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Information and Abstracts

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Scientific Program

Time	Event
08:45 – 09:15	Mounting of Posters
09:15 – 09:30	**Opening Ceremony** - Welcome speech by PVC, Prof. Wai Yee Chan - Welcome speech by Interim Dean of Science, Prof. Zuowei Xie
09:30 – 10:30	Keynote Lecture by Prof. William D. Jones
10:30 – 11:00	Group Photo and Tea Reception
11:00 – 11:25	**Activation of Functionalized Alkynes for Metalated Heterocyclic Complexes and Metallacycles** *Chi-Fung Yeung, City University of Hong Kong*
11:25 – 11:50	**Boron(III) Carbazosubphthalocyanines: Core-Expanded Antiaromatic Boron(III) Subphthalocyanine Analogues** *Yu-Man Chan, The Chinese University of Hong Kong*
11:50 – 12:15	**Novel Design of Amphotericin B-Conjugated Red-Emitting Carbon Dots Against *Candida albicans* Biofilms** *Regina Huang, Hong Kong Baptist University*
12:15 – 14:00	Lunch
14:00 – 15:15	Poster Session
15:15 – 15:40	**Selective Recognition and Detection of Catecholamines in Living Cells** *Ka-Yan Tong, The University of Hong Kong*
15:40 – 16:05	**AIE-Based Organic-Inorganic Integrated Nanosystems for Multimodality Bioimaging and Therapeutics** *Xuewen He, The Hong Kong University of Science and Technology*
16:05 – 16:30	**Ruthenium(II)-Catalyzed Enantioselective γ-Lactams Formation by Intramolecular C – H Amidation of 1,4,2-Dioxazol-5-ones** *Chun-Ming Chan, The Hong Kong Polytechnic University*
16:30 – 17:00	Closing Ceremony & Award Presentation
17:00 – 17:30	Dismounting of Posters

List of Abstracts

- *Keynote Lecture*

  Why Do Weaker Metal-Carbon Bonds Lead to More Stable Complexes? What's Going On?
  Prof. William D. Jones (University of Rochester, USA)

- *Postgraduate Student Oral Presentations*

  Activation of Functionalized Alkynes for Metalated Heterocyclic Complexes and Metallacycles (ORAL - 1)
  Mr. Chi-Fung Yeung (City University of Hong Kong)

  Boron(III) Carbazosubphthalocyanines: Core-Expanded Antiaromatic Boron(III) Subphthalocyanine Analogues (ORAL - 2)
  Mr. Joseph Y. M. Chan (The Chinese University of Hong Kong)

  Novel Design of Amphotericin B-Conjugated Red-Emitting Carbon Dots Against *Candida albicans* Biofilms (ORAL - 3)
  Ms. Regina Huang (Hong Kong Baptist University)

  Selective Recognition and Detection of Catecholamines in Living Cells (ORAL - 4)
  Ms. Ka Yan Tong (The University of Hong Kong)

  AIE-Based Organic-Inorganic Integrated Nanosystems for Multimodality Bioimaging and Therapeutics (ORAL - 5)
  Mr. Xuewen He (The Hong Kong University of Science and Technology)

  Ruthenium(II)-Catalyzed Enantioselective γ-Lactams Formation by Intramolecular C–H Amidation of 1,4,2-Dioxazol-5-ones (ORAL - 6)
  Mr. Chun-Ming Chan (The Hong Kong Polytechnic University)

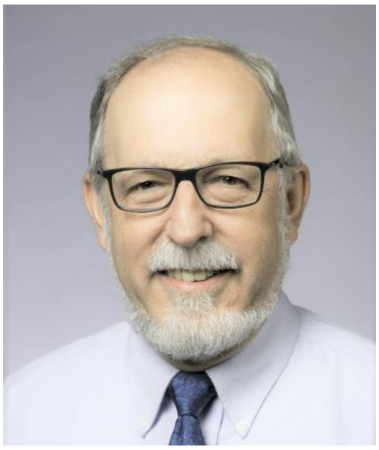
(To be continued on next page)

List of Abstracts (cont'd)

- *Poster Presentations (Total: 324)*

Analytical and Environmental Chemistry	(A&E - 1 to 48)
Inorganic Chemistry	(INORG - 1 to 70)
Organic Chemistry	(ORG - 1 to 58)
Physical Chemistry	(PHYS - 1 to 31)
Material Chemistry	(MAT - 1 to 40)
Biochemistry and Chemical Biology	(BIO - 1 to 77)

Keynote Lecture



Why Do Weaker Metal-Carbon Bonds Lead to More Stable Complexes? What's Going On?

William D. Jones, Department of Chemistry,
University of Rochester, Rochester, NY 14627
jones@chem.rochester.edu

Over the past 20 years substantial progress has been made in the understanding of the activation of C-H and other strong bonds by reactive metal complexes in low oxidation states. This talk will present an overview of the use of pentamethylcyclopentadienyl and trispyrazolylborate rhodium complexes for the determination of thermodynamic factors that influence the activation of arene and alkane C-H bonds. Insights into bond strengths, kinetic and thermodynamic selectivities, and the nature of the intermediates involved will be examined. The influence of substituent effects on the thermodynamics of bond activations will also be analyzed. Trends in the effects of ligand donor strength on C-H activation will be examined. Recent work in acceptorless dehydrogenation reactions will also be presented. A novel route for conversion of ethanol to butanol will also be presented.

Biography

William D. Jones was born in Philadelphia, Pennsylvania, in 1953, and was inspired to work in inorganic chemistry as an undergraduate researcher with Mark S. Wrighton at Massachusetts Institute of Technology (BS, 1975). He obtained a Ph.D. degree in chemistry at California Institute of Technology (1979), working with Robert G. Bergman and completing his final year at Berkeley. He moved to the University of Wisconsin as an NSF postdoctoral fellow with 2004 ACS President Chuck Casey, and in 1980 accepted a position as Assistant Professor at the University of Rochester. He was promoted to Associate Professor in 1984 and Professor in 1987, and is now the Charles F. Houghton Professor of Chemistry. Professor Jones has received several awards, including an Alfred P. Sloan Research Fellowship (1984), a Camille & Henry Dreyfus Foundation Teacher-Scholar Award (1985), a Royal Society Guest Research Fellowship (1988), a Fulbright-Hays Scholar (1988), a John Simon Guggenheim Fellow (1988), the ACS Award in Organometallic Chemistry (2003), and an ACS Cope Scholar Award (2009). He is a Fellow of the American Association for the Advancement of Science and the American Chemical Society. He also has served as an Associate Editor for *J. Am. Chem. Soc.* since 2003. Professor Jones' research interests include organometallic research in strong C-X bond cleavage, catalysis, model studies, mechanisms, kinetics, thermodynamics, and synthetic applications.

Activation of Functionalized Alkynes for Metalated Heterocyclic Complexes and Metallacycles

Chi-Fung Yeung, Lai-Hon Chung, Sze-Wing Ng, Hau-Lam Shek, Sheung-Ying Tse, Siu-Chung Chan, and Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong; acywong@cityu.edu.hk

Abstract

While the fascinating chemistry demonstrated by metalated N-heterocyclic carbene complexes highlights the significance of metalated heterocyclic chemistry, the development of other metalated heterocycles is falling behind, presumably because of the sparseness of general synthetic methodologies. Recently, we have been using metal-induced cycloisomerization of heteroatom-functionalized alkynes as a strategy to prepare metalated heterocyclic complexes. We will discuss the isolation of and calculations on novel metal complexes bearing chromene, chromone, indole, indoline, indolizine and indolizinone moieties prepared from reactions between alkynes and ruthenium complexes, with emphasis on their mechanistic insights into the ruthenium-induced alkyne transformations and applications in material design and drug discovery.

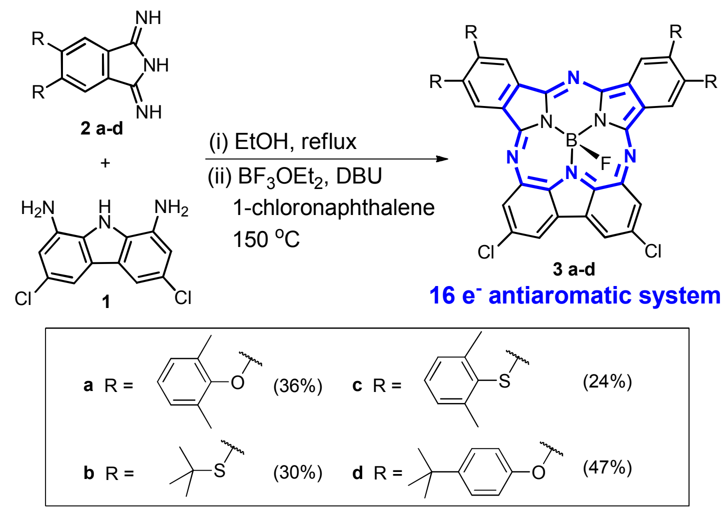
Boron(III) Carbazosubphthalocyanines: Core-Expanded Antiaromatic Boron(III) Subphthalocyanine Analogues

Joseph Y. M. Chan,[a] Takahiro Kawata,[b] Nagao Kobayashi,*[,b] and Dennis K. P. Ng*[,a]

[a] *Department of Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China. E-mail: dkpn@cuhk.edu.hk*

[b] *Department of Chemistry and Materials, Faculty of Textile Science and Technology, Shinshu University, Ueda 386-8567, Japan. Email: nagaok@shinshu-u.ac.jp*

Antiaromatic porphyrinoids with a 4n π-electron core have received considerable attention. Apart from their intrinsic interest, these compounds exhibit intriguing optical and electronic properties. They can serve as potential electrode-active materials in rechargeable batteries and ambipolar semiconductors for field-effect transistors. To date, a number of antiaromatic porphyrins have been prepared by core-modification. However, antiaromatic azaporphyrinoids are relatively scarce in the literature. In this presentation, we report a series of novel core-expanded subphthalocyanine analogues prepared through condensation of 1,8-diamino-3,6-dichlorocarbazole with of the corresponding disubstituted 1,3-diiminoisoindolines, followed by the treatment with $BF_3{\cdot}OEt_2$. These air-stable π-conjugated macrocycles, namely carbazosubphthalocyanines, possess two boron-containing seven-membered ring units and a 16 π-electron skeleton, which represent the first examples of antiaromatic subphthalocyanine analogues as supported by spectroscopic and theoretical studies.[1]



Scheme 1. Synthesis of boron(III) carbazosubphthalocyanines **3a**-**d**.

