natural products, medicinal compounds, and agrochemicals. Regioselective allylic C–H bonds functionalization for the construction of C(sp^3)–C(sp^3) bond offer the atom- and step-economical approaches for skeletal and functional diversification. Blakey[1], Rovis[2], and Glorius[3] 's groups reported Rh^{III}- and Ir^{III}-catalyzed intermolecular allylic C–H amidation of inactivated alkenes. Since then, Blakey's[4] group developed the enantioselective allylic C–H amidation mediated by chiral rhodium indenyl catalyst. Inspired by Rovis[5-6] previous exploration of the steric and electronic effects of cyclopentadienyl ligands for d^6 transition metal catalysts towards regiocontrolled cross coupling reactions, we examined a series of functionalized Cp ligands for the Rh^{III}-catalyzed highly branched-selective allylic C–H alkylation of unactivated alkenes with diazomalonates via intermolecular allylic carbene C–H functionalization.

Ligand mediated Branched-Selective Allylic Alkylation



>60 examples, up to 99% yields, >20:1 rr

References

1. Burman, J. S.; Blakey, S. B. *Angew. Chem., Int. Ed.* **2017**, 56, 13666–13669.
2. Lei, H.; Rovis, T. *J. Am. Chem. Soc.* **2019**, 141, 2268–2273.
3. Knecht, T.; Mondal, S.; Ye, J.; Das, M.; Glorius, F. *Angew. Chem., Int. Ed.* **2019**, 58, 7117–7121.
4. Caitlin; Kazerouni, A. M.; Park, B.; Poff, C. D.; Won, J.; Sharp, K. R.; Baik, M.-H.; Blakey, S. B. *J. Am. Chem. Soc.* **2020**, 142, 13996–14004.
5. Piou, T.; Romanov-Michailidis, F.; Romanova-Michaelides, M.; Jackson, K. E.; Semakul, N.; Taggart, T. D.; Newell, B. S.; Rithner, C. D.; Paton, R. S.; Rovis, T. *J. Am. Chem. Soc.* **2017**, *139*, 1296–1310.
6. Piou, T.; Tomislav Rovis. *Acc. Chem. Res.* **2017**, 51, 170–180.

Ruthenium-Catalyzed π-Selective Amidation of Nonactivated Distal Methylene C–H Bonds of Terminal Alkenes via Olefin Chain-Walking Isomerization

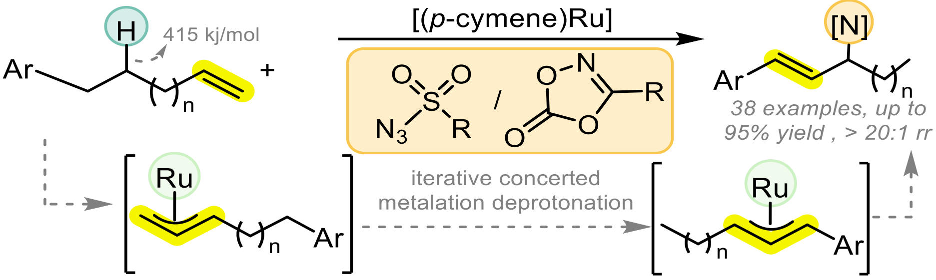
Yiu-Wai Yeung, Sing-Fung Hung, Chi-Ming Au, Marco Chan, Chun-Ming Chan* and Wing-Yiu Yu*

State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong

Corresponding email: fortunechunming.chan@polyu.edu.hk ; wing-yiu.yu@polyu.edu.hk

Abstract

Developing regiocontrolled strategies to transform nonactivated C–H bonds into amides is a significant area of interest. Intramolecular C–H functionalization by reactive metal-nitrene and amidyl radicals has been extensively exploited to accomplish exquisite control toward five- and six-membered ring formation.[1] Furthermore, delicate regiocontrol can be exercised by exploiting the difference in bond dissociation energies and steric properties of the tertiary (3°), benzyl, secondary (2°) and primary (1°) C–H bonds.[2-4] Yet, selective amidation of nonactivated methylene C–H bond is particularly problematic. Due to similar electronic and steric properties, regiocontrolled strategies that effectively differentiate the methylene C–H bonds for amidation remain elusive. We are inspired by the recent successes on allylic C–H amidation using electrophilic late transition metal ions such as Pd(II), Rh(III) and Ir(III) as catalysts via the π-allyl metal intermediates.[5-7] We surmised that exploiting chain-walking isomerization of the π -allyl metal intermediate would be a fruitful course for accomplishing control amidation at distal nonactivated methylene sites. Here, we report the development of the [(*p*-cymene)Ru(II)]-catalyzed π-selective amidation of nonactivated distal methylene C–H bonds of terminal alkenes via olefin chain-walking isomerization.



1. Noda, H.; Tang, X.; Shibasaki, M. *Helv. Chim. Acta* **2001**, 104, No. e2100104.
2. Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417.
3. Clark, J. R.; Feng, K.; Sookezian, A.; White, M. C. *Nat. Chem.* **2018**, *10*, 583.
4. Brunard, E.; Bouquet, V.; Van Elslande, E.; Saget, T.; Dauban, P. *J. Am. Chem. Soc.* **2021**, *143*, 6407.
5. Knecht, T.; Mondal, S.; Ye, J.-H.; Das, M.; Glorius, F. *Angew. Chem. Int. Ed.* **2019**, *58*, 7117.
6. Lei, H.; Rovis, T. *J. Am. Chem. Soc.* **2019**, *141*, 2268.
7. Kazerouni, A. M.; Nelson, T. A. F.; Chen, S. W.; Sharp, K. R.; Blakey, S. B. *J. Org. Chem.* **2019**, *84*, 13179.

Bifunctional N-Heterocyclic Carbene Organocatalysts in Asymmetric Catalysis

Yuxin Zhao, Yuxing Cai, Yichi Zhang, Yong Huang*

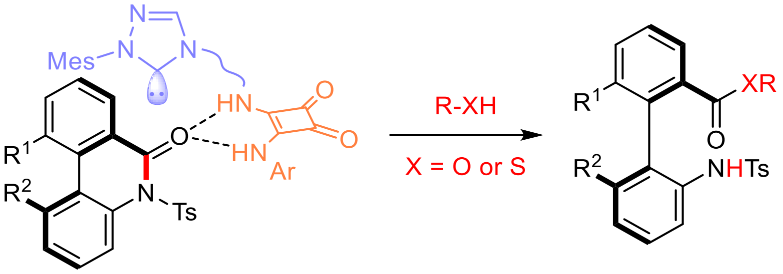
Department of Chemistry, The Hong Kong University of Science and Technology

Clear Water Bay, Kowloon, Hong Kong SAR, China

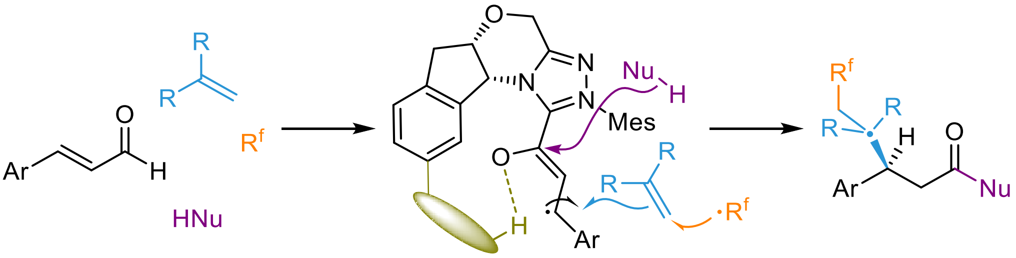
E-mail: yonghuang@ust.hk

Abstract

We developed a chiral bifunctional NHC-squaramide catalyst that achieved high enantiocontrol in challenging asymmetric transformation compared to traditional monofunctional NHC catalysts. In atroposelective nucleophilic ring-opening of *N*-Ts biaryl lactams, a series of axially chiral biaryl molecules was prepared[1]. In radical relay coupling, this bifunctional catalyst induced high facial selectivity in the coupling of congested tertiary carbon radicals and vinylogous ketyl radicals, delivering chiral carboxylates bearing an all-carbon quaternary center at the β-position[2].



chiral bifunctional NHC • axial chirality • up to 99% ee



chiral bifunctional NHC • radical relay coupling • up to 97% ee

Reference

1. Cai, Y.; Zhao, Y.; Tang, K.; Zhang, H.; Mo, X.; Chen, J.; Huang, Y. *Nat. Commun.* **2024**, *15*, 496.
2. 2. Zhao, Y.; Zhang, Y.; Huang, Y. *Angew. Chem. Int. Ed.* **2024**, *63*, e202409566.

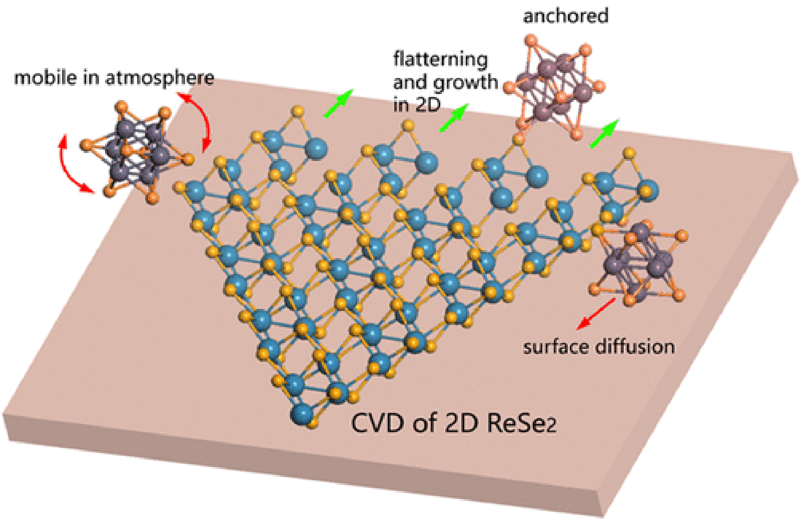
Unveiling the Critical Intermediate Stages During Chemical Vapor Deposition of Two-Dimensional Rhenium Diselenide

Xin Chen, Lok Wing Wong, Lingli Huang, Fangyuan Zheng, Ran Huang, Shu Ping Lau, Chun-Sing Lee, Jiong Zhao, Qingming Deng, Thuc Hue Ly
P5117, Yeung Kin Man Academic Building, CityU, HK, Email: thuchly@cityu.edu.hk

Abstract

Two-dimensional (2D) transition metal dichalcogenides (TMDs) are promising materials for numerous emergent applications. Here, we apply atomic-resolution scanning transmission electron microscopy (TEM) to resolve the intermediate stages during chemical vapor deposition (CVD) synthesis of 2D rhenium diselenide ($ReSe_2$). Contradictory to the conventional growth models proposed previously, stable intermediate species, viz., molecular metal chalcogenide clusters, are experimentally unveiled. These molecular clusters present in the chemical vapor deposition chamber can significantly alter the growth kinetics, mass transport, and surface anchoring sites. Our work resolved the critical question of whether nucleation occurs in atmosphere or on the solid surface. Besides, additional experiments show that the hydrogen environment in the CVD chamber can mitigate the aggregation problem of clusters, which is decisive for obtaining uniform 2D full films. Combined with density functional theory (DFT) calculations, the key reaction steps during growth are identified. Here, we show a clear picture of the debated growth mechanisms of 2D TMDs, expected to facilitate further optimization of CVD growth conditions to achieve stable mass production.

Reaction Dynamics of Disulfide Bond Cleavage in Hydrated Electron Clusters



Jia Yang Lim[1], Chiu Hwi Ng[2], Wai Kit Tang[2*], Chi-Kit Siu[1*]

[1] *Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon Tong, Hong Kong SAR, P. R. China*

[2] *Department of Chemistry, University of Malaya, 50603 Kuala Lumpur, Malaysia*

Chi-Kit Siu (chiksiu@cityu.edu.hk), Wai Kit Tang (wktang@um.edu.my)

Abstract

Hydrated electron, $e^{-}_{(aq)}$ is a potent reducing agent in organic synthesis and radiation chemistry, with noteworthy biological implications. Since its discovery over 40 years ago, reaction mechanisms involving $e^{-}_{(aq)}$ have been the subject of ongoing debate due to its inherently high structural variability which complicates experimental monitoring.[1] Reaction dynamics of a chemical model comprising a hydrated electron cluster with six water molecules, and a dimethyl disulfide, the prototypical molecule containing a S−S bond, $[CH_3SSCH_3(H_2O)_6^{\bullet-}]$ at 100K (comparable with temperature in a previous FT-ICR mass spectrometric study)[2] has been examined using density functional theory based molecular dynamics (DFT-MD) simulations performed with the CP2K Quickstep module. Intracluster electron transfer in $[CH_3SSCH_3(H_2O)_6^{\bullet-}]$ gives $[CH_3SSCH_3^{\bullet-}(H_2O)_6]$, in which the reduced $CH_3SSCH_3^{\bullet-}$ anion is greatly stabilized by the water cluster. Although adiabatic electron affinity of dimethyl disulfide is slightly positive (10 kJ mol^{-1}),[3] our DFT-MD simulations show that this process is barrierless and highly exothermic ($\Delta H = -166$ kJ mol^{-1}) which is comparable with value of -113 ± 13 kJ mol^{-1} based on the nanocalorimetry approach.[2] Our results show a considerable degree of solvent reorganization which transforms the cavity solvation (where the hydrated electron originally located) to a solvation network stabilizing the anionic S−S bond.

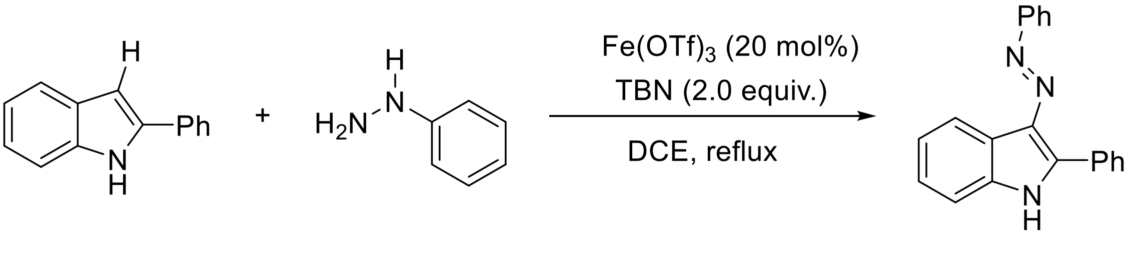
1. Herbert, J. M.; Coons, M. P. *Annu. Rev. Phys. Chem.* **2017**, *68*, 447-472.
2. Höckendorf, R. F.; Hao, Q.; Sun, Z.; Fox-Beyer, B. S.; Cao, Y.; Balaj, O. P.; Bondybey, V. E.; Siu, C.-K.; Beyer, M. K. *J. Phys. Chem. A.* **2012**, *116*, 3824-3835.
3. Carles, S.; Lecomte, F.; Schermann, J. P.; Desfrançois, C.; Xu, S.; Nilles, J. M.; Bowen, K. H.; Bergès, J.; Houée-Levin, C. *J. Phys. Chem. A.* **2001**, *105*, 5622-5626.

Theoretical studies of the reaction mechanism of iron(III) catalyzed synthesis of 3-amidoindole from 2-arylindoles

Feng Panxian
panxifeng2-c@my.cityu.edu.hk

abstract

Iron(III) trifluoromethansulfonate [Fe(OTf)$_3$] was explored experimentally to catalyze coupling reaction between phenylhydrazine and 2- phenylindole with TBN as additive and DCE as solvent, giving moderate to excellent yields. A reaction mechanism was proposed from experimental conclusions derived from different reaction conditions, mainly including [1,5]-hydrogen migration, coordination reaction, nucleophilic addition reaction and charge transfer. Reactants, proposed reaction intermediates and products were modeled with density functional theory (DFT) using B3LYP functional with 6-311+G(d,p) basis set by the Gaussian 16 quantum chemical package. Initially, the substituent on indole and hydrazine were changed from phenyl group to methyl groups for preliminary investigation. Relative energies of reaction intermediates were evaluated to determine the thermodynamic feasibility of each reaction step. In case of encountering chemically unreasonable barrier, alternative reaction pathway was explored. The main objective is to understand the role of Fe(OTf)$_3$ in activating the C-3 position of indole for the nucleophilic attack by hydrazine. Finally, solvent effect will be explored to explain the preference of dichloroethane over ethanol, tetrahydrofuran and methyl cyanide for the coupling Reaction.



Mechanistic Study of N_2O Reduction by CO on Single-Atom Transition Metal-Doped MoS_2: Insights from DFT

Ephrem G. Demissie and Chi-Kit (Andy) Siu*

Department of Chemistry, City University of Hong Kong, Hong Kong SAR, P. R. China
chiksiu@cityu.edu.hk

This study investigates the adsorption and catalytic decomposition of nitrous oxide (N_2O) by carbon monoxide (CO) using first-row late transition metal (TM) adatoms anchored on MoS_2 surfaces, employing density functional theory (DFT). The adsorption of N_2O occurs primarily through two coordination modes: η^1-NL (N-bound) and η^1-OL (O-bound). The η^1-NL mode exhibits stronger binding energies, ranging from −1.22 eV to −0.49 eV, compared to the η^1-OL mode, which shows binding energies ranging from −0.52 eV to −0.22 eV. Two distinct mechanisms for N_2O reduction by CO were examined: the stepwise mechanism and the concerted mechanism. The stepwise mechanism involves initial O-bound N_2O reduction, followed by CO reacting with the resulting metal oxide, and exhibits a lower energy barrier compared to the concerted pathway. For the η^1−NL coordination mode, direct dissociation of the strong N−O bond is challenging, necessitating an internal rotation that switches the coordination mode from N-bound to O-bound, requiring approximately 1 eV to overcome the energy barrier. The stepwise pathway for the N_2O−CO reaction is the most favorable, with the lowest activation energy observed on cobalt (Co) adatoms at 0.38 eV. When TM adatoms are initially bound with CO, the N_2O−CO reaction proceeds through stepwise pathways, involving a transition state with oxygen transfer from N_2O to CO. Although the oxidation of CO by N_2O is exothermic, it is kinetically unfavorable due to its higher energy barrier compared to the stepwise mechanism. This study highlights the potential of these TM adatoms as single-atom catalysts (SACs) for N_2O abatement, offering insights into the development of cost-effective alternatives to noble metal catalysts.

Facet-Junction Induced Strong Metal Support Interaction for Enhanced Alkaline Hydrogen Evolution Reaction

Wenqian Shen, Qiang Fu, Chi Shing Tsang, Lok Wing Wong, Xiaodong Zheng, Jiong Zhao, Thuc Hue Ly
P2407, Yeung Kin Man Academic Building, CityU, HK; wenqishen4-c@my.cityu.edu.hk

Abstract

Strong metal-support interaction (SMSI) plays a critical role in enhancing the catalytic performance of electrocatalysts. Currently, effective approaches to enhance the SMSI effect in supported electrocatalysts still need to be developed, and a comprehensive atomic-level understanding of the underlying reaction mechanisms remains unclear. In this study, a novel facet-junction strategy is proposed to enhance the SMSI between the loaded Ru atoms and the Co_3O_4 support. By modulating the ratio of exposed facet for (111)/(100) crystal plane in Co_3O_4, the hydrogen evolution reaction (HER) performance can be dramatically enhanced by 560% and could achieve a Pt-like HER activity with the overpotential of 45 mV. Detailed analysis with atomic-resolution integrated differential phase contrast (iDPC)-scanning transmission electron microscopy (STEM), atomic-resolution high angle annular dark field (HADDF)-STEM and electron energy loss spectroscopy (EELS) further proved that with proper (111)/(100) crystal plane ratio, the intensified charge distribution near the facet-junction region would modify the electronic structure around the active sites. This work provides new insights to enhance the SMSI and would contribute to the rational design of highly efficient electrocatalysts for water splitting.

Defect Engineering of Two-Dimensional Transition Metal Dichalcogenides for Hydrogen Evolution

MAN Ping, LEE Chun Sing, DENG Qingming*, ZHAO Jiong*, LY Thuc Hue*
Email: thuchly@cityu.edu.hk, jiongzhao@polyu.edu.hk

Abstract

Hydrogen energy presents a promising, environmentally friendly solution to future energy demands due to its high enthalpy and clean production methods. Electrocatalytic hydrogen evolution from water splitting stands out as one of the most sustainable methods, as it does not emit carbon dioxide. However, current commercial catalysts largely depend on expensive Pt-based noble metals, which are unsuited for large-scale implementation. Recent advances in two-dimensional materials, particularly transition metal dichalcogenides (TMDs) like MoS_2 and WSe_2, reveal their potential as alternative catalysts with properties comparable to Pt. Despite their advantages, these TMDs often exhibit limited active sites, particularly within the basal planes, hindering their catalytic efficiency. Research indicates that strategies such as phase and defect engineering can enhance performance, yet a comprehensive understanding of catalytic mechanisms remains elusive. Challenges such as insufficient theoretical foundations, immature preparation methods and high costs further obstruct the commercialization of these sustainable hydrogen production technologies. To tackle these challenges, we propose a novel salt-assisted chemical vapor deposition method for controllable synthesizing ultra-high-density vacancy-rich 2H-MoS_2 for electrocatalysis. Integrating on-chip microdevice configuration and theoretical methodologies to explore the role of defects on catalytic activity, thereby contributing to the effective application of TMDs in electrocatalysis.

References

1. Man P.; Jiang S.; Leung K. H.; et al. Advanced Materials, 2024, *36*, 2304808.
2. Man P.[+]; Huang L.[+]; Zhao J.*; Ly T. H.* Chemical Reviews, 2023, 12, 10990 –11046.
3. Man P.; Srolovitz D.; Zhao J.*; Ly T. H.* Accounts of Chemical Research, 2021, 54, 4191 – 4202.
4. Ly T. H.; Man P.; Leung K. H. 2023, 12, 28. Priority No. 18/522,053.

Electrodepositing 2D materials and study on electrocatalyst application

Ka Ho Leung, Ping Man, Thuc Hue Ly
P2407, Yeung Kin Man Academic Building, City University of Hong Kong;
khleung363-c@my.cityu.edu.hk

Abstract

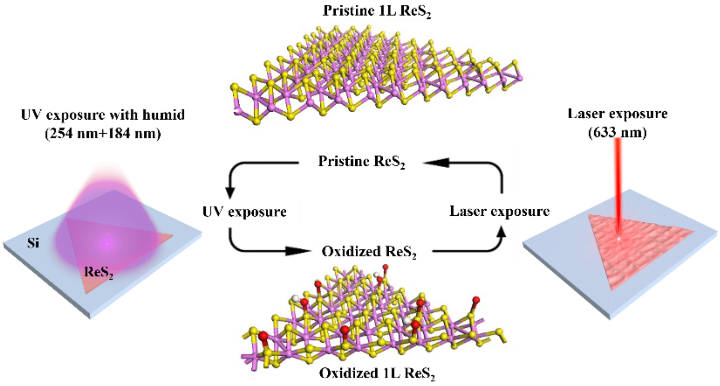
Hydrogen evolution reaction (HER) is one of the famous researched topics for next generation energy by producing the cleanest fuel hydrogen from water, platinum has been found as the best catalyst for HER but due to its high cost, scientists are finding possible alternatives for catalyzing HER. MoS_2 is one of the materials that is considered a competitive substitute due to its higher relative abundance for lower cost and comparable catalytic performance. In this project, a highly controllable and reproductive two-step synthesis route of MoS2film is proposed combined by electrodeposition and low temperature in-situ sulfurization, a few layers MoS2was successfully synthesized and shows comparable catalytic performance with comparison to MoS2synthesized by other methods. Despite the performance has to be improved for further application, the synthesized MoS2shows great potential and this work provides a possible way for controllable large-scale synthesis of MoS2.

Redox Photochemistry on Van Der Waals Surfaces for Reversible Doping in 2D Materials

Huang, L. L.; Yang, T. F.; Wong, W. W.; Zheng, F. Y.; Chen, X.; Lai, K. H.; Liu, H. J.;
Thi, Q. H.; Shen, D.; Lee, C.-S.; Deng, Q. M.; Zhao, J.; Ly, T. H.
Email: q.deng@hytc.edu.cn (Deng, Q. M.); jiongzhao@polyu.edu.hk (Zhao, J.)
thuchly@cityu.edu.hk (Ly, T. H.)

Abstract

Despite the van der Waals (vdW) surfaces are usually chemically inert, un-destructive, scalable, and reversible redox reactions are introduced on the vdW surfaces of 2D anisotropic semiconductors ReX_2 (X = S or Se) facilitated by photochemistry. Ultraviolet (UV) light (with humid) and laser exposure can reversibly oxidize and reduce ReX_2, respectively, yielding a pronounced doping effect with good control. The optical and electrical properties can be thereby reversibly tunable in wide ranges. Such optical direct-writing and rewritable capability via solvent/contaminant-free approach for chemical doping are compelling in the coming era of semiconductor.



References

1. Huang, L. L.; Yang, T. F.; Wong, W. W.; Zheng, F. Y.; Chen, X.; Lai, K. H.; Liu, H. J.; Thi, Q. H.; Shen, D.; Lee, C.-S.; Deng, Q. M.; Zhao, J.; Ly, T. H. *Advanced Functional Materials*, **2021**, 31, 2009166.
2. Huang, L. L.; Chen, H. L.; Ly, T. H. *US non-provisional patent*, **2024**, US 12, 104, 280 B2.