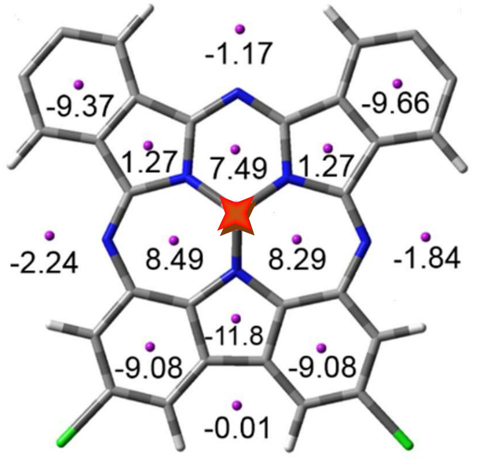


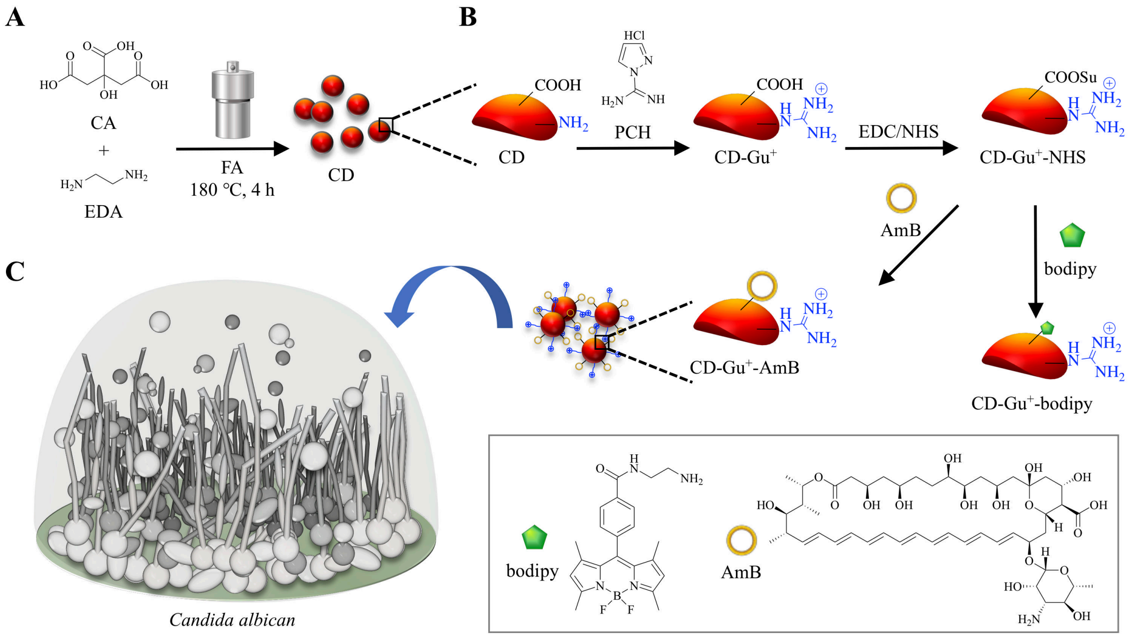
Figure 1. Computed NICS values (in ppm) for the DFT-optimized structure of **3a** at various positions.

1. Chan, J. Y. M.; Kawata, T.; Kobayashi, N.; Ng, D. K. P. *Angew. Chem. Int. Ed.* **2019**, *58*, 2272-2277.

Novel Design of Amphotericin B-Conjugated Red-Emitting Carbon Dots Against *Candida albicans* Biofilms

Regina Huang[1], Xuan Li[2], Ken Cham-Fai Leung[1]*
[1]Department of Chemistry and Partner State Key Laboratory of Environmental and Biological Analysis, The Hong Kong Baptist University, Hong Kong SAR, P. R. China.
Email: cfleung@hkbu.edu.hk
[2]Faculty of Dentistry, The University of Hong Kong, Hong Kong SAR, P. R. China.

Amphotericin B (AmB) can be applied to severe fungal-infected patients against *Candida albicans*, one of the most pervasive pathogenic microbes that cause oral candidiasis.[1,2] However, its bioavailability is significantly limited due to poor water solubility. Herein, the surface-engineered carbon dots (CD) are designed as drug "surveillance vehicles" to deliver and track AmB for the elimination of *C. albicans* biofilms. Recent progress shows that CD can tackle biofilm by facilitating the tracking of drug molecules and improve the bioavailability of AmB in aqueous solution. These findings contribute to developing novel carbon-based drug delivery systems in nanoscale for effective healthcare.



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2. Hamill, R. J., *Drugs* **2013**, *73* (9), 919-934.

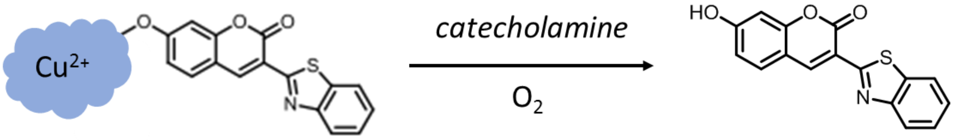
Selective Recognition and Detection of Catecholamines in Living Cells

Ka Yan Tong and Ho Yu Au-Yeung*

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

Email: hoyuay@hku.hk

Catecholamines (e.g. dopamine, adrenaline and noradrenaline) are small molecule neurotransmitters that involve in vital physiological processes and are tightly regulated in the human body. Catecholamine dysregulation is implicated in various neurodegenerative diseases such as Parkinson's disease, schizophrenia, psychosis and attention deficit hyperactivity disorder (ADHD). Selective recognition and detection of catecholamines is exceedingly challenging due to their small size, non-specific molecular shape and trivial chemical properties. We report here the development of a bioinspired, copper-based oxidative bond cleavage for the catecholamine-triggered release of a fluorescent reporter for selective and sensitive catecholamine fluorescent detection. Live cell imaging with the new probe successfully visualized the accumulation and depletion of dopamine in cellular models of neuron differentiation and Parkinson's disease. Complemented by morphological studies in the same experiment, catecholamine imaging using the new probe provides for the first time an integrative approach for studying important neuronal processes.



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AIE-Based Organic-Inorganic Integrated Nanosystems for Multimodality Bioimaging and Therapeutics

Xuewen He, Ben Zhong Tang*

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

Abstract: Multimodality imaging is highly desirable for accurate diagnosis by achieving high sensitivity, spatial−temporal resolution, and penetration depth with a single structural unit. However, it is still challenging to integrate fluorescent and plasmonic modalities into a single structure, as they are naturally incompatible because of significant fluorescence quenching by plasmonic noble-metal nanoparticles. Herein, we report a new type of silver@AIEgen (aggregation-induced emission luminogen) core−shell nanoparticle (AACSN) with both strong aggregated-state fluorescence of the AIEgen and distinctive plasmonic scattering of silver nanoparticles for multimodality imaging in living cells and small animals. The AACSNs were prepared through a redox reaction between silver ions and a redox-active AIEgen, which promoted synergistic formation of the silver core and self-assembly of the AIEgen around the core. The resulting AACSNs exhibited good biocompatibility and high resistance to environmental damage. As a result, excellent performance in fluorescence imaging, dark-field microscopy, and X-ray computed tomography-based multimodality imaging was achieved.

Simultaneously, RNA interference (RNAi) is demonstrated as one of the most powerful technologies for sequence-specific suppression of genes in disease therapeutics. Exploration of novel vehicles for small interfering RNA (siRNA) delivery with high efficiency, low cytotoxicity, and self-monitoring functionality is persistently pursued. By taking advantage of the above AIE-featured core−shell nanovehicles, we applied them for high-efficiency siRNA delivery and real-time monitoring of its intracellular behaviors. The thickness of AIE shell was optimized to achieve the best performance in target interference and tumor growth inhibition in vitro and in vivo. By harnessing the unique AIE fluorescence, real-time visualization of the cellular uptake and release of siRNA and long-term tracking of in vivo tumor tissue were also successfully demonstrated. Compared to the commercial transfection reagents, significant improvements were obtained in biocompatibility, delivery efficiency, and reproducibility, representing a promising future of this nanocarrier in RNAi-related cancer therapeutics.

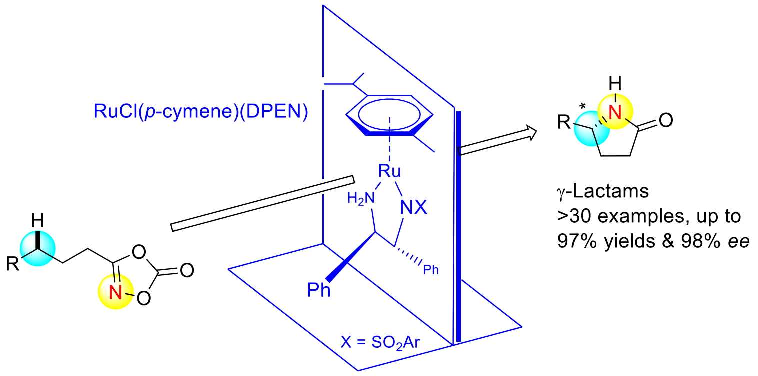
Keywords: *aggregation-induced emission (AIE), multimodality, core−shell, RNA interference, therapeutics*

Ruthenium(II)-Catalyzed Enantioselective γ-Lactams Formation by Intramolecular C – H Amidation of 1,4,2-Dioxazol-5-ones

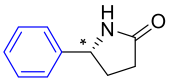
Chun-Ming Chan and Wing-Yiu Yu*

State Key Laboratory of Chemical Biology and Drug Discovery and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University

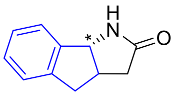
Abstract



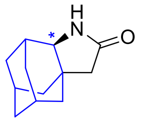
Selected examples



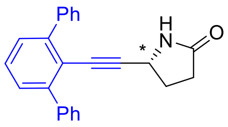
2a
92%, 94% *ee*



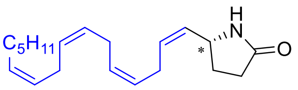
2m
97%, 98% *ee*
d.r. > 20:1



2n
63%, 51% *ee*
70%, 65% *ee*



5d
91%, 93% *ee*



5n
66%, 64% *ee*

We report the Ru-catalyzed enantioselective annulation of 1,4,2-dioxazol-5-ones to furnish γ-lactams in up to 97% yield and 98% *ee* via intramolecular carbonylnitrene C–H insertion. By employing chiral diphenylethylene diamine (dpen) as ligands bearing electron-withdrawing arylsulfonyl substituents, the reactions occur with remarkable chemo- and enantioselectivities; the competing Curtius-type rearrangement was largely suppressed. Enantioselective nitrene insertion to allylic / propargylic C–H bonds was also achieved with remarkable tolerance to the C=C and C≡C bonds.

References

Xing, Q.; Chan, C.-M.; Yeung, Y.-W.; Yu, W.-Y. *J. Am. Chem. Soc.* **2019,** *141*, 3849.

G-Quadruplex-Mediated Molecular Switching of Self-Assembled 3D DNA Nanocages

Dick Yan Tam, Hoi Man Leung, Miu Shan Chan, and Pik Kwan Lo*

Department of Chemistry, City University of Hong Kong, 83 Tat Chee Avenue, Kowloon Tong, Hong Kong**;** peggylo@cityu.edu.hk

Abstract

G-quadruplex is a G-rich DNA sequence forming specific structure in present of cations which naturally present in cells. This structure can be deformed by high temperature, lowering the cation concentration and ion-clelating ligands. Nowadays, researchers have applied this property to make various devices, eg. logic gate, switch, sensor, etc.. However, most of them are DNA in the form of single strand or origami. Therefore, we would like to explore the reversibility, catalytic activity as well as the biological properties in a self-assembled DNA nanostructure integrated with G-quadruplex sequence which diameter is only a few nanometers.

References

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Exploring Structural Characterization Methods for Isomeric Glycopeptides and Glycans using Tandem Mass Spectrometry

H. T. Wong, T.-W. Dominic Chan
Department of Chemistry, The Chinese University of Hong Kong, Hong Kong SAR
E-mail: twdchan@link.cuhk.edu.hk

Abstract

Glycosylation is one of the most important form of protein post-translational modifications and plays important roles many biological pathways such as cell−cell signaling, protein stability and solubility as well as interactions between ligands and receptors. Characterization of isomer structures of glycans attached on proteins is of great importance for better understanding of the roles of glycans.[1]

In this work, we are exploring methods for characterization and separation of isomeric carbohydrates. Glycopeptides released from bovine pancreatic ribonuclease B (RNase B) by tryptic digestion and glycans released by digestion using PNGase F were isolated from sample mixture by lectin-based solid phase extraction or HILIC Ziptip extraction. The isolated RNase B glycopeptides and glycans were subsequently analysed by MS/MS method electron capture dissociation (ECD), electron induced dissociation (EID) and collision induced dissociation(CID) and the derived structural information will be discussed. We also tried to use DMS as a separation method for isomeric glycopeptides or glycans prior to mass spectrometry analysis. Effect of compensation voltage (CV) and percentage change of modifier was tested.