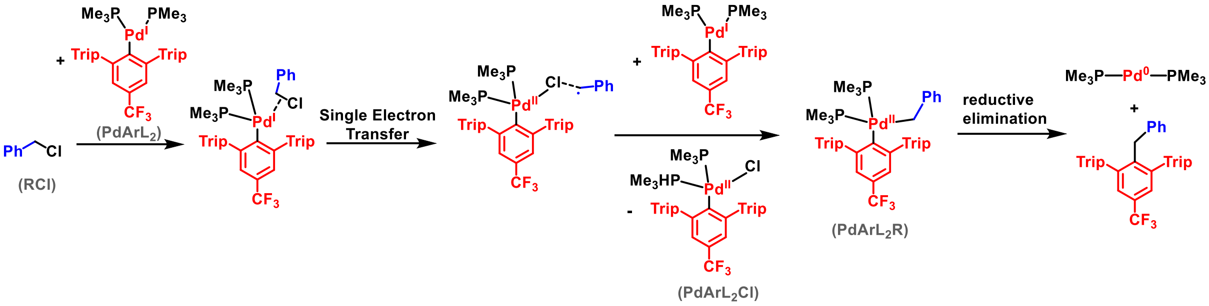
DFT study on the reactions of $(PMe_3)_2Pd^I(Ar^{Trip}\text{-}p\text{-}CF_3)$ with RX

Miaomiao ZHOU, Kai Chung Lau*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon Tong, Hong Kong, China; Email: miaomzhou2-c@my.cityu.edu.hk

Abstract

The capability of the Pd(I) aryl complex in activating the carbon-halogen bonds of organic iodide and benzyl halides have been proved by Deng et. al.[1] Reactivity studies revealed that mononuclear palladium(I) aryl complex **$PdArL_2$** (L=PMe_3, Ar= Ar^{Trip}-*p*-CF_3, Trip = 2,4,6-triisopropylphenyl) perform cross-coupling reactions with benzyl chlorides or bromides. Herein, the mechanism of **$PdArL_2$** with benzyl chlorides was explored, and DFT calculations point out that the cross-coupling products are likely formed from the sequential steps of the stepwise single electron transfer reaction of a Pd(I) aryl complex with benzyl chlorides involving one Pd(II) intermediate (**$PdArL_2Cl$**) followed by reductive elimination reactions of the resulting another Pd(II) intermediates (**$PdArL_2R$**).



Reference:

1. Xia, T.; Long, L.; Leng, X.; Chen, H.; Deng, L. *CCS Chem.* **2024**.

Computational Predictions of Structural and Energetic Properties of Carbon Rings

Ailin Gao and Kai-Chung Lau*
Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon,
Hong Kong; kaichung@cityu.edu.hk

Abstract

Both the DFT and high-level coupled-cluster theory including single and double excitations with a perturbative correction for triple excitations (CCSD(T)) have been performed to predict the molecular structural and energetic properties of neutral and cationic even-numbered cyclo[n]carbons (n=10−20). The analysis of computed BLA, BAA, and IEs has revealed a consistent trend across different calculation methods. Even-numbered cyclo[n]carbons were found to have singlet ground states. The Peierls transition was observed between cyclo[10]carbons and cyclo[18]carbons within the C4k+2 carbon ring series. Larger cyclo[n]carbons exhibited strong BLA, and BAA disappeared. For even-numbered cyclo[n]carbons, the DFT calculation confirms that the structure of the neutral and cationic cyclo[n]carbon ring is not affected by symmetry relaxation. IEs were predicted for both even and odd cyclo[n]carbons using computational methods. Even-numbered cyclo[n]carbons exhibited an oscillatory pattern in IEs for smaller ring sizes. Hückel aromatic cyclo[n]carbons were found to have higher IEs than adjacent antiaromatic cyclo[n]carbons. The IEs for both the aromatic and antiaromatic ring display trends of monotonic decrease in their respective series, the even aromatic 4k+2 series of IEs eases from 9.19 eV for C10 to 8.03 eV for C18, while the antiaromatic 4k counterpart declines from 8.13 eV for C12 to 7.78 eV for C20. Both the DFT and CCSD(T) calculations provide a comprehensive understanding of the ground state structures and properties of carbon rings. The results obtained at CCSD(T) calculations exhibit a reasonable agreement with experimental results. This study provides computational insights into the structures, energies, and aromaticity of cyclo[n]carbons.

Theoretical study of the reaction between Vanadium (I) ion and carbon dioxide in gas phase

CHENG Lin, LAU Kai Chung*
Department of Chemistry, City University of Hong Kong; Tat Chee Avenue, Kowloon Tong, Hong Kong, China; kaichung@cityu.edu.hk

Abstract

Carbon dioxide (CO_2) is an essential driving force of global warming that has attracted a large amount of attention for many years. In this project, the reaction of CO_2 and V^+ (at quintet and triplet state) in the gas phase ($^{3/5}V^+ + CO_2 \rightarrow {}^{3/5}VO^+ + CO$) is studied using the density functional theory of method (at B3LYP/aug-cc-pVQZ level) and coupled-cluster method (at CCSD(T)/aug-cc-pVTZ level). The potential energy surface (PES) of this reaction is obtained. The PES of the 3-dimensional scan between the $^{3/5}$INT1 and $^{3/5}$TS1 shows the quintet-to-triplet spin-crossing can occur before $^{3/5}$TS1 and a quintet-to-triplet spin-crossing point is located between the ^{5}INT1 and ^{3}TS1.

References

1. Huang, C.H. and Tan, C.S. *Aerosol and Air Quality Research,* **2014**, *14*, 480-499.
2. Al-Ghussain, L. *Environmental Progress & Sustainable Energy*, **2019**, *38*, 13-21.

Supramolecular Assembly Transformations of Hemiindigo Amphiphiles in Constructing Macroscopic Soft Scaffolds

Yikun Ren,[a,†] Leong-Hung Cheung,[a,†] Takashi Kajitani, Franco King-Chi Leung[a]*

[a] State Key Laboratory of Chemical Biology and Drug Discovery, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China.

*Corresponding Author: kingchifranco.leung@polyu.edu.hk (F.K.-C. Leung)

[†]These authors contributed equally to this work.

Abstract

Biological processes predominantly occur in water, where supramolecular assemblies, driven by noncovalent interactions, play a crucial role [1, 2]. Inspired by natural hierarchical structures, researchers have developed amphiphilic molecules that self-assemble into functional nanostructures [3]. Recent advancements in stimuli-responsive systems highlight light as an ideal stimulus due to its precision and non-invasive nature. However, traditional UV-responsive systems pose health risks while utilized in biosystems [4]. Although they gained photoswitching ability after structure modification under visible-light, indigoid compounds face challenges like poor hydrolytic stability and limited functionalization [5, 6]. This research focuses on hemiindigo, a compound capable of bidirectional switching under visible light, yet underexplored in bio-applications. We synthesized and characterized a series of hemiindigo amphiphile (HIA), and we developed macroscopic gels of HIA_n using a shear-flow method to evaluate their photoisomerization and potential as cell scaffolds. Our findings suggest that these HIA_n macroscopic gels could serve as innovative cell scaffolds with dual visible light-controlled photoswitching property, offering new opportunities for bio-compatible applications.

References

1. Ball, P., Water as an Active Constituent in Cell Biology. *Chemical Reviews* **2008,** *108* (1), 74-108.
2. Krieg, E.; Bastings, M. M. C.; Besenius, P.; Rybtchinski, B., Supramolecular Polymers in Aqueous Media. *Chemical Reviews* **2016,** *116* (4), 2414-2477.
3. Yuan, C.; Ji, W.; Xing, R.; Li, J.; Gazit, E.; Yan, X., Hierarchically oriented organization in supramolecular peptide crystals. *Nature Reviews Chemistry* **2019,** *3* (10), 567-588.
4. Sandri, A.; Tessari, A.; Giannetti, D.; Cetti, A.; Lleo, M. M.; Boschi, F., UV-A Radiation: Safe Human Exposure and Antibacterial Activity. *International journal of molecular sciences* **2023,** *24* (9).
5. Yau, J. C.-K.; Hung, K.-L.; Ren, Y.; Kajitani, T.; Stuart, M. C. A.; Leung, F. K.-C., Red-light-controlled supramolecular assemblies of indigo amphiphiles at multiple length scales. *Journal of Colloid and Interface Science* **2024,** *662*, 391-403.
6. Chau, M.-H.; Wong, W.-K.; Meng, S.; Kajitani, T.; Leung, F. K.-C., Supramolecular assembled macroscopic soft scaffolds of thioindigo amphiphiles as cell-material interfaces. *Dyes and Pigments* **2024,** *230*, 112334.

Hemi-Protonated Cytosine-Cytosine Base Pair Controls Ultrafast Excited State Dynamics in Human Telomere and c-MYC Promoter i-Motifs

Alvis Tsz-Kit Law[1], Qingwu Xiong[2], Joshua Chiu-Lok Chow[1], Chensheng Ma,[2,*] and Wai-Ming Kwok[1,*]

[1] *Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, P. R. China; wm.kwok@polyu.edu.hk*

[2] *College of Chemistry and Environmental Engineering, Shenzhen University, Shenzhen, Guangdong, P. R. China; macs@szu.edu.cn*

Abstract

Cytosine-rich DNA i-motifs are known for their susceptibility to form cyclobutene pyrimidine dimers (CPDs), which are highly mutagenic and directly associated with skin cancer.[1] Despite this link, the impact of i-motif structures on electron dynamics remains inadequately understood. In our preliminary exploration, we have scrutinized the excited state dynamics of the homo-oligomer dC_{20} i-motifs.[2] To delve deeper into their excited-state dynamics, i-motifs derived from human telomeric and c-MYC promoter sequences were examined using a combination of steady-state, femtosecond time-resolved fluorescence, and transient absorption spectroscopy. Our investigation reveals a sophisticated multichannel deactivation pathway involving charge recombination (CR) occurring within tens of picoseconds and proton-coupled electron transfer (PCET) within the hundreds of picoseconds timescale. Notably, our findings suggest that the charge transfer (CT) and PCET processes in the excited states of i-motifs predominantly occur within the hemi-protonated base pair. Furthermore, we observe that the characteristics of CT states within these hemi-protonated base pairs are notably influenced by the number of C–C+ base pairs present.

References

1. Douki, T.; Cadet, J. *Biochemistry (Easton)* **2001**, *40* (8), 2495-2501.

2. Ma, C.; Chan, R. C. T.; Chan, C. T. L.; Wong, A. K. W.; Chung, B. P. Y.; Kwok, W. M. *Chemistry, an Asian journal* **2018**, *13* (23), 3706-3717.

Acknowledgments

We highly appreciate financial support from the Research Grants Council of Hong Kong (15301721 and 15302423).

Ultrafast Broadband Time-resolved Fluorescence Study on the Förster Resonance Energy Transfer on Human Telomeric G-quadruplex Binding with Thioflavin T

Joshua Chiu-Lok Chow[1], Alvis Tsz-Kit Law[1], Chensheng Ma,[2,*] and Wai-Ming Kwok[1,*]

[1]*Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China;* *wm.kwok@polyu.edu.hk*

[2]*College of Chemistry and Environmental Engineering, Shenzhen University, Shenzhen, Guangdong, China;* *macs@szu.edu.cn*

Abstract

Though the human telomeric DNA sequence lacks genes, it plays a crucial role in safeguarding genes during human cell division to prevent mutation and oncogene formation.[1] The typical guanine (G)-rich sequences of telomeres can adopt a unique conformation known as the G-quadruplex (GQ). Consequently, sensing human telomeric DNA has become a prominent research area. Although GQs can emit detectable intrinsic fluorescence,[2] Thioflavin T (ThT) is a more effective and selective sensor for probing human telomeric GQs by amplifying the fluorescence signal.[3] Through the utilization of femtosecond broadband time-resolved fluorescence (fs-TRF), it has been observed that upon exciting the GQ HTD23 (5'-TAGGG[TTAGGG]$_3$) complexed with ThT in a potassium solution, the fluorescence emitted by the donor HTD23 can trigger Förster Resonance Energy Transfer (FRET) to the acceptor ThT.

References

1. Y. Xu, *Chemical Society Reviews*, **2011**, *40*, 2719-2740.
2. C. Ma, J. C.-L. Chow, A. K.-W. Wong, Q. Xiong, J. Chomchoei, and W.-M. Kwok, *The Journal of Physical Chemistry Letters*, **2023**, *14*, 5085-5094.
3. J. Mohanty, N. Barooah, V. Dhamodharan, S. Harikrishna, P. I. Pradeepkumar, and A. C. Bhasikuttan, *Journal of the American Chemical Society*, **2013**, *135*, 367-376.

Acknowledgments

We highly appreciate financial support from the Research Grants Council of Hong Kong (15301721 and 15302423).

Mechanochemical Fabrication of Full-Color Luminescent Materials from Aggregation-Induced Emission Prefluorophores for Information Storage and Encryption

H. Xie,[a] R. T. K. Kwok,[a] J. W. Y Lam,[a] J. Zhang,[b] and B. Z. Tang[a,b,]*
[a] Department of Chemistry, The Hong Kong Branch of Chinese National Engineering Research Center for Tissue Restoration and Reconstruction, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong
[b] School of Science and Engineering, The Chinese University of Hong Kong, Shenzhen, Guangdong 518172, China *Email: tangbenz@ust.hk

Abstract

The development of luminescent materials through mechanochemistry represents a fascinating yet complex frontier in materials science. In this study, we present a methodology for synthesizing brightly luminescent polymers via the mechanochemical coupling of aggregation-induced emission (AIE) prefluorophores with generic polymers. We synthesized a range of AIE moieties tethered to the 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) radical, which initially exhibit weak fluorescence due to intramolecular quenching. However, the mechanical coupling of these prefluorophores with macromolecular radicals generated through ball milling of generic polymers significantly enhances the fluorescence of the resulting materials. We carefully evaluate the tunable emission of the AIE-modified polymers, which spans a broad spectrum from the visible to the near-infrared region. This study highlights the potential of these materials in stimuli-responsive systems, particularly for applications in information storage and encryption displays. By simplifying the conventional synthesis of luminescent polymers, our approach offers a new paradigm in the field of AIE-based materials with promising implications for advanced technological applications.[1]

Reference

1. Xie, H.; Wang, J.; Lou, Z.; Hu, L.; Segawa, S.; Kang, X.; Wu, W.; Luo, Z.; Kwok R. T. K.; Lam J. W. Y.; Zhang J.; Tang B. Z. J. Am. Chem. Soc. 2024, 146, 18350−18359.

Is the Whole Equal to, or Greater than, the Sum of its Parts? The Similarity and Difference between Molecules and Aggregates

Jin Wang, Wenlang Li, Xinwen Ou, Xinmeng Chen, Jianyu Zhang, Shengyi Yang,
Ryan T. K. KWOK*, Jacky W. Y. LAM *, Ben Zhong Tang*

Department of Chemistry, and the Hong Kong Branch of Chinese National Engineering Research Center for Tissue Restoration and Reconstruction, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR 999077, P.R. China. Email: chjacky@ust.hk; tangbenz@cuhk.edu.cn

Abstract

Reductionism and holism are two well accepted philosophical approaches to understanding the relationship between the whole and its parts. Herein, by manipulating the aggregation process of a tetraphenylethene derivative called TPE-NS with ionic interactions, two obtained aggregates, named TPE-NS-a and TPE-NS-b, exhibited completely different structure-determined behaviors. Specifically, the aggregate structure of TPE-NS-a was determined by its single molecule with free conformation in solution, while the distorted molecule conformation in TPE-NS-b was dictated by the united aggregate, which finally determined the performances of aggregates. Photochromism (PC) and photoluminescence (PL) were found to be inactive in TPE-NS-a and TPE-NS-b, respectively, which was similar to the solution. However, PL in TPE-NS-a and PC in TPE-NS-b were active, which was distinguished to solution. Investigating the structure-property relationship both in the single molecule and the aggregate states, and further exploring the transformation of these relationship before and after aggregation, was coined as a feasible approach to understand when the whole is equal to or greater than the sum of its parts.

References

1. J. Wang, W.L. Li, X.W Ou, X.M. Chen *et al. Matter*, **2024**, *7*, 2551–2566.

Bright and Ultralong Organic Phosphorescence via Sulfonic Acid Functionalization for High-Contrast Light-Writing Display

Xin Li, Zhihong Guo*, Jacky W. Y. Lam*, Ben Zhong Tang*
Department of Chemistry, The Hong Kong University of Science and Technology, Hong Kong. Prof. Zhihong Guo: chguo@ust.hk; Prof. Jacky W. Y. Lam: chjacky@ust.hk; Prof. Ben Zhong Tang: tangbenz@ust.hk.

Abstract

It is challenging to achieve room temperature phosphorescence (RTP) in pure organics with both high efficiency and long lifetime.[1] While much effort has been placed on discovering efficient phosphor skeletons, the importance of phosphor functionalization in enhancing the RTP performance has not received adequate attention. Herein, we demonstrate that functionalization of phosphors with sulfonic acid can ensure both bright and ultralong RTP, outperforming other substituents. The unique trigonal pyramidal structure of sulfonic acid group allows for more effective (n, π*) transitions to enhance intersystem crossing efficiency. Its highly polarized S–O bonds render strengthened hydrogen bonding interactions and a narrower confinement within the poly(vinyl alcohol) (PVA) matrix, to minimize the non-radiative dissipation. Furthermore, its excellent water-solubility contributes to the outstanding transparency of PVA film (over 97%), yielding high-quality optical imaging with a high contrast ratio of 48.0 and a low blurriness of 0.24. By leveraging these advantages, light-writing displays with sharp imaging, high sensitivity and exceptional rewritability are demonstrated.[2]

References

1. Zhao W., Tang B. Z. et al. Room-Temperature Phosphorescence from Organic Aggregates. *Nat. Rev. Mater.* **2020**, *5*, 869–885.
2. Li X., Tang B. Z. et al. Bright and Ultralong Organic Phosphorescence via Sulfonic Acid Functionalization for High-Contrast Light-Writing Display. *J. Am. Chem. Soc.* **2025**, under review.

Development of Controllable Hetero-Pauson-Khand Polymerization to Functional Stimuli-Responsive Poly(γ-lactam)s

Wutong DU, Xinyue LIU, Feiyi SUN, Jacky W.Y.Lam, Jinglei YANG, Ben Zhong TANG
Department of Chemistry, The Hong Kong University of Science and Technology;
maeyang@ust.hk, tangbenz@cuhk.edu.cn

Abstract

Polymers containing lactam structures play a crucial role in both natural biological systems and human life, and their synthesis, functions and applications are of utmost importance for biomimetics and the creation of new materials. In this study, we developed an efficient heterogeneous Pauson–Khand polymerization (h-PKP) method for the controlled synthesis of main-chain poly(γ-lactam)s containing α, β-unsaturated γ-lactam functionalities using readily available internal alkynes and imines. The molecular weights of the resulting poly(γ-lactam)s can be precisely controlled by adjusting the ratio of phenyl formate and nickel. These polymers exhibit high solid-state luminescence and demonstrate rapid and sensitive dual responsiveness to light and acid stimuli. The unique dual-emission peaks observed in poly(N−H/γ-lactam)s obtained through post-treatment under acidic conditions demonstrate a mechanism of aggregation-induced intermolecular excited-state proton transfer specific to lactam structures. The efficient one-pot synthetic method for poly(γ-lactam) provides a novel strategy for constructing polymers with γ-lactam structures in the main chain and the simple and efficient post-modification method offer a versatile toolbox for functionalizing poly(γ-lactam)s to expand their potential applications.

References

1. Du, W.T.; Liu, X.Y; Sun, F.Y.; Lam, J. W. Y.; Yang, J.L; Tang, B. Z.; *Angew. Chem. Int. Ed.* **2025**, 64, e202413275.

Hot Electron Photocatalysis Enabled by Enhanced Auger Effect in Non-toxic n-type Quantum Dots

Jianning Feng, Kezhou Fan, Qinxuan Cao, Wenfei Liang, Pui Ying Wong, Jie Xue, Kin Ting Chang, Kam Sing Wong, and Haipeng Lu*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, 999077, Hong Kong, China (SAR)
haipenglu@ust.hk

Abstract

Colloidal semiconductor nanocrystals, or quantum dots (QDs), have gained prominence as versatile photocatalysts for organic transformations.[1] However, one of the major drawbacks is the reliance on toxic lead and cadmium metals, limiting their broad applications in solar-to-chemical conversion. Additionally, existing systems primarily utilize bandedge carriers for less challenged photoredox reactions, while harvesting hot carriers for chemical transformations is rarely explored. To address these issues, non-toxic, cost-effective, and recyclable $CuInS_2$ QDs and non-stoichiometric ZnCuInS QDs are utilized as potent photoreductants for the generation of aryl radical from aryl halides (Ar-I, Ar-Br, Ar-Cl), following by reductions (up to −2.90 V vs. SCE) or cross couplings (C-C, C-P, C-B and C-S), enabled by Auger hot electron. Compared with $CuInS_2$ QDs, ZnCuInS QDs greatly shorten the reaction time to one fourth, and significantly increase the product yields ten times. The remarkable efficiency observed in ZnCuInS QDs can be attributed to the enhanced Auger effect in n-type semiconductors. Our research highlights the potential of directly utilizing Auger hot electrons for extreme-reduction potential organic transformations under mild conditions with non-toxic QDs.

References

1. Cao, Q.; Feng, J.; Chang, K. T.; Liang, W.; Lu, H. Emerging Opportunities of Colloidal Quantum Dots for Photocatalytic Organic Transformations. *Advanced Materials n/a* (n/a), 2409096.

Recent Studies in Molecular Vibrational Polaritons by Ultrafast Spectroscopy

Peiyu Zhu, Teng-Teng Chen
Postal Address: 7134, Academic Building, HKUST, Clear Water Bay, Kowloon, HK
Email Address: tentengchen@ust.hk

Abstract

Molecular vibrational polaritons (MVPs) arise when molecular vibrational modes strongly couple with cavity photon modes, providing a means to manipulate chemical reaction rates and pathways. Foundational work by Thomas Ebbesen demonstrated that vibrational strong coupling (VSC) can slow reactions such as silyl deprotection by more than fivefold[1,2]. Subsequent ultrafast spectroscopic studies, notably by Wei Xiong's group and his colleagues[3,4], have revealed detailed insights into polariton dynamics in systems like $W(CO)_6$ and $Fe(CO)_5$. Recent advancements in photonic architectures—including dual and confined cavity designs as well as plasmonic substrates—have potential to enhance coupling efficiency and clarify energy transfer processes between polaritonic and dark modes. This poster consolidates concrete experimental findings on polariton lifetimes, energy transfer mechanisms, and altered reaction energetics, while addressing challenges such as dark mode dominance, and highlights promising avenues for precise chemical control and quantum simulation.

References

1. T. W. Ebbesen, Acc. **2016**, Chem. Res. 49 (11), 2403-2412 .
2. A. Thomas, J. George, A. Shalabney, M. Dryzhakov, S. J. Varma, J. Moran, T. Chervy, X. Zhong, E. Devaux, C. Genet, J. A. Hutchison and T. W. Ebbesen, Angew. Chem. **2016,** Int. Ed. 55 (38), 11462-11466.
3. B. Xiang, R. F. Ribeiro, M. Du, L. Chen, Z. Yang, J. Wang, J. Yuen-Zhou and W. Xiong, Science, **2020**, 368 (6491), 665-667.
4. T.-T. Chen, M. Du, Z. Yang, J. Yuen-Zhou and W. Xiong, Science **2022**, 378 (6621), 790-794 .

Orbital Entropy as a Descriptor Evaluating Calculation Quality and Interaction in Chemistry Systems

Hu Chenyu
Postal address: huchenyu@connect.hku.hk

Abstract

Despite its successful application on many chemistry systems, density functional theory (DFT) still suffers from the limitation in describing open shell systems and molecules at near bond-breaking structure. The concept of orbital entropy from quantum information theory has shown its potential for analyses of the bonding structure of some simple chemistry systems.1 Herein, the insufficiency of DFT calculations is demonstrated from the perspective of orbital entropy. Besides, we would like to explore the applications of orbital entropies in analyzing catalytic reactions between reactant and catalyst. Furthermore, we will make use of orbital entropy as another descriptor besides energy for evaluation and to promote efficiency of configuration interaction methods.

Reference

1. Boguslawski, K.; Tecmer, P.; Barcza, G.; Legeza, Ö.; Reiher, M. *Journal of Chemical Theory and Computation,* **2013**, *9,* 2959 – 2973.

Quantum Chemical Prediction for Protein Correlation Energies with Projected Atomic Orbitals

Shaowei NIE, Yin ZHUO

Department of Chemistry, The University of Hong Kong 999077, P. R. China;
u3010751@connect.hku.hk

Abstract

Exact computation of correlational energies is extremely expensive for large molecule systems, such as proteins. Based on our previous T-dNN model[1], we furtherly exploit the locality of both real and orbital spaces by introducing projected atomic orbitals (PAOs)[2] The cost of density-fitting 3c2e integral generation, which is the most time consuming step in the feature generation, has been reduced. For 1-D molecules such as (Gly)n, about 30% AOs are truncated out. Combined with protein fragmentation methods[3], we are able to predict the correlation energies of large proteins by training on small fragmentations.

References

1. Ng, W.; Liang, Q.; Yang, J. *J. Chem. Theory Comput*, **2023**, *19*, 5439-5449.
2. Pulay, P. *Chem. Phys. Lett*, **1983**, *100*, 151-154.
3. Wang, T.; He, X.; Li, M, et al. *Nature*, **2024**, *635*, 1019-1027.