Reference

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Gas chromatography-mass spectrometry based profiling reveals six monoglycerides as markers of used cooking oil

Guodong Cao[a], Dongliang Ruan[a,b], Yanjun Hong[a,b]*, Zongwei Cai[a,b] *

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

[b] HKBU Institute of Research and Continuing Education, Shenzhen, China

Email:zwcai@hkbu.edu.hk & Email: yjhong@hkbu.edu.hk;

Abstract:

Under deep frying conditions, edible oil will release a variety of deterioration chemicals that have been implicated in many diseases. Unscrupulous traders may refine used cooking oil and adulterate it as qualified edible oil, thus posing threats to public health. This research aimed to discover the chemical markers of used cooking oil by using gas chromatography-mass spectrometry (GC-MS) based profiling. Our results suggested that six monoglycerides could be used as endogenous markers to discriminate used cooking oil from fresh edible oil. Accumulation behaviors of those markers in continuous heating process were observed. A quantitative GC-MS method was further developed for the six monoglycerides with good accuracy, precision and reproducibility. This method enabled the authentication of commercial olive oil adulterated with 1% deep fried oil. Abnormally high levels of the monoglycerides markers had also been determined in 116 gutter oil samples. Therefore, quantitation of six monoglycerides markers by GC-MS could be a promising approach for elucidating the degradation state of edible oil, authenticating commercial oil products adulterated with used cooking oil, as well as screening of gutter oil.

Keywords:

GC-MS profiling; Used cooking oil; Endogenous markers; Monoglycerides;

Reference:

Cao, G., Ruan, D., Chen, Z., Hong, Y., & Cai, Z. (2017). Recent developments and applications of mass spectrometry for the quality and safety assessment of cooking oil. *TrAC Trends in Analytical Chemistry*.

Photo-pTyr-scaffold approach for drug mechanism analysis of tyrosine kinase inhibitors

Qian Kong[1], Bizhu Chu[2], Pengfei Li[*], Ruijun Tian[*], Zongwei Cai[*]

[1] State Key Laboratory of Environmental and Biological Analysis, Department of Chemistry, Hong Kong Baptist University, Hong Kong SAR, China
[2] Southern University of Science and Technology, Shenzhen,China

*E-mail: lipf@sustc.edu.cn, tian.rj@sustc.edu.cn, zwcai@hkbu.edu.hk

Abstract

Tyrosine kinases regulate cell proliferation, differentiation, death, and other physiological processes by mediating the cell signal transduction. Recently, a variety of tyrosine kinases be used as drug targets on targeted therapy and the EGF receptor (EGFR) is the first receptor to be proposed for cancer therapy. EGFR inhibitors bind to the tyrosine kinase domain at the ATP binding sites competing with ATP and disrupting the kinase activity, so that to abrogate downstream signaling proteins. However, the mechanism of action and influence on downstream proteins has not to be clarified. In this research, we investigate the differences between two EGFR inhibitors – Erlotinib that has been approved by the FDA in 2004 and Tyrphostin AG1478 that still in the clinical trial process. Based on the work foundation of our lab, a photo-pTyr-scaffold approach was taken to detect the downstream protein changes of EGFR signaling after tyrosine kinase inhibitors (TKIs) blockage.

Owing to the binding capacity of the SH2 domain with phosphorylated tyrosine proteins, a Src superbinder protein with modified SH2 domain was introduced. A trifunctional probe with a photoreactive group and an enrichment group was engineered with the superbinder protein and then be used for phosphorylated tyrosine protein capture. Using this approach, the drug-induced changes in the phosphorylation state of the captured changes were investigated. Through the function and interaction network analysis of these proteins, the mechanism of the inhibitors could be clarified. The downstream signaling pathway and phosphosites analysis show the difference of these two inhibitors and facilitate the mechanism exploration. The data suggest that our approach is a valuable tool for drug discovery.

Keywords：Tyrosine kinase inhibitors, Photo-pTyr-scaffold, Phosphorylated proteins

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Application of MALDI MS Imaging for Rapid Poly-bacterial Antibiotic Susceptibility Test

Xiaojian Shao, Yisu Wang, Kangning Ren*, Zongwei Cai*

Department of Chemistry, Hong Kong Baptist University, Hong Kong, SAR China

Corresponding authors: zwcai@hkbu.edu.hk; kangningren@hkbu.edu.hk

Abstract

Bacteria could cause severe infections that are fatal to human health. To get the correct antibiotics for treatment of infections, current clinical practice generally requires over 2 days for bacterial identification and antibiotic susceptibility test. Herein, we proposed to develop a platform that integrates microchip and MALDI MS imaging to reduce the time to 12 hours and simultaneously accomplishes bacterial identification and poly-bacterial antibiotic susceptibility test. The microchip utilized multiple channels for infusion of different antibiotics, thereof greatly streamlining the processes for cell culture and antibiotic treatment. After transferred onto ITO glass, the bacteria cells were treated by solvents to extract the proteins and then MALDI matrix was applied onto it to get proteins as mass fingerprint.

As a proof of concept, *S. aureus* and *P. aeruginosa* were co-cultured on the microchip and treated with ampicillin, which could cause specific toxicity towards *S. aureus*. As a result, we identified the bacterial mixture as *S. aureus* and *P. aeruginosa* by analyzing the mass fingerprint using bacterial identification software called BacteriaMS. Moreover, concentration-dependent change of proteins was observed by MALDI MS imaging and those proteins were found specific to *S. aureus* while there is no such trend for *P. aeruginosa*, suggesting that our platform could be used for antibiotic susceptibility test. Our integrated platform could afford a robust solution for rapid bacterial identification and antibiotic susceptibility test, which is a promising tool for further clinical uses.

Effects of acute ambient $PM_{2.5}$ exposure on heart in C57BL/6J diet-induced obesity mouse model

Yuanyuan Song[1], Yanhao Zhang[1], Zenghua Qi[2], Ruijin Li[3], Zongwei Cai[1,2,*]

[1] State Key Laboratory of Environmental and Biological Analysis, Department of Chemistry, Hong Kong Baptist University, Hong Kong SAR, China.

[2] School of Environmental Science and Engineering, Guangdong University of Technology, Guangzhou, China

[3] Institute of Environmental Science, Shanxi University, Taiyuan, China.

Air pollution, one of the toughest challenges that humans are confronted with, has raised great public concern. The particulate matter (PM) with an aerodynamic diameter less than 2.5 *μm* ($PM_{2.5}$) is one of the most critical air contaminants and a key indicator of air pollution.The epidemiological studies reported that those people who have obesity and diabetes were more susceptible to $PM_{2.5}$, they were more likely to be infected than normal people. In this study, the effects of $PM_{2.5}$ exposure on heart in diet-induced obesity mice were investigated. The 4-weeks male C57BL/6J mice were fed with normal or high fat chows for one month until the weights of high fat groups were 25% percent heavier than normal groups. Then the normal and fat groups were both divided into two groups, and one groups were exposed to phosphate buffered solution (PBS) and another were exposed to Taiyuan winter $PM_{2.5}$ sample (175 $\mu g.m^{-3}$) through intratracheal instillation every three days for one month. The results showed that the body weight and blood glucose were not obviously changed, but the heart rate and blood pressure were significantly increased after $PM_{2.5}$ exposure in obese mice groups. To reveal the mechanism more clearly, metabolomics and lipidomics were conducted in mice serum and heart. Phenylalanine metabolism pathway was significantly changed in serum of $PM_{2.5}$ treated obese mice. As the precursors of catecholamines, the increase of phenylalanine and tyrosine induced the release of dopamine, epinephrine and norepinephrine, which played important roles in regulating cardiovascular system. At the same time, the proinflammatory cytokines were significantly increased both in hypothalamus and heart of $PM_{2.5}$ treated obese mice, suggesting that $PM_{2.5}$ exposure aggravated inflammation of obese mice and activated phenylalanine metabolism pathway to change the heart rate and blood pressure. Furthermore, besides small molecular metabolites, the levels of free fatty acids were also increased in serum of $PM_{2.5}$ treated obese mice, correspondingly, the content of triacylglycerol (TG) was observed to be accumulated in heart. While the increase of metabolites in TCA cycle and decrease in glycolysis as well as the mRNA expression of CPT1 also showed the elevation of fatty acids oxidation and inhibition of glucose oxidation in obese mice, suggesting that $PM_{2.5}$ exposure disrupted energy metabolism and caused cardiac lipotoxicity in obese mice.

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Prenatal exposure to ambient fine particulate matter induces dysregulations of lipid metabolism in adipose tissue in male offspring

Peisi Xie[1], Chao Zhao[1], Wei Huang[1], Ting Yong[1], Arthur C.K. Chung[1], Kaiwu He[2], Xiangfeng Chen[3], Zongwei Cai[1]*

1. State Key Laboratory of Environmental and Biological Analysis, Department of Chemistry, Hong Kong Baptist University, Hong Kong, P.R., China

2. Key Laboratory of Modern Toxicology of Shenzhen, Shenzhen Center for Disease Control and Prevention, Shenzhen 518055, China

3. Shandong Analysis and Test Center, Qilu University of Technology (Shandong Academy of Sciences), Jinan, Shandong, China

*Corresponding author: CAI Zongwei, Email: zwcai@hkbu.edu.hk

Abstract

Prenatal exposure to ambient fine particles (diameter < 0.25 μm, $PM_{2.5}$) has been found to be associated with abnormal growth and development in offspring.[1] However, the effects of $PM_{2.5}$ on the lipid metabolism of adipose tissue in offspring are unclear. In the present study, we established a mouse model of prenatal exposure to $PM_{2.5}$ by intratracheal instillation to pregnant C57BL/6 female mice with $PM_{2.5}$ suspension or normal saline. We found that prenatal exposure to $PM_{2.5}$ of a mouse model reduced body weight in adult male offspring after 6 weeks old. Histological analysis showed that the adipocyte size was significantly reduced in epididymal adipose tissue (eWAT) in male offspring, but not in brown adipose tissue. The expression levels of genes related to fatty acid synthesis (ACC1, ACSL1) and oxidation (PPARα) in eWAT were also significantly decreased. In addition, downregulation of pro-inflammatory cytokines (TNFα, IL-1β, IL-6) was also observed. Lipidomics analysis of eWAT demonstrated that prenatal exposure of $PM_{2.5}$ reduced lysophosphatidylcholines (LPC), phosphatidylcholines (PC), phosphatidylethanolamines (PE), sphingomyelins (SM), and ceramides (Cer), indicating that metabolic pathways, including SM-Cer signaling and glycerophospholipids remodeling, were disrupted. In summary, prenatal exposure to $PM_{2.5}$ was associated with the dysregulations in lipid metabolism of eWAT and pro-inflammatory response in male offspring.

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Magnetic covalent organic framework as adsorbent and new matrix for enrichment and rapid determination of PAHs and their derivatives in $PM_{2.5}$ by surface-assisted laser desorption/ionization-time of flight-mass spectrometry

Yanhao Zhang,[a] Yuanyuan Song,[a] Jie Wu,[b] Ruijin Li,[ad] Di Hu,[a] Zian Lin*[b] and Zongwei Cai*[ac]

[a] State Key Laboratory of Environmental and Biological Analysis, Department of Chemistry, Hong Kong Baptist University, Hong Kong SAR, China.