Accurate Neural Network Fine-Tuning Approach for Transferable Ab Initio Energy Prediction across Varying Molecular and Crystalline Scales

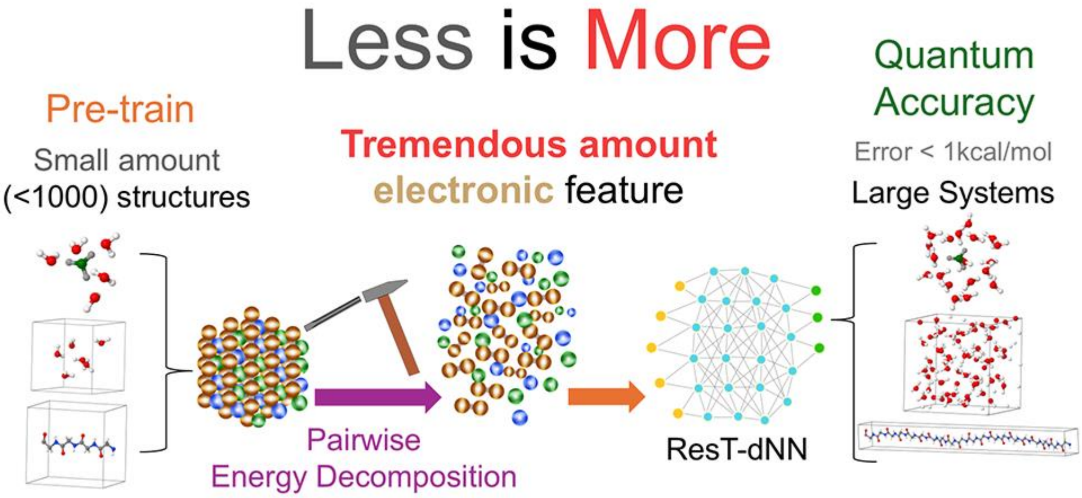
Wai-Pan Ng[1], Zili Zhang[†], Jun Yang
Department of Chemistry, The University of Hong Kong, Hong Kong, P.R. China
Hong Kong Quantum AI Lab Limited, Hong Kong, P.R. China
juny@hku.hk

Abstract

Existing machine learning models attempt to predict the energies of large molecules by training small molecules, but eventually fail to retain high accuracy as the errors increase with system size.[1] Through an orbital pairwise decomposition of the correlation energy, a pretrained neural network model on hundred-scale data containing small molecules is demonstrated to be sufficiently transferable for accurately predicting large systems, including molecules and crystals.[2] Our model introduces a residual connection to explicitly learn the pairwise energy corrections, and employs various low-rank retraining techniques to modestly adjust the learned network parameters. We demonstrate that with as few as only one larger molecule retraining the base model originally trained on only small molecules of $(H_2O)_6$, the MP2 correlation energy of the large liquid water $(H_2O)_{64}$ in a periodic supercell can be predicted at chemical accuracy. Similar performance is observed for large protonated clusters and periodic poly-glycine chains. A demonstrative application is presented to predict the energy ordering of symmetrically inequivalent sublattices for distinct hydrogen orientations in the ice XV phase. Our work represents an important step forward in the quest for cost-effective, highly accurate and transferable neural network models in quantum chemistry, bridging the electronic structure patterns between small and large systems.

---

[1] W.-P. N. and Z. Z. contributed equally to this study.



References

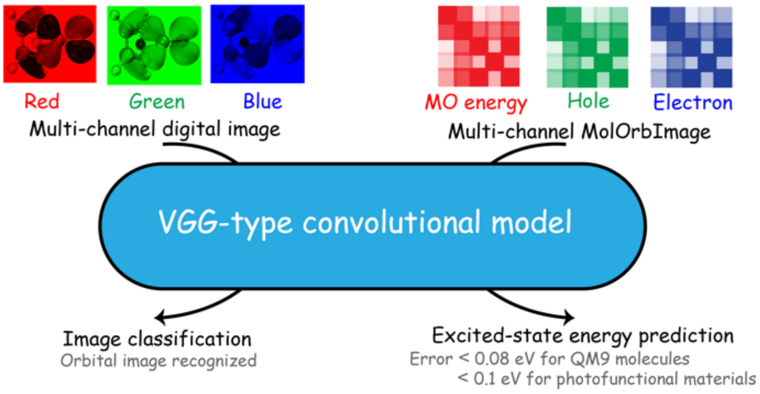
1. Liang, Q.; Yang, J. *J. Chem. Theory Comput.* 2021, *17*, 6841–6860.
2. Ng, W.-P.; Liang, Q.; Yang, J. *J. Chem. Theory Comput.* 2023, *19*, 5439–5449.

Encoding Hole–Electron Information in the Multi-Channel MolOrbImage for Machine-Learned Excited-State Properties of Practical Photofunctional Materials

Ziyong Chen and Vivian Wing-Wah Yam*
Department of Chemistry, The University of Hong Kong, Hong Kong
wwyam@hku.hk

Abstract

We present a novel class of one-electron multi-channel molecular orbital images (MolOrbImages) designed for the prediction of excited-state energetics in conjunction with the state-of-the-art VGG-type machine-learning architecture.[1] By representing hole and electron states in the excitation process as channels of MolOrbImages, the revised VGG model achieves excellent prediction accuracy for both low-lying singlet and triplet states, with mean absolute errors (MAEs) of <0.08 and <0.1 eV for QM9 molecules and practical photofunctional materials with up to 560 atoms, respectively. Remarkably, the model demonstrates exceptional performance (MAE < 1 kcal/mol) for the T_1 state of QM9 molecules, making it a non-system-specific model that approaches chemical accuracy. The general rules attained, for instance, the improved performance with well-defined MO energies and the reduced overfitting concern via the inclusion of physically insightful hole−electron information, provide invaluable guidelines for the further design of orbital-based descriptors targeting molecular excited states.



References

1. Chen, Z.; Yam, V. W.-W. *J. Am. Chem. Soc.* **2023**, *145*, 24098–24107.

Photothermal Cavitation-Driven Micromotor Penetrate Cell Membrane

Binglin Zeng[1], Jialin Lai[1], Jingyuan Chen[1], Yaxin Huang[1], Qingxin Guo[1], Chao Huang[1],
Xiaofeng Li[1], Changjin Wu[2], Shuai Li[3*], and Jinyao Tang[1*]
1. Department of Chemistry, The University of Hong Kong, Hong Kong, China
2. Department of Mechanical Engineering, The University of Hong Kong, Hong Kong, China
3. College of Shipbuilding Engineering, Harbin Engineering University, Harbin, China
E-mail: lishuai@hrbeu.edu.cn; jinyao@hku.hk

Abstract

Photothermally-driven micro/nanomotors efficiently convert light into mechanical motion, making them highly attractive for biomedical applications due to their exceptional biocompatibility and safety. However, one mystery of the photothermally-driven micro/nanomotor is the wide range of reported light intensities applied, ranging from 1 W cm^{-2} to over 10^5 W cm^{-2}. To address this mystery, we systematically investigated the propulsion of carbon microbottle-based micromotor under three illumination conditions: continuous laser, pulsed laser, and scanning laser, where a new cavitation-driven mechanism is identified. Using a high-speed camera, we find that the instantaneous deposition of laser energy on the micromotors can lead to transient and localized evaporation of the solvent, creating cavitation bubbles to drive micromotors with ultrafast speed, where instantaneous velocity over 1 m s^{-1} is observed. Through precise modulation of the scanning orientation and intensity of laser, directional propulsion and targeted explosions of the microbottles are achieved, where the instant force is strong enough to penetrate live cell membranes. Finally, the cavitation-driven micromotors are exploited as gene transfection tools, where targeted cytoplasmic transfection is demonstrated.

Photoredox Bath Induced Phase Separation and Universal Material 3D Nanoprinting

Xiaofeng Li[1], Binglin Zeng[1], Jialin Lai[1], Yaxin Huang[1], Dongdong Jin[2], Mingliang Li[1], Qingxin Guo[1], Yingnan Cao[1], Wei Wang[3], Lu Shi[4], Jinhong Guo[5], Xing Ma[2*] and Jinyao Tang[1*]

1. Department of Chemistry, The University of Hong Kong; Hong Kong, China.
2. Sauvage Laboratory for Smart Materials, School of Integrated Circuits, Harbin Institute of Technology (Shenzhen); Shenzhen, 518000, China.
3. School of Materials Science and Engineering, School of Integrated Circuits, Harbin Institute of Technology (Shenzhen); Shenzhen, 518000, China.
4. The M.O.E. Key Laboratory of Laboratory Medical Diagnostics, The College of Laboratory Medicine, Chongqing Medical University; Chongqing, 400000, China
5. School of Sensing Science and Engineering, Shanghai Jiao Tong University; Shanghai, 200000, China.

Email: maxing@hit.edu.cn; jinyao@hku.hk

Abstract

Phase transitions are ubiquitous for all materials and living matter, where the molecular interaction dictates the formation of various phases and their properties. The ability to control such interaction would enable the on-demand phase transition and materials with novel responsive properties. While canonical intermolecular forces are commonly behind this control, dissipative chemical reactions may induce effective interaction and phase transition, which has rarely been studied. In this research, we show that the photoredox process causes substantial apparent attractions between molecules without net chemical reaction, leading to Avrami-like aggregation and phase transition. More importantly, the photoredox solution acts as an active bath, allowing any immersed inert colloids and solute molecules to partially inherit the active nature of the bath, thereby inducing similar attraction and leading to aggregation and phase separation. With this universal process, the photoredox bath ink is formulated, allowing general materials to be patterned by laser direct writing with diffraction-limited resolution. We demonstrated that the nanostructures composed of DNA, protein, and enzyme, as well as the operational organic electronic components, such as conductive nanowires, field-effect transistors, and logic gates, can all be directly printed from formulated photoredox baths.

Photoredox Molecular Swimmer

Jialin Lai[1,2], Binglin Zeng[1], Xiaofeng Li[1], Mingliang Li[1], Qiujiang Liang[1], Chenyu Hu[1], Jun Yang[1*], Lang Rao[2*] and Jinyao Tang[1*]
1. Department of Chemistry, The University of Hong Kong, Hong Kong, China;
2. Institute of Chemical Biology, Shenzhen Bay Laboratory, Shenzhen, China.
juny@hku.hk; lrao@szbl.ac.cn; jinyao@hku.hk

Abstract:

Recent decades have seen a surge in nanometer and molecular-scale machines, from the 2016 Nobel Prize-winning molecular machines to modern active colloids and microswimmers that convert chemical or light energy into mechanical work. However, achieving propulsion at the molecular scale is highly challenging, raising debates about the feasibility of molecular swimmers compared to colloidal nanomotors. This study demonstrates that under photoredox conditions, dye molecules deviate from Brownian motion, exhibiting mechanical propulsion. Further experiments suggest a non-reciprocal interaction between the photoredox center and redox shuttle molecules. The propulsion mechanism likely stems from directional solvent pumping, driven by a Brownian ratchet effect enabled by pseudo-periodic surface potential shifts during photoredox reactions. Notably, with excellent biocompatibility, these photoredox molecular swimmers can modulate lipid droplet transport and regulate cell membrane permeability in live cells. Given the simplicity and ubiquity of photoredox systems, our findings establish a promising molecular engine for the next generation of autonomously moving molecular robots.

Tunable lasers from colloidal assembly

Chao Huang[1], Jinyao Tang[1*]
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong;
Email: jinyao@hku.hk

Abstract

Self-assemblies refer to highly ordered structures, and in some cases, they can even form crystals from individual components. The macroscopic properties of materials predominantly hinge upon these assembled crystal structures. Recent investigations have demonstrated that the self-assemblies of colloidal particles hold the potential to achieve a continuously adjustable laser threshold. Here, we present a novel photonic architecture that enables the manipulation of laser action by precisely controlling the self-assemblies of colloidal particles. We employ optoelectronic tweezers, which offer a versatile and universal strategy for organizing particles. Our research reveals that due to the integration of the spherical lens effect and light-actuated alternating current (AC) electroosmosis, colloidal particles can be effectively driven by the illumination.

Furthermore, by carefully adjusting the illumination conditions, we can induce the formation of various two-dimensional (2D) Bravais lattices. Simultaneously, the laser modes can be manipulated both reversibly and in real-time according to the 2D Bravais lattices formed by the colloidal particles. In conclusion, our optically guided dynamic colloidal assemblies provide a straightforward but highly effective strategy for exploring the modes of random lasing, the coupling of cavities, and the tunable photonic band gap. This approach opens new possibilities for the development of advanced photonic devices and applications.

Modular Micromotor Fabrication with Self-Focusing Lithography

Qingxin Guo[1], Binglin Zeng[1]*, Yingnan Cao[1], Xiaofeng Li[1], Jingyuan Chen[1], Wei Wang[2] and Jinyao Tang[1]*

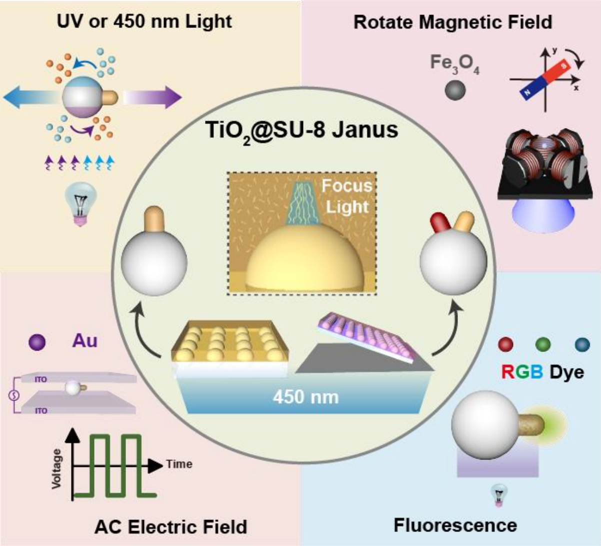
1. Department of Chemistry, The University of Hong Kong, Hong Kong, China.

2. School of Materials Science and Engineering, School of Integrated Circuits, Harbin Institute of Technology (Shenzhen); Shenzhen, 518000, China.

E-mail: binglin@hku.hk; jinyao@hku.hk

Abstract

In this study, we present a modular fabrication approach for micromotors with a particle-tip structure based on the self-focusing lithography induced by an array of TiO_2 microspheres. By adjusting the tip composition or loading, precise programming of motor functionality is achieved, allowing for various capabilities such as photoredox reaction-induced propulsion, fluorescent imaging, electric and magnetic navigation. Furthermore, we demonstrate the flexibility of this fabrication method by selectively loading materials onto two tips to achieve multifunctionality within a micromotor unit. This study proposes a straightforward and versatile approach for modular functional micromotors.



References

1. Guo, Q.; Zeng, B. *; Cao, Y.; Li, X.; Chen, J.; Wang, W.; Tang, J.* *Small Methods*, **2024,** 202401388.

Active Colloidal Phase Transitions under Optically Controlled Effective Temperature

Jingyuan Chen,[1] Shaobin Zhuo,[2] Binglin Zeng,[1] Zhigang Li[2*] and Jinyao Tang[1*]
[1]Department of Chemistry, The University of Hong Kong, Pokfulam, Hong Kong, China.
[2]Department of Mechanical and Aerospace Engineering, the Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China.
Email: mezli@ust.hk; jinyao@hku.hk

Abstract

Colloids can be utilized as model "gigantic atoms" to emulate phase behaviors at the atomic scale for its easy observation and slower dynamics. Photoactive colloids have recently been demonstrated with on-demand directional interactions as well as tunable dynamics, which are particularly suitable to emulate the phase transition due to their excellent controllability. In this study, we demonstrate that light can induce effective temperature up to a few thousand Kelvins on photoactive colloids, wherein temperature-dependent phase behavior emerges. By inducing directional interaction and optically controlled effective temperature with light illumination, the phase transition between zigzag band, liquid, and vapor, distinguished by their orientational order, can be precisely controlled. Further addition of passive colloids analogous to reactant atoms with different sizes causes "chemical reaction" between the two colloid species, leading to the formation of binary colloid compounds with various stoichiometric ratio. The effect of different "dopant atom" sizes on the melting point of the binary phase is reproduced in an active colloidal system.

Guanidinium-appended Microgels for Controlled Intracellular Protein Delivery

Henry Chak Man YAU and Kou OKURO
okuro@hku.hk

Abstract

Intracellular protein delivery holds great therapeutic potential, yet conventional delivery methods face significant challenges in efficient cellular uptake and preventing undesired protein leakage from carriers.[1,2] Here, we developed a novel microgel system functionalized with guanidinium ions (μGu-gel) that can efficiently encapsulate and protect therapeutic proteins through multivalent salt-bridge interactions with the protein surface.[3] Using carbonic anhydrase as a model protein, we demonstrated that μGu-gels maintained protein stability and activity for over one week, with no detectable leakage under physiological conditions. The encapsulated protein showed responsive release behavior starting at glutathione concentrations of 2 mM, enabling controlled release under intracellular conditions (typically 1–10 mM).[4] Given that guanidinium ions strongly interact with cell membranes to facilitate cellular uptake,[5] this stimulus-responsive carrier system provides a promising platform for efficient intracellular protein delivery in therapeutic applications.

References

1. Leader, B.; Baca, Q. J.; Golan, D. E. *Nat. Rev. Drug Discov.*, **2008**, *7,* 21–39.
2. Porello, I.; Cellesi, F. *Front. Bioeng. Biotechnol.*, **2023**, *11*, 1211798.
3. Mogaki, R.; Hashim, P. K.; Okuro, K.; Aida, T. *Chem. Soc. Rev.*, **2017**, *46*, 648–6491.
4. Lu, S. C. *Biochim. Biophys. Acta* **2013**, *1830*, 3143–3153.
5. Man, M. H. K.; Yau, H. C. M.; Okuro, K. *Mater. Chem. Front.*, **2025**, *in press*.

Guanidinium-appended γ-cyclodextrin: efficient fullerene solubiliser for enhanced photodynamic therapy

Mervyn Ho Kong MAN, Henry Chak Man YAU and Kou OKURO
okuro@hku.hk

Abstract

Efficient solubilisation of inherently hydrophobic fullerenes in aqueous media is crucial for their photodynamic therapy (PDT) applications.[1–3] In particular, fullerenes are promising as photosensitisers for PDT due to their absorption of tissue-permeable visible light, photochemical stability and exceptionally high quantum yields in the generation of cytotoxic singlet oxygen.[4] We demonstrated the efficacy of guanidinium-appended *γ*-cyclodextrin (CD^{Gu}) as a novel solubiliser for C_{60} and C_{70} fullerenes, achieving exceptionally high aqueous concentrations of 3.1 mM and 0.37 mM, respectively, through simple mechanical mixing in the presence of Na^+ ions.[5] The resulting complexes, $CD^{Gu}\supset C_{60}$ and $CD^{Gu}\supset C_{70}$, enabled efficient fullerene transfer to cell membranes, a critical factor for PDT efficacy. Notably, $CD^{Gu}\supset C_{70}$ exhibited excellent $^1O_2$ generation (quantum yield $\Phi_\Delta = 0.77$ at 630 nm) and induced >90% cell death with only 5 min of white light exposure *in vitro*.

References

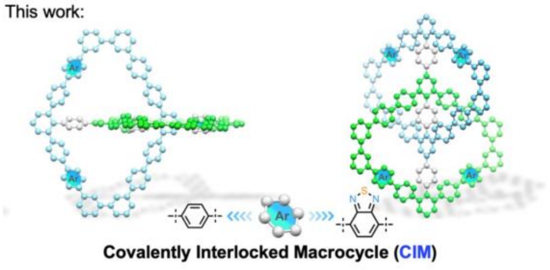
1. Biswas, R.; Batista Da Rocha, C.; Bennick, R. A.; Zhang, J. *ChemMedChem*, **2023**, *18*, e202300296.
2. Ikeda, A. *J. Inclusion Phenom. Macrocyclic Chem.*, **2013**, *177*, 49–65.
3. Nakamura, E.; Isobe, H. *Acc. Chem. Res.*, **2003**, *36*, 807–815.
4. Hamblin, M. R. *Photochem. Photobiol. Sci.*, **2018**, *17*, 1515–1533.
5. Man, M. H. K.; Yau, H. C. M.; Okuro, K. *Mater. Chem. Front.*, **2025**, *in press*.

Covalently interlocked rigid conjugated macrocycles (CIMs)

Biao Xia,[1] Junzhi Liu[1],*
[1] *Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, China*
E-mail: juliu.hku.hk

In the past 30 years, carbon allotropes of sp^2 hybridized carbon, including fullerene (**0D**), carbon nanotubes (**1D**) and graphene (**2D**), have been hot topics in carbon nanostructure research. Although the precise synthesis of unique 3D carbon nanostructures is extremely challenging, their extraordinary electronic, optical and magnetic properties have stimulated considerable interest among scientists. This article reports the synthesis of a novel class of conjugated interlocked macrocycles (**[2]CIM**) and their detailed characterization of their physicochemical properties.

Conjugated carbon nanostructures have properties that can be adjusted with structural modification, so in the future the 3D structural framework of **[2]CIM** can be further optimized and modified to further improve its physical and chemical properties. This work not only provides a window for in-depth study of the optical and electromagnetic properties of this new type of three-dimensional conjugated molecules but also paves the way for the precise synthesis of cubic graphite and Mackay crystals at the molecular level.



References

1. Dumslaff, B., Reuss, A. N., Wagner, M., Feng, X., Narita, A., Fytas, G., and Müllen, K. *Angew. Chem. Int. Ed.* **2017**, *56*, 10602-10606.
2. Ejlli, B., Nußbaum, P., Rominger, F., Freudenberg, J., Bunz, U. H., and Müllen, K. *Angew. Chem. Int. Ed.* **2021**, *60*, 20220-20224.

Structural design in ordered ionic covalent organic frameworks for fast ion transport

Huan Xu, Chang Shen, Yao Li, Han Deng and Zhengxiao Guo*

Postal address: Department of chemistry, The university of HongKong, Pokfulam, Hong Kong SAR, P. R. China, email: zxguo@hku.hk

Abstract

Covalent Organic Frameworks (COFs) are a class of ionic conductors with well-defined channels and structural robustness, offering advantages such as low diffusion energy barriers and excellent temperature tolerance compared to classical conductors[1]. However, challenges remain, including: (1) the low concentration of mobile ions in the nanochannels of COFs, which hinders efficient ionic conduction; and (2) the high energy barrier for ionic migration within the COF nanochannels. To address these limitations, the present work proposes three strategies: (1) the use of multi-site (ether) dissociation salts to increase the concentration of mobile ions; (2) the development of a cationic-type COF to enhance the cation transference number; and (3) the in-situ synthesis of ionic COF gels or membranes to improve the interface. Experimental results demonstrate that these approaches can effectively enhance the ionic conductivity of COFs while maintaining their inherent advantages, thereby advancing the development of efficient and robust ionic conductors for next-generation energy storage and electrochemical devices.

References

1. Xiao-Xue W, Xi-Wen C, Ma-Lin L, De-Hui G, Cheng-Lin M and Ji-Jing X. *Chem*, **2023**, *9*, 394-410.

Three-Dimensional Covalence Organic Frameworks via a D_{6h} Knot with 12 Arms at Gram-Scale

Chang Shen and Zhengxiao Guo*

Department of Chemistry, The University of Hong Kong (zxguo@hku.hk)

Abstract

The valency of core building blocks for the synthesis of three-dimensional covalence organic frameworks (3D COFs) are normally 4, 6, and 8, therefore, 3D COFs are rare because few building blocks can offer multiple connection sites and symmetry for the 3D framework extension. Meanwhile, the product of COFs at the gram scale is still a challenge and only 100 mg < of COFs can be obtained in one-pot synthesis for most reported articles. Herein, hexakis(3,5-diformylphenyl) benzene, a D_{6h} knot with 12 arms performed like a hexagonal prism has been designed and synthesized, using a bottom-up [12 + 2], [12 + 3], and [12 + 4] construction approach, we rationally designed and synthesized three brand-new three-dimensional **HKUCOF-1**, **HKUCOF-2**, and **HKUCOF-3** with ***asc***, ***aea***, and ***shp*** topology respectively at gram-scale. This work propelled the valency of COF chemistry to twelve.

References

1. Yaghi, O. M. *Science*. **2005**, *310*, 1166-1170.
2. Yaghi, O. M. *Science*. **2007**, *316*, 268-272.
3. Yaghi, O. M. *Science*. **2020**, *307*.

Electrochemical Recovery of Gold and Copper from E-Waste: A Selective and Sustainable Approach

Fatima Arshia[1], Zhengxiao Guo[1]*
[1]Department of Chemistry, The University of Hong Kong,
Hong Kong island, Pokfulam Road, Hong Kong SAR, China; zxguo@hku.hk

Abstract

The rapid accumulation of electronic waste (e-waste) poses severe environmental and resource challenges due to its high content of valuable metals, particularly gold (Au) and copper (Cu). Conventional recovery techniques, such as hydrometallurgy, pyrometallurgy, and solvent extraction, suffer from inefficiencies, high energy consumption, and environmental hazards. This study proposes a hybrid electrochemical strategy integrating reduced graphene oxide-polyaniline (rGO/PANI) and CoNi-LDH electrocatalysts to selectively recover Au and Cu from acidic leachates of e-waste. The high conductivity and redox-active nature of PANI facilitate rapid metal ion adsorption and electrochemical reduction, while CoNi-LDH enhances Cu recovery efficiency through controlled electrodeposition. The system effectively mitigates competitive metal deposition and hydrogen evolution reactions (HER), improving selectivity and yield. Electrochemical characterization, including cyclic voltammetry (CV) and chronopotentiometry, confirms the enhanced performance of the hybrid electrode system, reducing the overpotential and increasing metal recovery rates. The findings provide a scalable, cost-effective, and environmentally friendly solution for sustainable metal recovery from e-waste, paving the way for future advancements in electrochemical recycling.

References

1. Fu, K.; Liu, X.; Zhang, X.; Zhou, S.; Zhu, N.; Pei, Y.; Luo, J. *Nat. Commun.*, **2024**, *15*, 6137.
2. Ye, X.; Wang, J.; Zhang, L.; Chen, Y.; Zhao, H.; Liu, T.; Guo, Q.; Zhou, F.; Huang, Z.; Yang, J.; Li, Y. *ACS Appl. Mater. Interfaces*, **2022**, *14*, 9544–9556.

Multi-scale Modeling of Hydroxyl Radical Reactions with Isoprene in the Gas Phase and at the Air-Water Interface

Tianren ZHU, Ying-Lung Steve TSE
Department of Chemistry, the Chinese University of Hong Kong, Hong Kong, China
E-mail: tianren04@link.cuhk.edu.hk, stevetse@cuhk.edu.hk

The hydroxyl radical (·OH) plays a crucial role in the atmospheric chemistry of organic compounds, significantly impacting air pollution and climate. Its reactions with isoprene, the most abundant atmospheric volatile organic compound (VOC), lead to the formation of ozone and secondary organic aerosols (SOAs) through a series of oxidation products. While these reactions are ubiquitous, the mechanisms, particularly at the air-water interface, remain poorly understood.[1]

To delineate the key physical and chemical aspects of ·OH and isoprene reactions in gas phase and at the air-water interface on the molecular scale, we utilize a multi-scale modeling strategy. This approach utilizes quantum mechanical (QM) data from relatively small systems as a reference to parametrize more efficient empirical valence bond (EVB) models[2], enabling simulations of these ·OH and isoprene reactions for bigger sizes and longer time scales in various chemical environments. Our work will provide insights into the molecular details that are difficult to obtain from experiment, and also provide useful information for other thermodynamic models commonly used by atmospheric scientists. This research is supported by a General Research Fund from the Research Grants Council of Hong Kong (GRF 14301922).