[b] Ministry of Education Key Laboratory of Analytical Science for Food Safety and Biology, Fujian Provincial Key Laboratory of Analysis and Detection Technology for Food Safety, Department of Chemistry, Fuzhou University, Fuzhou, Fujian, P.R. China.

[c] Guangzhou Key Laboratory of Environmental catalysis and Pollution Control, School of Environmental Science and Engineering, Institute of Environmental Health and Pollution Control, Guangdong University of Technology, Guangzhou, China

[d] Institute of Environmental Science, Shanxi University, Taiyuan, China.

E-mail: zianlin@fzu.edu.cn; zwcai@hkbu.edu.hk

Abstract

A magnetic covalent organic framework nanomaterial (Fe_3O_4@COFs) served as an adsorbent for enrichment and a new matrix for SALDI-TOF-MS analysis of PAHs and their derivatives in $PM_{2.5}$. The unique properties of Fe_3O_4@COFs in terms of high enrichment ability and matrix-free interference made it possible for sensitive analysis of low-concentration organic small-molecule pollutants in complex environmental samples.

Reference

Chemical Communications, 2019, DOI: 10.1039/C9CC00384C

Gestational exposure to benzotraizoles and benzothiazoles in relation to birth weight: a repeated measures study

Yanqiu Zhou[1], Zongwei Cai [1]*

[1] State Key Laboratory of Environmental and Biological Analysis, Department of Chemistry, Hong Kong Baptist University, Hong Kong SAR, P.R. China

Email:zwcai@hkbu.edu.hk

Abstract

Although animals and *in vitro* studies provided evidence for the reproductive toxicity of benzotriazoles and benzothiazoles (BTs), human epidemiology data on the developmental effect of gestational exposure to BTs remain sparse. We therefore investigated the association of prolonged exposure to BTs during pregnancy with fetal growth and explored the critical window of vulnerability. Participants consisted of 856 pregnant women drawn from a prospective birth cohort between 2014 and 2015 in Wuhan, China. Urinary concentrations of BTs were measured in samples (n = 2568) collected at three trimesters (13.1 ± 1.1, 23.7 ± 3.2, and 35.7 ± 3.4 gestational weeks). For overall infants, prolonged exposure to benzothiazole was associated with decreased birth weight (β = -87.0, 95% CI = -115 to -18.7 at the fourth quartile, p = 0.013). Notably, although tests for multiplicative interaction (exposure*sex) were only marginally significant (p for interaction = 0.064), we observed that prolonged exposure to 1-H-benzotriazole were associated with increased birth weight among girls (β = 82.8, 95% CI = -15.6 to 181, p = 0.099) but decreased birth weight among boys (β = -20.5, 95% CI = -124 to 83.4, p = 0.699). In agreement with findings from repeated measures analysis, trimester-specific analyses revealed that the magnitude and/or direction of the relationships did not vary by time point of exposure during pregnancy. A significant negative association between benzothiazole exposure and birth weight was observed across three trimesters (β = -79.5, 95% CI = -142 to -16.7; β = -74.8, 95% CI = -137 to -12.5; β = -69.3, 95% CI = -131 to -7.76 for the first, second and third trimester, respectively). Based on longitudinal exposure during pregnancy, this study indicated gestational exposure to BTs may pose adverse effects on fetus development.

Optical properties, source apportionment and health implications of humic-like substance ($HULIS_{WS}$) in fine particulate matter ($PM_{2.5}$) in Hong Kong

Yiqiu Ma, Yubo Cheng, Binyu Kuang, Jianzhen Yu, Di Hu*

Address: Hong Kong Baptist University, Kowloon Tong, Kowloon, Hong Kong, P. R. China.; E-mail: dihu@hkbu.edu.hk

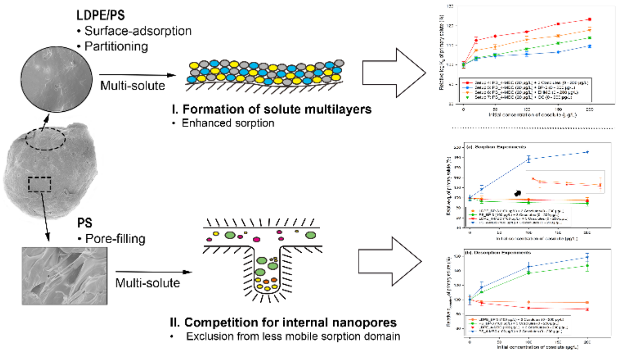
Water-soluble humic-like substances ($HULIS_{WS}$) are a significant component of water-soluble organic matter (WSOM) in atmospheric fine particles ($PM_{2.5}$). In this study, the mass concentration, optical properties, and reactive oxygen species (ROS)-generation potential of $HULIS_{WS}$ were investigated in $PM_{2.5}$ samples collected in Hong Kong, and they all showed higher levels on regional days than on long regional transport (LRT) days and local days. Positive matrix factorization (PMF) analysis was conducted. Four primary sources (biomass burning, marine vessels, industrial exhaust and vehicle emissions), and two secondary sources (secondary organic aerosol formation and secondary sulfate) were identified. Most sources showed higher contributions to $HULIS_{WS}$ and the DTT activity of $HULIS_{WS}$ on regional days than LRT and local days, except marine vessels with higher contributions on local days than on LRT and regional days. Secondary processes were the major contributor to $HULIS_{WS}$ mass concentration throughout the year, followed by biomass burning and industrial exhaust. Biomass burning was found to have the highest contribution to extrinsic DTT activity of $HULIS_{WS}$, followed by secondary processes.

Fate and Biological Effects of Microplastics-mediated Chemical Exposure in the Co-occurrence of Environmental Contaminants

Wai-Kit Ho and Kelvin Sze-Yin Leung*
Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong SAR, P. R. China.
E-mail address of corresponding author: s9362284@hkbu.edu.hk

Abstract

Sorption studies of organic pollutants by microplastics (MPs) in single-solute systems are well established in the literature. However, actual aquatic environments always contain a mixture of contaminants. In this regard, prediction of the fate and biological effects of MPs-mediated chemical exposure require a better understanding of altered sorption and desorption behaviors caused by the co-occurrence of multiple organic contaminants. Herein, we showed that distinctly different sorption behaviors were exhibited in multi-solute systems as both competitive and synergistic sorption behaviors have been observed. The relative contribution of the two opposite effects is controlled by the hydrophobicity and molar ratio of both solutes, together with inherent sorptivity of MPs. We also showed that the bioaccessibility of primary solute was significantly elevated in the presence of cosolute, even though competitive sorption was observed in the same conditions. These findings supplemented the current research gaps on sorption mechanisms and interactions of multiple organic contaminants on MPs, which are critical for a comprehensive environmental risk assessment of both MPs and hazardous anthropogenic contaminants.



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Fate of UV filter Ethylhexyl methoxycinnamate in rat model and human urine: metabolism, exposure and demographic associations

Huang Yanran, Kelvin Sze-Yin Leung

Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong

Email: s9362284@hkbu.edu.hk

Abstract

Ethylhexyl methoxycinnamate (EHMC) is one of the most frequently used UV filters in sunscreens and other cosmetic products. Its ubiquitous presence in various environmental matrices and its endocrine disrupting properties have been widely reported. However, we know little about the effect of EHMC exposure on humans, mainly due to its fast metabolism. In this study, urine and plasma of EHMC-dosed rats were analysed to identify its major metabolites. Five metabolites were found, with four firstly reported. Two metabolites were putatively identified as 4-methoxycinnamic acid (4-MCA) and 4’-methoxyacetophenone (4’-MAP). Quantitative results revealed that their excretion concentrations were much higher than the parent compound. Because of these high concentrations, for the human biomonitoring study, EHMC and these two metabolites were detected simultaneously in urine samples from Chinese children and adolescents. The results indicated wide exposure to EHMC, 4-MCA and 4’-MAP. The correlation between urinary concentration of EHMC and 4-MCA as well as 4-MCA and 4’-MAP provided important clues as to the sources and metabolic pathways among these three compounds. Several demographic factors were also assessed with the exposure level. As the first human exposure study of EHMC in a Chinese population, this report would help to establish an exposure database facilitating health risk assessment of EHMC.

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Dual-functional magnetic liposome for on-site delivery and MRI imaging in brain

Zhen-Zhen Dong, Hung Wing Li

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

Abstract

Reactive oxygen species (ROS) play important roles in lots of pathological and physiological processes.[1,2] Among the ROS family, hydrogen peroxide (H_2O_2) is the principal member, which is generated from activation of NADPH oxidase complexes,[3,4] acting as an crucial messenger for proliferation, cellular growth, and differentiation. However, the excessive generation of H_2O_2 takes part in many serious diseases, such as, neurodegenerative disorders, cancer, cardiovascular diseases and so on. Hence, it is of great significance to establish a sensitive strategy for H_2O_2 detection in living biological systems. Here, we designed a new fluorescent probe for rapid detection of H_2O_2 with high sensitivity and good specificity. The proposed probe could achieve ratiometric sensing of H_2O_2 with a detection limit of 21 nM in vitro. It also was successfully applied into HeLa cells for H_2O_2 imaging in a wide range and rapid response time. Besides its good biocompatibility and low toxicity, this probe is a desired tool for H_2O_2 detection and imaging, holding the potential to further application in disease diagnosis and therapy.

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A reaction-based luminescent switch-on sensor for the detection of OH$^-$ ion in simulated wastewater

Chun Wu[a] and Dik-Lung Ma*[a]
Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong, China.
E-mail: edmondma@hkbu.edu.hk (Dik-Lung Ma).

A series of luminescent iridium(III) complexes were synthesized and evaluated for their ability to interact with hydroxide ions in semi-aqueous media at ambient temperature. Upon the addition of OH$^-$, a nucleophilic aromatic substitution reaction takes place at the bromine groups of the N^N ligand of complex **1**, resulting in the generation of a yellow-green luminescence. Complex **1** showed a 35-fold enhanced emission at pH 14 when compared to neutral pH, and the detection limit for OH$^-$ ions was 4.96 μM. Complex **1** exhibited high sensitivity and selectivity, long-lived luminescence and impressive stability. Additionally, we have demonstrated the practical application of complex **1** to detect OH$^-$ ions in simulated wastewater.

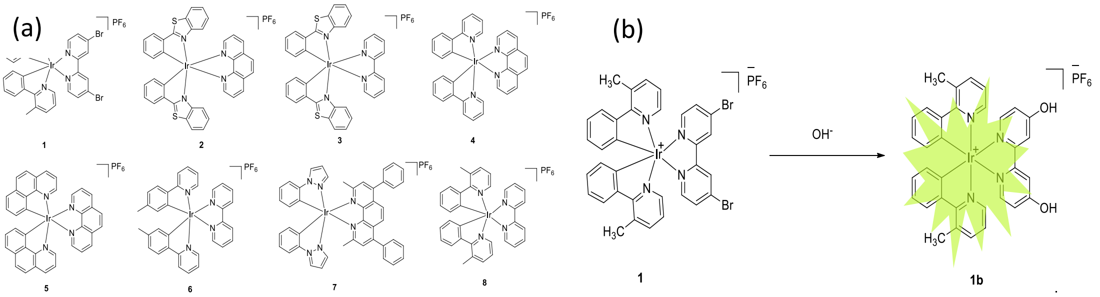

Fig. 1 (a) Chemical structures for complexes **1–8**. **(b)** Schematic mechanism for hydroxide detection by complex **1**.

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Reliable and reusable whole-polypropylene plastic microfluidic de-vices for rapid, low-cost antimicrobial susceptibility test

Han Sun[a], Chiu-Wing Chan[a], Yisu Wang[a], Kangning Ren[a,b]*

[a] Department of Chemistry, Hong Kong Baptist University. Waterloo Rd, Kowloon, Hong Kong, China.

[b] HKBU Institute of Research and Continuing Education, Shenzhen, China.

Email: kangningren@hkbu.edu.hk

Abstract:

Antimicrobial resistance (AMR) has increasingly become a major threat to modern medicine, and it is primarily caused by the misuse or abuse of antibiotics. Antimicrobial susceptibility test (AST) is a promising way to help the optimal use of antibiotics and potentially reduces AMR. However, conventional ASTs usually suffer from the lack of insufficient quantifi-cation capability, efficiency and affordability, and they are lengthy and need several days to complete, need several days for observing and analyzing the macroscopic growth of bacterial colonies. Herein, we demonstrate a reliable whole-polypropylene (PP) microfluidic chip with satisfactory resolution and high fidelity for AST that shows several advantages compared to PDMS chips. A deepened chamber is developed to improve the precision of AST and reduce the effect of shear stress of flow during cell curling, which is examined by both numerical simulations and experiments. Our system allows reliable tracking of individual cells and obtaining AST results within 2-3 hours. Unlike PDMS chips, the whole-PP chips can be conveniently recycled for multiple rounds of usage, and can be remelted and refabricated if it is out of service, which largely decreases the cost and is environmental-friendly. The PP chips provide a practical solution to upgrade the culture-based AST and benefit the battle against AMR through helping doctor to prescribe the effective narrow-spectrum antibiotic; it will also be useful for other applications where a reliable, solvent resistant, anti-fouling, yet affordable microfluidic chip is needed.

Development of Molecularly Imprinted Polymers for Extraction and Preconcentration of Urinary Spermine as Prostate Cancer Biomarker

Yan Ho Fung, Ka-Leung Wong*

Department of Chemistry, Faculty of Science,
Hong Kong Baptist University, Kowloon Tong, Kowloon, Hong Kong
Email: klwong@hkbu.edu.hk

Abstract

Polyamines are multifunctional organic cations that have been studied extensively on their associations with cancer for the past decades. Through the pilot study of prostate cancer (PCa), the urinary spermine (Spm) have demonstrated its usefulness to be biomarker for the differentiation between PCa and non-malignant benign prostatic hyperplasia (BPH) patients.[1] Conventional quantitative detection of urinary spermine content techniques include chromatographic and electro-migration methods coupling with different detectors, for example, UPLC-MS/MS, chemiluminescence based HPLC, etc.[2] However, the above techniques require expensive instrument and complicated sample preparation. Nevertheless, the applicability of newly developed chemosensor, nanoparticle and inorganic complexes-based probes for urinary Spm are limited by the complex matrix and composition of urine, posed difficulty in sample clean-up for efficient detection. Recently, molecularly imprinted polymers (MIPs) have been widely applied as artificial molecular recognition media for the highly selective adsorption and/or concentration/extraction of targeting compounds.[3] In this work, Spm-imprinted acrylic acid-based MIPs are prepared by polymerization. Their structures, morphologies, adsorption efficiency and selectivity to Spm are characterized and discussed.

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Direct Immunomagnetic Detection of Low Abundance Cardiac Biomarker by Aptamer DNA Nanocomplex

Ka Wang Wong,[†] *Dinggeng He,*[†] *Di Xu,*[†] *Man Shing Wong*[†] *and Hung-Wing Li*[†,*]

[†]*Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong*

*Corresponding author e-mail: hwli@hkbu.edu.hk

An early and rapid diagnosis of acute myocardial infraction (MI) by serum biomarker quantification is vital for boosting up treatment efficacy and survival rate; however, it still remains challenging due to ultralow biomarkers content and the emergent nature of the disease. In view of these challenges, a single-step target capturing method for cardiac Troponin I (cTnI), the major cardiac biomarker of MI, was developed. The detection of target cTnI was performed by coupling the capture antibody modified magnetic silica nanoparticle (mSiO2) and an aptamer-based DNA nanostructure produced by hybridization chain reaction (aptHCR). cTnI in sample was first directly captured by mSiO2 and aptHCR in 30 minutes. The as formed nanocomplex was then labelled by a customized DNA turn on fluorescent dye SPM. By reading the strengthened fluorescent signal using total internal reflection fluorescence microscope (TIRFM), the detection platform has accomplished an impressive LOD of 8.5 fM with high specificity towards cTnI. The advantages of the short immunoreaction time (30 min) and the pre-treatment free property of the method have addressed the urgent diagnostic requirements of MI. The detection platform offers a potential solution to tackle insufficient sensitivity and tedious turnaround time of clinically approved assays for cTnI detection.

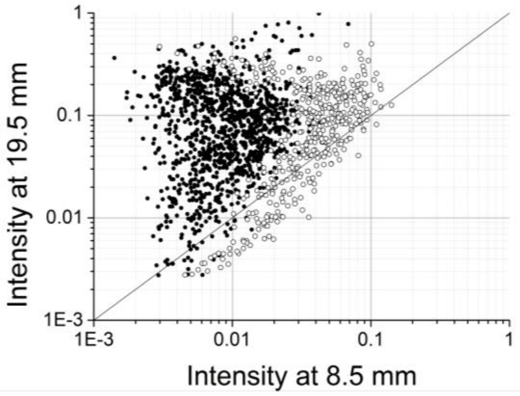
Double-Viewing-Position Single-Particle ICP-AES for the Selection of ICP Sampling Depth with precise intensity measurement

Ka-Him Chun, Wing-Tat Chan*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong SAR.
e-mail: wtchan@hku.hk (Wing-Tat Chan)

ABSTRACT:

Single-particle inductively coupled plasma–mass spectrometry (SP-ICP-MS) have widely been used for the characterization of nanoparticles (typical size range = 10 – 10^2 nm). However, calibration with standard solutions for particle-size determination sometimes introduces systematic error as the sensitivity (atoms/count) of nanoparticles is generally lower than that of standard solutions.[1,2] With an appropriate correction factor, calibration using standard solutions is possible but is only applicable over a small size range (3 orders of magnitude in mass) [3]. The main reason is that particle vaporization is not instantaneous and large particles are incompletely vaporized in the ICP.

A double-viewing-position single-particle inductively coupled plasma–atomic emission spectrometry (SP-ICP-AES) has been developed to study particle vaporization in the ICP.[4] , Ytterbium(III) oxide particles (200 – 2000 nm) were used as test particles. The Yb II emission (λ = 328.94 nm) at two positions (8.5 and 19.5 mm above the load coil (ALC)) were measured to give a pair of temporal emission peaks for each particle (double-peak). Correlation of intensities of the two peaks in a 2D plot shows a large variation in intensity at 8.5 mm ALC. As the boiling point of Yb_2O_3 is approximately equal to the ICP gas temperature at 8.5 mm ALC, the degree of vaporization (DOV) of the particles is low. In addition, the temperature at the rim of the ICP central channel is 400 K higher than that at the center, leading to a large variation in DOV. Confining the particles to a smaller radial dimension of the ICP central channel using a sheath gas device effectively reduces the variation in intensity. Experimental and simulated the correlation plots will be examined to study the key parameters in single-particle measurement. Criteria of selecting optimum sampling position will also be discussed.



Correlation plot of 200 – 2000 nm Yb_2O_3 in double-viewing-position SP-ICP-AES. Particles were introduced to the center (●) and to the rim (○) of the central channel using a sheath gas device.

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Electrospray single-cell inductively coupled plasma – mass spectrometry (ES-SC-ICP-MS)

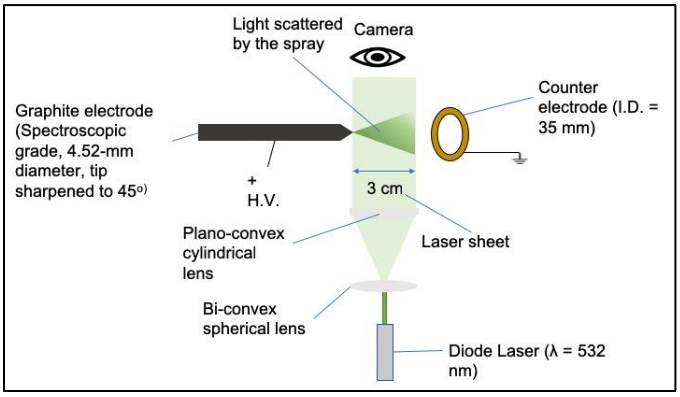
Marco Cheuk-Hei Wong and Wing-Tat Chan

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong SAR. E-mail: wtchan@hku.hk (Wing-Tat Chan)

Abstract

Single-cell inductively coupled plasma – mass spectrometry (SC-ICP-MS) is a powerful technique for the determination of the elemental contents of individual cells. The distribution of cellular elemental contents can be used to evaluate the physiological state[1] and the heterogeneity of the cells[2]. Typical sample preparation procedures for SC-ICP-MS involves repeated centrifugation and resuspension of the biological cells in water or buffer solutions to remove interfering elements in the culture solutions. However, the biological cells suffer from severe mechanical stresses during the centrifugation process [3], as well as osmotic stresses across the cell membrane due to the difference in electrolyte concentration between the cell and the cleaned medium[4]. These stresses may induce changes in the elemental contents of the cells and cell.

To minimize the stresses introduced to the sample cells during the preparation procedures, a novel sample introduction system by electrospray is proposed. A 1-µL aliquot of sample cell suspension is placed on the tip of the graphite electrode. A potential ranging from 7 kV to 10 kV was applied to the graphite electrode to produce a spray with a current less than 1.5 µA. The spray of a 1-µL aliquot of cell suspension can sustain for a few minutes, which is long enough for a typical time-resolved measurement for SC-ICP-MS. The spray was visualized by laser scattering (wavelength = 532 nm) (Fig.1). The spray angle was approximately 49° and is insensitive to the applied potential and the distance between the graphite tip and the counter electrode. The sprayed cells appeared to be intact and well-separated as individual cells. The spraying efficiency was estimated to be 18% and was improved to 30% when the pH was adjusted below the pK_a of the cell surface carboxylic group. Characteristics of the electrospray system will be presented.



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Shotgun Proteomics and Quantitative Pathway Analysis of the Mechanisms of Action of Dehydroeffusol, a Bioactive Phytochemical with Anticancer Activity from *Juncus effusus*

I-Sheng Chang†, Lai-King Sy†, Bei Cao, Ching Tung Lum, Wai-Lun Kwong, Yi-Man Eva Fung*, Chun-Nam Lok* and Chi-Ming Che*

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

*Email: eva.fungym@hku.hk; cnlok@hku.hk; cmche@hku.hk.

ABSTRACT: Dehydroeffusol (DHE) is a phenanthrene isolated from the Chinese medicinal plant *Juncus effusus*. Biological evaluation of DHE reveals *in vitro* and *in vivo* anticancer effects. We performed a shotgun proteomic analysis using liquid chromatography-tandem mass spectrometry to investigate the changes in the protein profiles in cancer cells upon DHE treatment. DHE affected cancer-associated signaling pathways, including NF-κB, β-catenin, and endoplasmic reticulum stress. Through quantitative pathway and key-node analysis of the proteomics data, activating transcription factor 2 (ATF-2) and c-Jun kinase (JNK) were found to be the key components in DHE's modulated biological pathways. Based on the pathway analysis as well as chemical similarity to estradiol, DHE is proposed to be a phytoestrogen. The proteomic, bioinformatic, and chemoinformatic analyses were further verified with individual cell-based experiments. Our study demonstrates a workflow for identifying the mechanisms of action of DHE through shotgun proteomic analysis.