Reference

1. Martins-Costa, M. T. C.; Ruiz-López, M. F. *Chem. Phys. Chem.*, **2020**, *21*, 2263–2271.
2. Warshel, A.; Weiss, R. M. *J. Am. Chem. Soc.*, **1980**, *102*, 6218–6226.

On-Water Catalysis Near the Air-Water Interface

Yutong Yang[1] and Ying-Lung Steve Tse*,[1]

[1] Department of Chemistry, The Chinese University of Hong Kong, Sha Tin, Hong Kong, China
*E-mail: stevetse@cuhk.edu.hk

Abstract

"On-water" catalysis, with no additional substances added to the reaction mixture, can accelerate a reaction by up to several hundred times when it occurs at or near a water interface formed with either air or another hydrophobic solvent[1]. This phenomenon has been observed in various systems, including water-oil emulsions and atmospheric aerosols. Its widespread occurrence and immense potential indicate the necessity for a comprehensive understanding of its mechanisms. Here, we focus on a reaction between CH_3Cl and ·OH radical, which acts as the main sink of CH_3Cl in the atmosphere. Studying reactions can be challenging when it comes to obtaining molecular details through experiments alone. However, molecular dynamics (MD) simulations can provide valuable insights into the mechanisms at the molecular level. In our research, an efficient reactive model based on the empirical valence bond (EVB) theory[2] is parameterized, which enables us to achieve converged results for the free energy change of the reaction. Thus, the kinetics of the reaction near the interface can be obtained to study the origin of the catalytic effect. We hope this work can pave the way for further advancements in modeling approaches for studying reactions at/near liquid interfaces. We would like to acknowledge the funding support of The Research Grants Council of Hong Kong (CUHK 14302221) and the support from the Department of Chemistry of CHUK.

References

1. Narayan, S.; Muldoon, J.; Finn, M. G.; Fokin, V. V.; Kolb, H. C.; Sharpless, K. B. *Angew. Chem. Int. Ed.*, **2005**, *44 (21)*, 3275-3279.
2. Warshel, A.; Weiss, R. M. *J. Am. Chem. Soc.*, **1980**, *102*, 6218–6226.

Developing Efficient and Accurate Molecular Simulation Models for Studying Refrigerants

Haihui WANG, Ying-Lung Steve TSE
Department of Chemistry, the Chinese University of Hong Kong, Hong Kong, China
E-mail: 1155226709@link.cuhk.edu.hk, stevetse@cuhk.edu.hk

The properties of refrigerants in their gaseous and liquid states, as well as their coexistence characteristics, are fundamental to the cooling process. Traditionally, these properties have been studied through experimental methods, which can be time-consuming, costly, and limited in providing molecular-level insights. While molecular simulations have significantly advanced our understanding of refrigerants at the atomic scale[1], traditional models still face challenges in accurately predicting properties across different temperatures and pressures. Quantum mechanical calculations offer greater accuracy but are computationally expensive.

To address these limitations, we aim to develop "multi-scale" models in which reference data from expensive quantum calculations are utilized to parameterize more efficient but still accurate models to calculate and analyze the properties of pure and mixtures of hydrofluoroolefin and natural refrigerants by using our optimized polarizable model to calculate and analyze the properties of pure and mixtures of hydrofluoroolefin and natural refrigerants.

References

1. Gabriele R., *J. Phys. Chem. B*, **2012**, *116*, 5744-5751.

Building Accurate and Efficient Molecular Simulation Models for Studying Warm Cloud Seeding

Guangzhi HE, Ying-Lung Steve TSE
Department of Chemistry, the Chinese University of Hong Kong, Hong Kong, China
E-mail: 1155201356@link.cuhk.edu.hk, stevetse@cuhk.edu.hk

Climate change has intensified extreme weather events including both droughts and floods, prompting efforts to develop effective mitigation strategies. Recently, different parts of the world including China have been experimenting with cloud seeding to induce precipitation. While cold cloud seeding with agents like silver iodide (AgI)[1.] has been extensively studied, the molecular mechanisms underlying warm cloud seeding, which involves the coalescence of water droplets without ice formation, remain poorly understood.

This project seeks to bridge this knowledge gap by developing simulation models to study warm cloud seeding. Our methodology integrates expensive quantum mechanical (QM) calculations to generate reference data on small scales and use the data for parametrizing classical force fields that will be used for larger length and time scales. By investigating the effects of inorganic salts and charged organic matter on water droplet behavior, including water uptake and coalescence dynamics, we aim to enhance our understanding of droplet interactions in the atmosphere and the properties at the air-water interface, thereby providing deeper insights into warm cloud seeding and its potential applications.

This research was supported by a General Research Fund from The Research Grants Council of Hong Kong (14300823).

References

1. Vonnegut, B., *J. Appl. Phys.*, **1947**, *18*, 593–595.

Modeling Reactions Near Liquid-Liquid Interfaces
with Empirical Valance Bond Theory

Weida FENG, Ying-Lung Steve TSE
Department of Chemistry, the Chinese University of Hong Kong, Hong Kong, China
E-mail: 1155168640@link.cuhk.edu.hk, stevetse@cuhk.edu.hk

Heterogeneous reactions, including those near liquid-liquid interfaces, play a significant role in production and everyday life, yet our understanding of them at the molecular level remains inadequate. Our group is interested in developing reactive molecular models for studying reactions near liquid-liquid interfaces.

While quantum mechanical (QM) calculations can naturally describe reactions, they are often so computationally demanding that only small time and length scales are accessible. To compensate for this deficiency, we have been developing more efficient empirical valence bond (EVB) models[1] using QM reference data. In the poster, we will present our modeling strategy and progress of modeling the reaction between CH_3Cl and CN^- in the water-dichloromethane interface system.

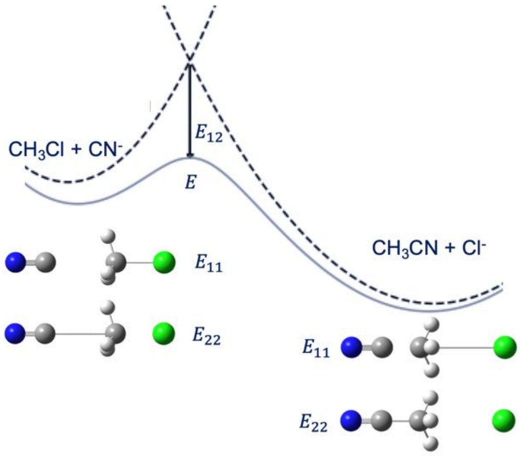


Figure 1: Modeling the S_N2 reaction using a two-state EVB model

We gratefully acknowledge the financial support provided by The Research Grants Council of Hong Kong (GRF 14300823).

References

1. Warshel, A.; Weiss, R. M. *J. Am. Chem. Soc.*, **1980**, *102*, 6218–6226.

Development of a Re-Moldable Lignin-Based Polyurethane with Enhanced Sustainability

Chun-Bong YUEN, and To NGAI
Department of Chemistry, The Chinese University of Hong Kong, HKSAR, China
1155120611@link.cuhk.edu.hk, tongai@cuhk.edu.hk

Abstract

Lignin-based polyurethane (LPU) is a potential alternative to traditional petroleum-based plastic. However, the unique three-dimensional structure and strong covalent bonds make them difficult to soften and mold under heat, limiting their ability to be reused and recycled. In this study, we report on the development of a re-moldable lignin-based PU (RMLPU) that is achieved by generating a thermally reversible covalent bond between the diisocyanate / furan alcohol modified lignin with the 6 or 12 carbon-bismaleimide linkers, through a Diel-Alder reaction. The RMLPU contained up to 38.05% lignin content. Additionally, the furfuryl alcohol, diamine, and maleic anhydride used to produce the RMLPU were plant-based, resulting in an overall plant-based content of up to 80%. The RMLPU exhibited a tensile strength of 14 MPa with a contact angle of 90°, the materials also showed nearly no water absorption at room temperature for 140 hours. Importantly, the material can soften when heated to 170°C and harden when cooled back to room temperature, enabling heat moldability. The TGA results showed that the material was stable even heated up to 290°C. This study provides a method for modifying lignin and creating thermally reversible cross-linking, offering a feasible alternative to traditional plastics and enhancing the sustainability of materials manufacturing.

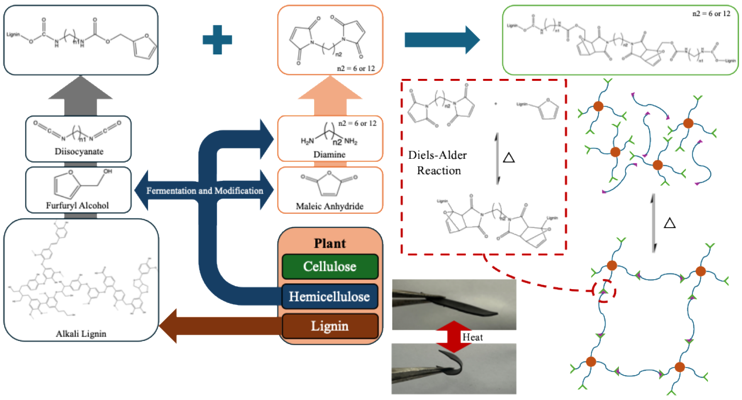


Fig. 1 Overview of Re-Moldable Lignin-based Polyurethane Production.

Hollow Paint: A Scalable Waterborne Lightweight Passive Radiative Cooling (PRC) Paint

Shiwei Qin, Manhin Kwok and To Ngai
Department of Chemistry, The Chinese University of Hong Kong, Shatin, Hong Kong
1155201341@link.cuhk.edu.hk

Abstract

Passive radiative cooling (PRC) is a promising eco-friendly cooling technology without any energy consumption. However, recent PRC technology is hindered by complicated synthetic process and high cost. In this work, a scalable waterborne lightweight PRC paint has been prepared facilely by combing low-density silica hollow spheres (SH) and $BaSO_4$ pigments with water-based polyacrylate emulsion binder. We experimentally proved that SH with ~1 um diameters provided the highest reflectivity, comparing with other sizes (300 nm, 4 um and 20 um). As shown in Figure 1(a) and (b), without sacrificing solar reflectivity, the higher the SH ratio, the lower the final dry coating density and the higher the coating emissivity. The lightweight paint presented good sedimentation resistance in the one-year storage test. With the appropriate estimated pigment volume concentration (ePVC) and $BaSO_4$: SH ratio, the final dry coating presented high solar reflectivity up to 95% and high emissivity up to 0.93. In the outdoor experiments, the cooling temperature was around 5 °C (Figure 1d).

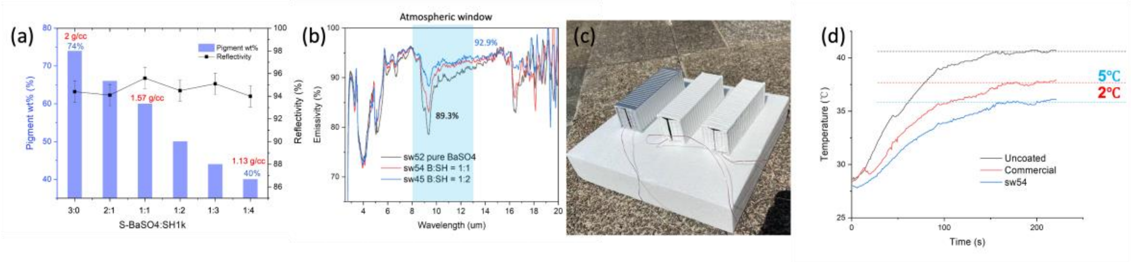


Figure 1. (a) the effect of $BaSO_4$: SH1k ratio on total pigment weight percentage and dry coating reflectivity; (b) the bare uncoated, commercial white paint coated and our paint coated metal models under sunlight; (c) the temperature measurement of three models

Improved Sunscreen Formulations Utilizing Cinnamate-Functionalized Hollow Microspheres for Enhanced UV Protection

Fangyuan Ge[1], Man-hin Kwok[1], and To Ngai[1]*
[1]*Department of Chemistry, The Chinese University of Hong Kong, Shatin N.T., Hong Kong, China*. 1155184284@link.cuhk.edu.hk

Abstract

Solar radiation plays a crucial role in numerous aspects of life on Earth.[1] However, excessive exposure to sunlight, especially ultraviolet (UV) radiation, can pose serious health risks.[2] To minimize the harmful effects of UV radiation, sunscreen plays a vital role in sun protection strategies. Sunscreen agents are essentially divided into two main categories: inorganic and organic UV filters. However, there is an increasing health concern regarding to organic UV filters used in cosmetic products, including poor photostability and forming dangerous radicals.[3] Inorganic UV filters are growing popularity in sun care market but white mark leaving on the skin has yet been solved. To meet these challenges, we reported here a method for the preparation of hollow microspheres using Cinnamate-functionalized cellulose nanocrystals (Cin-CNCs) and inorganic nanoparticles (SiO_2 or TiO_2) through the Pickering emulsion template to improve the efficacy and the safety of sunscreens. These Cin-functionalized hollow microspheres exhibited good water dispersibility and superior photostability compared to conventional organic UV filters. In contrast to inorganic UV filters, they had higher transparency and higher UV shielding properties due to the grafting of Cin groups and their hollow structure. Cin-CNCs/SiO_2 and Cin-CNCs/TiO_2 hollow microspheres exhibited higher UV protection ability than SiO_2 and TiO_2 nanoparticles. Therefore, these hollow microspheres are expected to be used in cosmetic formulations.