Gold@Metal Sulfide Core-Shell Nanoparticles: Rational Design of Substrates for Surface-assisted Laser Desorption Ionization – Mass Spectrometry

Yu-Hong Cheng and Kwan-Ming Ng*

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong S.A.R., P.R. China
**Corresponding author: kwanmng@hku.hk*

Abstract

Gold@Semiconductor core-shell nanoparticles are extensively applied in solar cell development and catalytic applications attributed to their high light harvesting efficiency and intrinsic charge separation property. Possessing characteristic localized surface plasmon resonance (LSPR) property, the gold core efficiently absorbs visible radiation resulting in a collective oscillation of the conducting electrons and induces the generation of excitons in the semiconductor shell. The electron–hole pairs generated would then be separated according to the band structure of the core-shell system. Herein, four types of Gold@Metal Sulfide nanoparticles (Au@Ag_2S, Au@CdS, Au@ZnS, and Au@PbS) with distinctive band structures were synthesized and applied as substrates for Surface-assisted Laser Desorption Ionization – Mass Spectrometry (SALDI–MS). Utilizing the light harvesting and charge separation properties of the Gold@Metal Sulfide nanoparticles, the laser energy could be effectively absorbed and the separated charges could be transferred to the analytes for ionization. With this rational design of Gold@Metal Sulfide SALDI substrate via the manipulation of electronic structures, optical absorption features, and heat transfer properties, the MS sensitivity could be improved for more than three times when compared to a standard SALDI method using gold nanoparticles as substrate.

Gold Nanoparticle Mass Tags for the sensitive detection of Cervical Cancer marker proteins via Laser Ionization Mass Spectrometry

Siu-Chung Toby Tam, Yu-Hong Cheng, Kwan-Ming Ng*

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong.
*Corresponding Author: kwanmng@hku.hk

Abstract

Infections by high-risk HPV types 16 and 18 are responsible for 70-80% of cases of cervical cancer worldwide, where oncoproteins E6 and E7 play a critical role in carcinogenesis[1]. Herein, a mass spectrometric approach using gold nanoparticles (AuNPs) was employed for the detection of E7 oncoproteins in solid-phase sandwich immunoassays. Utilizing their plasmonic properties, AuNPs undergo explosive ionization when irradiated to generate abundant reporter ions during MS analysis for strong signal amplification. When attached to a molecular probe e.g. antibodies, AuNPs can function as mass tags to enable detection and imaging of analytes as demonstrated in our recent study[2]. To improve their analytical performance, the role of polyethylene glycol (PEG) as a stabilizing agent for AuNPs in biological media was studied. 20nm AuNPs were modified with various ratios of antibody-conjugated PEG vs. carboxylate-PEG stabilizer to influence the degree of specific vs. non-specific binding. Optimization yielded a 50 times improvement in terms of signal-to-noise (S/N) for the detection of low femtomole levels of E7 oncoprotein, whilst the detection limit of this method achieved low attomole levels.

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Investigation of DNA-Protein Cross-Links in Toxicant Exposed Cells by Isotope-Dilution Liquid Chromatography Tandem Mass Spectrometry

Yat-Hing Ham, Long Jin and Wan Chan*

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

Abstract

DNA–Protein Cross-Links (DPC) are formed by reacting DNA lesions and proteins. In general, the association between DNA and protein is reversible. However, when there is an abasic site created in the DNA strands, DPC may occur. The irreversible binding of protein to DNA will impair normal cellular functions, as it inhibits gene transcription and replication, which may eventually result in cell death[1-2]. Although DPC is commonly known, the affected protein profile and the chemical structures of DPC in general cells are not clear. To investigate the proteins involved in DPC formation, DNA-protein complexes were extracted from human cells, which were then examined with liquid chromatography-tandem mass spectrometry (LC-MS/MS) as a high-throughput proteomic analysis. To explore the chemical structures of DPC, isolated DNA-protein complexes were hydrolysed and analysed with LC-MS/MS. The conformations of the formed adducts such as 2'-deoxyribose-cysteine or 2'-deoxyribose-lysine were revealed. The study will increase our understanding to the mechanism and effect of DPCs, revealing more about the basic principle of DNA lesions.

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Development of Dispersive Solid Phase Extraction Method for Determination of Aristolochic Acids in Water Samples

Ka Ki Tung and Wan Chan*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, Hong Kong; Email: chanwan@ust.hk

Abstract

Aristolochic acids (AAs) are carcinogen and nephrotoxin naturally produced by the *Aristolochia* plants. Previous study showed that decaying *A. Clematises* released free AAs and contaminated the cultivation soil in the Balkan Peninsula.[1] We postulate AAs might leached to the water bodies and contaminated the drinking water of the local residents.[1] We initiated the study by developing a dispersive solid phase extraction method to adsorb and concentrate AAs from contaminated water samples, then desorbed by using acid/heat treatment, and analyzed by using a highly sensitive and selective high-performance liquid chromatography coupled with tandem mass spectrometric method. We detected in this study for the first time AAs in the water samples collected from Serbia, indicating drinking water maybe one of the exposure pathways of AAs to human causing the Balkan endemic nephropathy. Our result provide evidence for a new human exposure pathway to AAs from contaminated drinking water.

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Determining Geographic Origins of Red Ginseng using Metabolomics

Ailsa, Chui-ying Yuen, Siu-wai Wan, Chi-on Chan, Daniel, Kam-Wah Mok
Email: bcdaniel@polyu.edu.hk

Abstract

Red ginseng (or called Hongshen in Chinese) is the steamed dried root and rhizome of *Panax ginseng* C.A. Mey [1] and is a famous Chinese medicine for tonifying *qi*. Red ginseng has two main production sites, northern part of China and South Korea. The red ginseng from these two regions are different in the quality and price [2]. Previous studies used the isotopic ratios including hydrogen, carbon and nirogen to differentiate those ginseng collected between China and Korea [3]. However, this technique may require specialized instrument and it does not provide information related to the quality of red ginseng. In this study, metabolomics analysis of red ginseng samples collected in China and Korea was performed using UPLC-orbitrap-MS. Multivariate analysis was carried out to identify the key metabolites for differentiation of the red ginsengs from these two geographical origins. Our results showed that 24 metabolites including sugars, fatty acids, ginsenosides were tentatively identified. The results suggested that metabolomics profile of red ginseng could provide more comprehensive information to differentiate Chinese and Korean red ginseng.

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Mechanistic Study on Inhibition of Ebselen and L-captopril towards New Delhi Metallo-β-lactamase (NDM-1) by Mass Spectrometry

Li-Wen Huang, Pui-Kin So, Sheng Chen, Zhong-Ping Yao

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University; E-mail: zhongping.yao@polyu.edu.hk.

Abstract

New Delhi metallo-β-lactamase (NDM-1) belongs to class B β-lactamase, which is a class of zinc-bound enzymes. The widespread NDM-1 renders severe antibiotic resistance towards nearly complete spectrum of β-lactam antibiotics in the market. Unfortunately, the inhibitors for NDM-1 are not available in the clinic yet. Several compounds, e.g., Ebselen and L-captopril, show potent inhibition towards NDM-1, but their inhibition mechanisms have been rarely reported. In this study, we used mass spectrometry (MS) coupled with hydrogen deuterium exchange (HDX-MS) to elucidate the conformational dynamics of the inhibitory interactions between NDM-1 and Ebselen/L-captopril. Electrospray ionization (ESI) MS showed a 1:1 NDM-1/Ebselen complex with one zinc ion replaced and a 1:1 NDM-1/L-captopril complex without the removal of any zinc ions, suggesting different mechanistic characters of these two inhibitors. Interestingly, the results from HDX-MS showed that the loop covering residues 211-228 exhibited significant decreased deuterium exchange for both Ebselen and L-captopril complexed NDM-1, indicating that the flexibility of this loop was effectively reduced upon inhibition and the conformational dynamics of this loop could be vital for the activity of NDM-1. These results allow us to obtain insights into the inhibition of NDM-1 that cannot be obtained by using other techniques and provide new evidence for design of inhibitors.

Acknowledgements: This work was supported by Hong Kong RGC GRF (No. 15304117) and CRF (No. C5031-14E).

Rapid Quantitation of Compositions of Blended Oils by Matrix-assisted Laser Desorption/Ionization Mass Spectrometry and Partial Least Squares Regression

Suying Li, Tsz-Tsun Ng, Zhong-Ping Yao*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University; *zhongping.yao@polyu.edu.hk*

ABSTRACT

Authentication of edible oils is an important issue for ensuring food quality and safety. Mislabeling of oil compositions for better profits is a problem frequently encountered in the market of blended oils. However, authentic method for quantitation of blended oils is still lacking. Matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) has been proved to be an effective tool for profiling triacylglycerols (TAGs) in edible oils,[1] enabling rapid classification of edible oils based on their MALDI-MS spectral patterns and statistical analysis.[2] In this study, we applied partial least squares regression (PLS-R) to analyze the MALDI-MS spectra of blended oils and established a protocol for quantifying all compositions of each blended oil simultaneously. The accuracy and precision of the established approach were measured and were comparable to those obtained by using the conventional gas chromatography flame ionization detector (GC-FID) method. Different types of blended oils, including binary, ternary and quaternary blended oils as well as 10 commercial blended oil products, have been successfully analyzed, demonstrating a rapid, simple and effective approach for quantitative determination of compositions of blended oils.

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Hydroponic Uptake and Translocation of Aristolochic Acids in *Allium Fistulosum*

Chun-Kit Au and Wan Chan*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, Hong Kong; Email: chanwan@ust.hk

Abstract

Aristolochic Acid Nephropathy (AAN) were reported worldwide due to chronic consumption of the Aristolochic Acids (AAs) contaminated agricultural products.[1] These carcinogenic and nephrotoxic persistent soil pollutants derived from the decomposition of the *A. Clematitis* seeds were absorbed, transferred and accumulated in the food crops. [2,3] However, the detailed uptake response of AAs remains unclear. This hydroponic study investigated the degree of root uptake and translocation of AAs in *Allium Fistulosum* under different pH conditions across its optimal growth range. Results indicated lower absorption in alkaline medium ascribable to the ion-trapping mechanism. It is anticipated that the result from the study could put forward effort on the substantial application in the agricultural practice.