References

1. Santos, A. C.; Marto, J.; Chá-Chá, R.; Martins, A. M.; Pereira-Silva, M.; Ribeiro, H. M.; Veiga, F. Materials Today Chemistry, 2022, 23, 100709.

2. Ngoc, L.T.N.; Tran, V.V.; Moon ... Tran VV, Moon J-Y, Chae M, Park D, Lee Y-C. Cosmetics 2019, 6, 64.

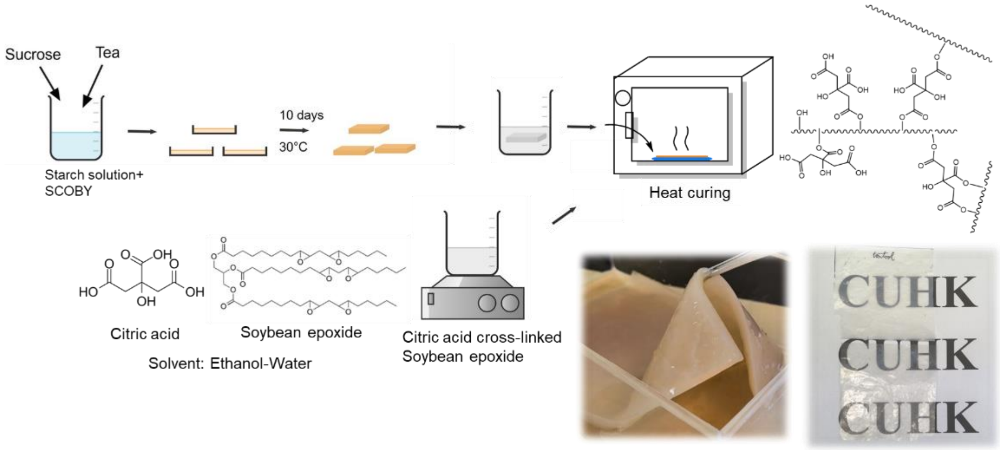
3. Geoffrey, K.; Mwangi, A. N.; Maru, S. M. Saudi Pharm J 2019, 27, 1009-1018.

Development of Translucent, Water- and Oil-Resistant Bacterial Cellulose through Interpenetrating Strategy for Packaging Applications

Hio Lam CHONG, To NGAI
Department of Chemistry, The Chinese University of Hong Kong, HKSAR, China
1155141304@link.cuhk.edu.hk, tongai@cuhk.edu.hk

Abstract:

The increasing global demand for eco-friendly single-use materials has spurred interest in cellulose-based packaging as a sustainable alternative to traditional plastics. Bacterial cellulose (BC), synthesized through the static cultivation of a symbiotic culture of bacteria and yeast (SCOBY), offers advantages in biodegradability and mechanical strength but often lacks transparency. This study explores the modification of BC using Epoxidised soybean oil (ESO) to enhance its physical properties based on pristine BC. The BC-ESO films demonstrated a four-fold reduction in water vapor permeability and a water contact angle of 102°, indicating improved hydrophobicity. Notably, visible light transmission increased from 6.1% for neat BC to 50.5% for the 1:3 ESO-CA BC mixture at a thickness of 0.1 mm. This work highlights the potential of leveraging microbial fermentation and bio-based resins to develop high-performance, transparent films, providing a scalable and accessible solution for sustainable packaging applications.



[Overview of Pristine BC packaging]

Molecular Orbital Tuning of Pentacene-Based Organic Semiconductors through *N*-Ethynylation of Dihydrodiazapentacene

Li Zhang, Yujie Zhao, Jiasheng Li, Yuang Fu, Boyu Peng,* Jun Yang, Xinhui Lu, Qian Miao*

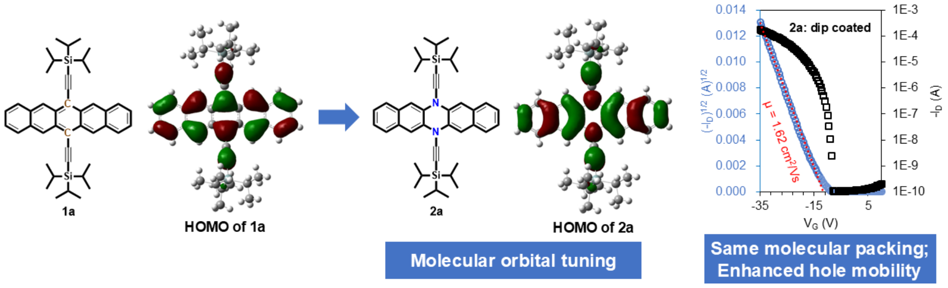
Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

*Email: pengboyu@zju.edu.cn; miaoqian@cuhk.edu.hk

Abstract

Charge transfer integral and reorganization energy are crucial factors in determining the rate of charge transport in organic semiconductors, as described by Marcus theory.[1] The charge transfer integral is governed by electronic coupling between neighboring semiconductor molecules, which depends on both the relative positions of interacting molecules and the phase and nodal properties of π-orbitals.

This study explores the concept of molecular orbital tuning for organic semiconductors through the use of *N,N'*-diethynylated derivatives of 6,13-dihydro-6,13-diazapentacene **2a**.[2] Compound **2a** maintain the same molecular geometry and π–π stacking as its parent pentacene derivative **1a**, but exhibits altered frontier molecular orbital. Theoretical calculations indicate that **2a** could enhance the hole mobility of the parent compound by improving the hole transfer integral. OFET devices for **2a** demonstrated a hole mobility exceeding 1 $cm^2\ V^{-1}\ s^{-1}$, more than twice that of the devices for **1a**.



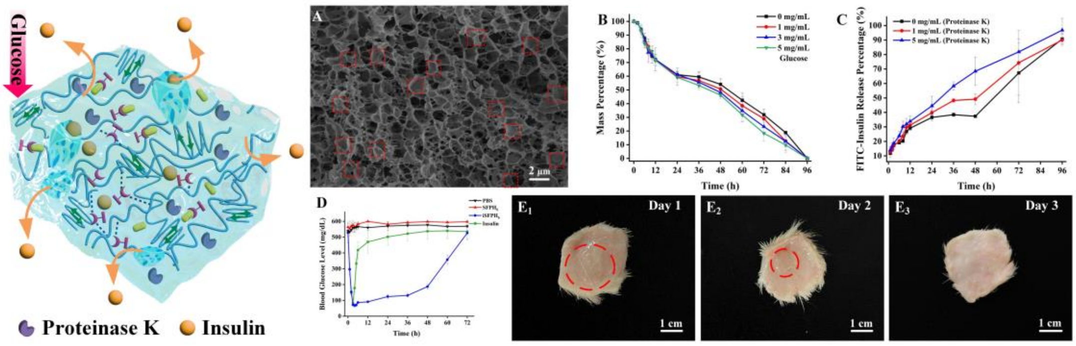
References

1. Brédas, J. L.; Calbert, J. P.; da Silva Filho, D. A.; Cornil, J. Natl. *Acad. Sci. U.S.A.* **2002**, *99*: 5804-5809.
2. Zhang, L.; Zhao, Y.; Li, J.; Fu, Y.; Peng, B.; Yang, J.; Lu, X.; Miao, Q., *J. Am. Chem. Soc.* **2025**, *147*, 3459-3467.

A Fully Biodegradable and Self-Regulating Injectable Silk Fibroin Hydrogel for Glucose-Responsive Insulin Delivery

Mingshuang Zhang[1,2], Mingyu Xing[1], Xinlu Li[1], Kangning Ren[2], Ya Wang[1]*
1Department of Life Sciences, BNU-HKBU United International College, Zhuhai, Guangdong 519087, China
2Department of Chemistry, Hong Kong Baptist University, Hong Kong, China
*Email: yawang@uic.edu.cn

As a common chronic disease, diabetes impacts over 500 million individuals worldwide.[1] We present an intelligent glucose-responsive injectable hydrogel system composed of silk fibroin (SF) and phenylboronic acid (PBA) via Green Chemistry. PBA accelerates hydrogel gelation by forming hydrogen bonding with SF and forms borate esters with glucose to disrupt the cross-linked network and achieve insulin release. Moreover, the glucose-responsive enzymatic degradation of hydrogel facilitates insulin release under hyperglycemic conditions. *In vitro* tests showed that 68.02% insulin was released in 5 mg/mL glucose solution at 48 h, 1.82 times greater than that in 0 mg/mL solution (37.35%). After one single subcutaneous injection of insulin-loaded hydrogel in TDM1 Wistar rats, the blood glucose homeostasis is restored in 2 h and maintained for 48 h. Notably, the hydrogel was fully degraded *in vivo* within 72 h, demonstrating an excellent match between its function and degradation kinetics. This system combines minimally invasive delivery with glucose-responsive release, offering a promising alternative to diabetes management.



References

1. Hossain M.J.; Al-Mamun M.; Islam M.R. *Health Sci Rep*. **2024**, *7*, e2004.

Mechanistic investigation of sensitized europium luminescence: excited states dynamics and luminescence lifetime thermometry

Tsz-Lam Cheung,[a] Zhijie Ju,[b] Wenchao Zhang,[b] David Parker,[a] Renren Deng [b]

a. Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong; davidparker@hkbu.edu.hk

b. State Key Laboratory of Silicon and Advanced Semiconductor Materials, Institute for Composites Science Innovation, School of Materials Science and Engineering, Zhejiang University, Hangzhou

rdeng@zju.edu.cn

Variations in intracellular temperature are of great importance in investigative cell pathology and physiology, which may allow early disease detection at the cellular level via real-time temperature mapping.[1] Temperature-dependent emission lifetime variation is a promising signalling mechanism for microscopic thermometry. However, the underlying sensitisation mechanism for photosensitisation and the details of excited state dynamics that could explain thermal-sensitive behaviour remain unclear. Here, we present the first molecular example of a water-soluble europium complex, **[Eu.L^1]$^-$**, that operates over physiological temperature range (298-318 K, pH 4.5-7.0) and exhibits high relative thermal sensitivity (1.2% K^{-1} at 298 K) based on temperature-dependent lifetime variation.[2] The underlying mechanism has been extensively investigated using transient absorption spectroscopy and variable temperature time-resolved luminescence methods. Additionally, the rates of key energy transfer processes have been described by different models, demonstrating highly efficient ligand sensitization and thermally activated back energy transfer processes.

References

1. Brites, C.D.S.; Millán, A.; Carlos, L.D. *Handbook on the Physics and Chemistry of Rare Earths,* **2016**, *49*, 339–427.
2. Cheung, T.-L.; Ju, Z.; Zhang, W.; Parker, D.; Deng, R. *ACS Appl. Mater. Interfaces* **2024**, *16*, 43933–43941

Oral abstract list

UNIVERSITY	STUDENT		NO.
HKU	YAO	Yueliang	Oral-1
HKBU	LUO	Shihui	Oral-2
CityU	LI	Shuchang	Oral-3
PolyU	MA	Xiaohao	Oral-4
CUHK	YUAN	Dingdong	Oral-5
HKUST	ZHU	Zheng	Oral-6

Poster abstract list

UNIVERSITY	STUDENT		NO.
CityU	CHANG	Tristan Juin Han	InoOrg-5
CityU	CHEN	Xin	MatPhy-1
CityU	CHENG	Lin	MatPhy-11
CityU	DEMISSIR	Ephrem Gizachew	MatPhy-4
CityU	FENG	Panxian	MatPhy-3
CityU	GAO	Ailin	MatPhy-10
CityU	HUANG	Lili	InoOrg-6
CityU	HUANG	Lingli	MatPhy-8
CityU	IO	Kai Wa	InoOrg-19
CityU	JIANG	Katherine Gui-Min	InoOrg-7
CityU	LEE	Lawrence Cho-Cheung	InoOrg-8
CityU	LEUNG	Ka Ho	MatPhy-7
CityU	LEUNG	Peter Kam-Keung	InoOrg-9
CityU	LI	Pan	InoOrg-10
CityU	LI	Tsun Yin	InoOrg-20
CityU	LIM	Jia Yang	MatPhy-2
CityU	MAK	Chiu Lam Eunice	InoOrg-11
CityU	MAN	Ping	MatPhy-6
CityU	SHEN	WENQIAN	MatPhy-5
CityU	SHENG	Yiqi	InoOrg-18
CityU	SHUM	Justin	InoOrg-12
CityU	WANG	Jiahao	InoOrg-13
CityU	XU	Jun-Wen	InoOrg-14
CityU	YEUNG	Chi Fung	InoOrg-21
CityU	YIP	Alex Man-Hei	InoOrg-15
CityU	ZHENG	Wei	InoOrg-17
CityU	ZHOU	Miaomiao	MatPhy-9
CUHK	CHEN	Pinyou	AnaBioEnv-2
CUHK	CHONG	Hio Lam	MatPhy-47
CUHK	CHUNG	Chak Him	InoOrg-24
CUHK	FENG	Weida	MatPhy-43
CUHK	GE	Fangyuan	MatPhy-46
CUHK	HAN	Yongxu	AnaBioEnv-78
CUHK	HE	Guangzhi	MatPhy-42
CUHK	HU	Danna	AnaBioEnv-61
CUHK	HU	Kaiqi	AnaBioEnv-74

Author Index

Author Index

Author Index