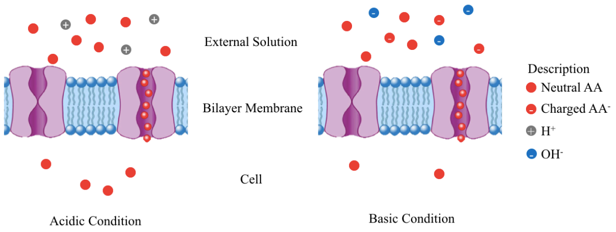

Figure 1: Illustration of the Ion-trapping Mechanism

Figure 2: The Hydroponic *A. Fistulosum*

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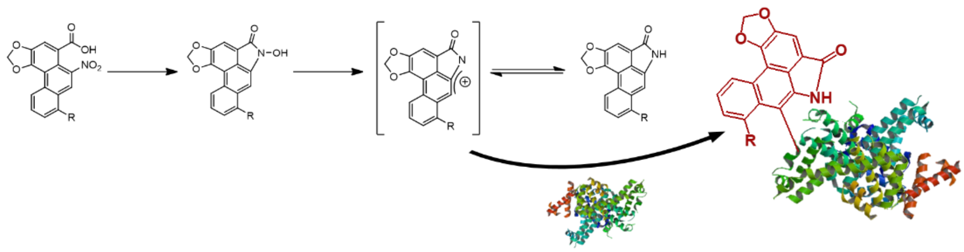
Albumin Adducts of Aristolochic Acids: Potential Biomarkers of Exposure to Aristolochic Acids

Chi-Kong Chan, Jiayin Zhang and Wan Chan*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, Hong Kong
Email: chanwan@ust.hk

Abstract

Aristolochic acids (AA) are carcinogenic and nephrotoxic phytochemicals present in *Aristolochia* species, and they are known to play a crucial role in the development of aristolochic acid nephropathy and Balkan endemic nephropathy[1]. Through the metabolic activation mediated by cytochrome P450 enzymes and peroxidases, AA generate highly reactive metabolites that exert genotoxicity in human[2]. These metabolites could also be implicated in protein-binding, while the binding mechanism remains unexplored. In this study, we first identified the formation and structure of covalent adducts between AA-I and glutathione, as well as between AA-I and *N*-acetylcysteine following *in vitro* incubations. Using our previously developed liquid chromatography-tandem mass spectrometric method, we optimized the hydrolysis method with bovine serum albumin and biomonitored the hydrolysis products of AA-I-protein, aristolactam-I, and in blood serum albumin of AA-I-dosed rats. Our results demonstrate that AA-I-albumin adducts could be an alternative biomarker of exposure to AA, which may provide a convenient method to biomonitor human exposure to AA from contaminated food and traditional Chinese medicines.



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Quantitation of Advanced Glycation End-products in Oxidative Stressor Exposed Cells by Liquid Chromatography-Tandem Mass Spectrometry

Sum Kok WONG[1] and Wan CHAN[1,2]

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

Email: chanwan@ust.hk

Abstract

Advanced Glycation End-products (AGEs) were linked to aging and many human degenerative diseases such as diabetes. Among numbers of reported AGEs, the representative analytes are N_ε-carboxy-methyl-lysine (CML) and N_ε-carboxy-ethyl-lysine (CEL). These products could be formed by reacting the amino side chain of lysine with glyoxal (GO) or methylglyoxal (MGO), respectively, while CML could also be generated by fragmentation of glycated protein from oxidation (Fig. 1). We investigated in this study the potential role(s) of CML and CEL in oxidative-stress related disease and explored their possible use as biomarker for disease risk assessment. We have initiated the study by detecting them in oxidant-exposed *E. coli*, then progress to identify them in protein isolated from toxicants exposed animal tissues.

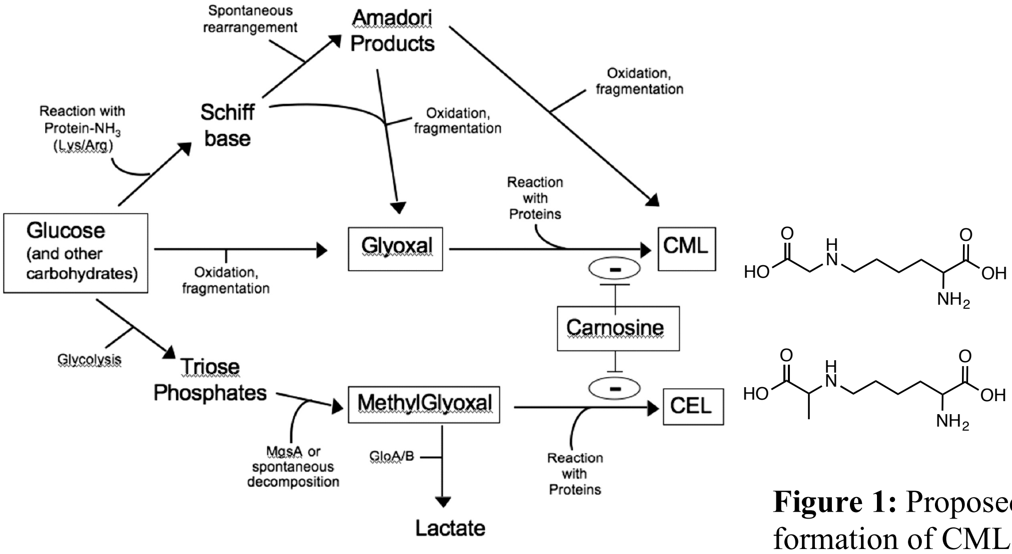

Figure 1: Proposed model for formation of CML and CEL

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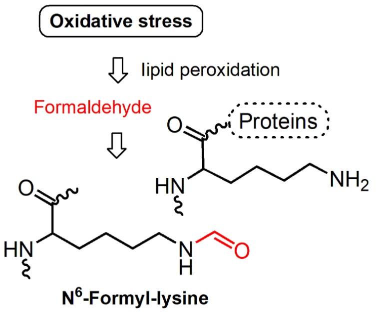
Quantification of *N*⁶-formyllysine in Oxidant-exposed Cells by LC-MS/MS with Stable Isotope Dilution Method

Yao ZHAO and Wan CHAN*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong;
Email: chanwan@ust.hk

Abstract

Epidemiological studies have shown that oxidative stress is associated with the development many human diseases, including cancers. During oxidative stress, formaldehyde is generated in lipid peroxidation and other pathways, which further reacts with lysine residues in protein to form *N*^{6}-formyllysine.[1] Because of the high chemical stability, FLys is being used as a biomarker for assessing the risk of formaldehyde exposure and oxidative stress associated diseases.[2] We have developed and validated an isotope-dilution liquid chromatography-coupled tandem mass spectrometry (LC-MS/MS) method for the rigorous quantification of FLys in purified protein and in protein isolated from oxidant-exposed cells. A dose-dependent formation of FLys was observed in cells exposed to benzoquinone, ferrous iron and aristolochic acids.



Lysine formylation as potential marker signature for Oxidative stress-induced human diseases

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Micro flow reactors with an integrated optical trace oxygen sensor

Ka Yuet Anna Leung and Stefan Nagl*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, Hong Kong SAR, P. R. China; E-mail: chnagl@ust.hk

Abstract

Oxygen is involved in a vast amount of chemical processes, and its presence may be either desirable or interfering. The luminescence-optical oxygen sensor is a prime tool for real-time oxygen measurement as it features non-invasiveness, full reversibility, precise and accurate measurements, ease of miniaturization, and imaging capability of oxygen on various scales. However, most developed oxygen sensors up to date cater to biological studies only and are not compatible with chemical processes that use organic solvents and non-polar condition, limiting their use in chemical synthesis.

We tested various optical sensor films for trace oxygen detection with respect to their analytical parameters and compatibility with organic solvents. Good results were obtained with a sensing film of 1 % (w/w) palladium(II)-5,10,15,20-tetrakis-(2,3,4,5,6-pentafluorphenyl)-porphyrin in Hyflon AD 60 that was spin-coated on glass slides. It shows a limit of detection below 10 p.p.m.v. of oxygen in gas phase under atmospheric pressure, a K_{SV} of around 4.8×10^{-3} p.p.m.v.$^{-1}$ and good resistance to non-polar environments.

Currently we are working on suitable microfabrication procedures in order to integrate the sensor into micro flow reactors in order to obtain a multifunctional platform for chemical synthesis in the absence of oxygen where the oxygenation status of the employed solutions can be precisely monitored by the sensor.

Improved microfluidic platforms with precise temperature control and monitoring for melting curve analysis

Xuyan LIN, Chenyu CUI, Stefan NAGL*

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

Abstract

Melting curve analysis (MCA) on microfluidic chips has attracted significant interest because it uses minute amounts of sample and potentially very short analysis times in the screening of genetic mutations. The shortest analysis are potentially afforded by space-domain on-chip MCA, but this requires real-time spatially resolved simultaneous monitoring of temperature and the DNA fluorescence signal. Herein, we developed a microfluidic chip integrated with a microheater and luminescent temperature sensor for MCA, giving information about the thermal gradient through optical imaging. A microheater for Joule heat generation was fabricated by Pt sputtering and a lift-off process on a 1’ square glass chip. The luminescent sensor film was fabricated from poly(styrene-co-acrylonitrile) with 1% tris(1,10-phenanthroline) ruthenium(II), that was blade coated on a glass surface at a thickness of about 3 μm. A PDMS microfluidic channel structure was fabricated on top of it. The temperature sensor was calibrated using luminescence lifetime measurements from 25 to 95 °C. The fluorescence in the DNA and the temperature spectral channel, respectively, can be imaged in a customized assembly, and is currently being used to screen for mutations in a variety of DNA samples.

High quality thin films doped with perovskite nanocrystals for non-contact thermal imaging in aqueous solutions

Zhangdi Lu[1], Yanxiu Li[2], Wenting Qiu[1], Andrey L. Rogach*[2] and Stefan Nagl*[1]
[1]Department of Chemistry, The Hong Kong University of Science and Technology, Kowloon, Hong Kong S.A.R. China; E-mail: chnagl@ust.hk
[2]Department of Materials Science and Engineering, and Center for Functional Photonics (CFP), City University of Hong Kong, 83 Tat Chee Avenue, Kowloon, Hong Kong S.A.R. China; E-mail: andrey.rogach@cityu.edu.hk

Abstract

Perovskite quantum dots have gained enormous attention in many application areas due to their unique optical properties. The applications of perovskite nanocrystals as temperature sensors require suitable embedding matrices, film quality and stability of perovskite crystals. We investigated various matrices for their ability to form functional composite films with embedded $CsPbBr_3$ nanocrystals (NCs) in different concentrations. These were immobilized on glass substrates by spin coating, characterized and applied as solid-state thermal sensors in aqueous environment. The film morphology of $CsPbBr_3$ – Hyflon AD 60 was found to be highly uniform based on fluorescence microscope images. The $CsPbBr_3$ NCs loading inside this highly hydrophobic fluorinated polymer showed complete water resistance for at least one month and exhibited good stability, strong thermal sensitivity (0.86% K^{-1}) and reversibility between 293 and 353 K. It also revealed high photostability at different temperatures. This perovskite film is currently applied on microfluidic devices for thermal mapping but may also find various other applications.

In-Situ Monitoring of Escherichia Coli Growth on Digital Microfluidics by Optical Chemosensors for Rapid Antibiotic Susceptibility Testing

Wenting Qiu and Stefan Nagl* E-mail: chnagl@ust.hk

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

Overuse and abuse of antibiotics in human and animal health care in the past few decades lead to a significant increase in antibiotic resistance among world-wide bacterial species. The minimum inhibitory concentration (MIC) of an antibiotic is the lowest concentration that inhibits the visible growth of a bacterium. MIC is a critical value for antimicrobial susceptibility testing, and normally is performed using tubes, microplates or agar plate-based broth dilution methods. Those methods are labor-intensive and time-consuming, typically they require more than 24 hours to determine the result. Digital microfluidics (DMF) is a droplet-based automation and miniaturization technology. Here we show DMF devices with integrated optical chemical sensor layers for pH and DO for rapid MIC determination of various antibiotics via automatic on-chip broth dilution.

We designed a set of electrode arrays comprising a culture region, detection region, sample region and reservoir region which can automatically perform two-fold serial antibiotic dilution and cell culture with real-time readout of culture medium conditions.

The DO probe Platinum tetrafluorophenylporphyrin (PtTFPP) was embedded in Hyflon AD 60 perfluoropolymer with a contact angle of over 120° which facilitates droplet manipulation and exhibits good sensitivity to oxygen in both gas phase and liquid phase at 37 ℃ with K_{sv} values of 0.1641 hPa^{-1} and 0.460 L/mg, respectively. It also showed good photostability, immersed in water after 1 h continuous 405 nm LED illumination, the intensity decrease was only 5%. The device could be stored under ambient temperature for over one month without significant changes in their optical properties.

To construct hydrophilic DMF surface regions for pH sensing, a pH probe consisting of Fluorescein covalently attached to poly-(2-hydroxyethyl methacrylate) (pHEMA) was deposited on a ‘lift-off’ surface. The FITC-pHEMA calibration indicated a pK_a value of 6.591, affording good sensitivity in the range of pH 5 to 8, fulfilling the requirements for cell culture monitoring.

We realized real-time and in-situ recording of DO and pH change during E. coli growth exposed to an antibiotic concentration gradient using a dedicated imaging system and a 37 ℃ temperature-controlled enclosure. Using the DMF with integrated optical sensors we could screen for MIC of antibiotics with a cycle time of only 3 to 4 h and using less than 10 μL culture, which is a decrease of a factor of more than 10 compared to standard microplate-based assays.

Fabrication of long-range chemical concentration gradient generator

Zeyu Liu, Jacqueline Cheryl Sabrina, Hongkai Wu*

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

E-mail: chhkwu@ust.hk

Abstract

Microfluidics technology has been used extensively to develop complex and stable flow-based and diffusion-based concentration gradient generator to study different biological and chemical process. Flow-based gradient generators can generate stable gradient in temporal and spatial, but the dynamic flow makes cells in a continuous shear stress which is not fitted with true microenvironment. Diffusion-based gradient generators developed only cover small distance up to few mm and done in 2D environment. Therefore, it is necessary to develop a concentration gradient that can represent the actual environment with long- range chemical concentration. This study focuses on developing a long-range chemical concentration gradient generator through diffusion with channel that extends to few cm long and suspended in a 3-dimensional configuration. The device was fabricated from multiple components – agarose gel, 3D printed molds, metal wire, and glass spacers. Then the resulting concentration gradient was imaged by confocal fluorescence microscopy. Generated concentration gradients demonstrated a high linearity after seven minutes, followed by the levelling off of the concentration gradient. This study shows that it is possible to create concentration gradient with longer range and 3D. The addition of inlet and outlet on the reservoirs could be useful for maintaining a stable concentration gradient.

Investigation of employing strawberry DNA as carrier DNA to enhance DNA extraction efficiency via Recombinase polymerase amplification (RPA)

Dong WANG[1], Ho Nam CHAN[1], Wong Kee Hang[1]

[1] The Hong Kong University of Science and Technology

dwangan@connect.ust.hk

Abstract

Emerging evidence has suggested both Polymerase chain reaction (PCR) and Recombinase polymerase amplification (RPA) for amplifying deoxyribonucleic acid (DNA) have one common limitation that a minimum concentration of target DNA is needed. Carrier DNA such as poly-(A) carrier RNA and salmon sperm DNA have been invented to enhance the yield of target DNA after in the extraction process. However, the cost and the ease of purchasing such carriers are concerns. This project aims to evaluate the capability of strawberry DNA as the carrier DNA for Bacillus subtilis 168 (bacteria) DNA extraction via RPA. The pure strawberry DNA were extracted by cetyl trimethylammonium bromide based (CTAB) method. Our study revealed that strawberry DNA was able to be employed as the carrier DNA in order to enhance the yield of bacteria DNA after extraction and time needed for obtaining RPA respond was shortened after strawberry DNA was used as carrier DNA. To the best of our knowledge, this project is the first to examine whether strawberry DNA can be used to be a carrier DNA. Results also demonstrated that pure strawberry DNA was required to obtain positive results in RPA and be the carrier DNA. Principle of RPA shown in Figure 1.

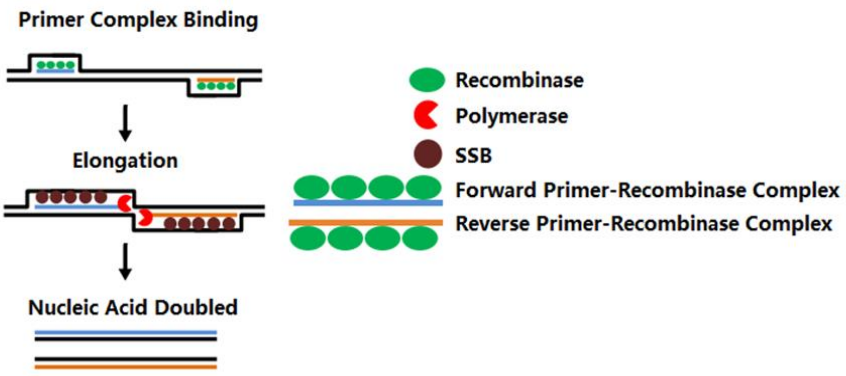

Figure 1. Diagram showing the principle of RPA

Single Cell Pipette based on Microfluidic Chip

Qiaoyi WANG, Sean Alan MICHAEL, Hongkai WU*

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

Abstract

Trapping and manipulating cells with high spatial and temporal precision is crucial for single cell isolation and analysis. Current trapping techniques mainly include the use of external fields, surface patterning, and hydrodynamic trapping. While the two former methods can produce single cell arrays with good resolution, they cannot work as a point source technique. Hydrodynamic traps, however, especially for those adapting resistive-based trapping mechanism, can capture one single cell with high efficiency under proper geometries[1]. This enables us to fabricate a single-cell pipette that can trap single cells selectively and efficiently, and thus transfer and precisely release the captured cells onto designated 2D substrates or into 3D space. In our work, Quake valves[2] and a simple mild negative pressure system are employed to precisely control the flow of fluids in the pipette. This single-cell pipette will be easy to handle, require minimal equipment, and can be applied to meet different task demands (e.g., high-throughput, multiplexity, 3D cell printing and droplet formation with 1 cell/drop) when combing with microfluidic components. In the future, it is promising for our single-cell pipette to be developed into commercial products for single-cell manipulation.

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Field observations of hydroxy diacids and investigation of their formation link with aliphatic diacids through heterogeneous oxidation

Yuk Ying Cheng[1], Yee Ka Wong[2], Jian Zhen YU*[1,2]

[1] Department of Chemistry, Hong Kong University of Science and Technology

[2] Division of Division of Environment and Sustainability, Hong Kong University of Science and Technology

*Corresponding author email: jian.yu@ust.hk

Abstract

Recent chamber studies have suggested that oxygenated organic aerosol might be further oxidized within aerosol atmospheric lifetime. The oxidation transformation of the oxygenated organic compounds would change the composition of the aerosol and thus alter the hygroscopicity to affect the radiation balance of the Earth. This influences both the climate and the air quality. Laboratory studies indicated that the major heterogeneous oxidation functionalization product of aerosol-phase aliphatic DCAs was the corresponding hydroxy DCAs (hDCAs). We therefore focused our field investigation on hydroxyl DCAs and report in this work their abundance, correlation and effect of estimated LWC and sulfate on their abundance. Good correlations were observed between DCAs and hDCAs, supporting that DCAs might be one of the major precursors for hDCAs (R~0.5-0.9). Seasonal variations in the correlation slopes were noted, which might indicate a switch of reaction mechanisms, precursors or sources. The effect of estimated LWC and sulfate was illustrated through the contour plots. Three clusters were identified in the contour plots representing three episodic events that occurred during the summer sampling period. The episodic formation of dicarboxylic acids was more associated with concentration of sulfate since all episode events occurred when there was relatively high abundance of sulfate but not higher estimated LWC. Long range transport contribution might explain that higher LWC were not associated with higher abundance of DCAs. More efforts are needed to understand the formation conditions and mechanisms for hydroxyl dicarboxylic acids.

Water-soluble inorganics in $PM_{2.5}$ and PM_{10} and precursor gases at an urban area in Hong Kong: Long-term trends and composition variability

Ka Yuen CHEUNG[1] and Jian Zhen YU[1,2]
[1] Division of Environment and Sustainability, The Hong Kong University of Science and Technology, Clearwater Bay, Kowloon, Hong Kong
[2] Department of Chemistry, The Hong Kong University of Science and Technology, Clearwater Bay, Kowloon, Hong Kong
*Corresponding author email: jian.yu@ust.hk

Gravimetric analysis has long been used to monitor the trends of the bulk aerosol mass in both $PM_{2.5}$ and PM_{10} while offline chemical speciation analysis of filter-based samples offered daily or lower frequency measurements. However, long-term and chemical speciated aerosol measurements with high temporal resolution are in limited availability. The Monitor for AeRosols and Gases (MARGA 2S, Applikon B.V., NL) allows for the identification and quantification of water-soluble inorganics (WSIs) in $PM_{2.5}$ and PM_{10} (NH_4^+, NO_3^-, SO_4^{2-}, Cl^-, Na^+, K^+, Mg^{2+}, Ca^{2+}) and precursor gases (HCl, HONO, HNO_3, SO_2 and NH_3) at hourly resolution.

The present study covers 4-year continuous observations of $PM_{2.5}$, PM_{10} and their precursor gases using the MARGA 2S at the Yuen Long Air Quality Monitoring Station (YLAQMS) in Hong Kong from July 2013 to June 2017. YLAQMS is one of the representative urban sites with heavy traffic flows. Major secondary inorganic aerosols (SIAs) including ammonium, nitrate and sulfate were found to be the dominating species of WSIs in $PM_{2.5}$ while nitrate was also found to make the largest contribution to the WSIs in PM_{Coarse} (PM_{10}-$PM_{2.5}$) in the sampling site. Our results confirm that nitrate, as a significant component in fine particle, could also have comparably abundant presence in the coarse particle. This provides evidence of considerable processing of sea spray and crustal dust aerosol species, particularly Na^+, Mg^{2+} and Ca^{2+}, in the coarse mode with HNO_3. Nitrate could be formed by heterogeneous reactions of HNO_3 with particulate even in ammonium poor regime and facilitated by a local source and/ or transport of crustal dust and sea spray aerosol. Our study also investigates the partitioning behaviours of nitrate between fine and coarse modes in order to quantify factors and processes governing nitrate in $PM_{2.5}$ and PM_{Coarse}.

The preliminary results of temporal variations, composition variability and factors affecting nitrate in fine and coarse mode will be shown. The results of this analysis support for the study of SIAs formation mechanisms in different regimes.

Acknowledgements

This work is supported by the Hong Kong Environmental Protection Department (HKEPD). We thank HKEPD for provision of the MARGA 2S data. The content of this study does not necessarily reflect the views and polices of the HKSAR Government, nor does mention of trade names or commercial products constitute an endorsement or recommendation of their use.

Temporal variation of Non-Polar Organic Compounds in $PM_{2.5}$ over 5 years (2014 -2017) in Hong Kong

Chow Wing Sze, Jian Zhen Yu*

Department of Chemistry, Hong Kong university of Science & Technology, Clear Water Bay, Kowloon, Hong Kong;

*Corresponding author: chjianyu@ust.hk

Abstract

Particulate matter 2.5 ($PM_{2.5}$) is one of the major components in air pollution in Hong Kong. It is important to know the major contributing sources and the chemical composition for formulating control strategies and for assessing health impact of $PM_{2.5}$ pollution. Among all the species, non-polar organic compounds (NPOCs) including polycyclic aromatic hydrocarbons (PAHs), hopanes and straight-chain alkanes (n-alkanes) can contribute one fifth to a quarter of $PM_{2.5}$ aerosol. The changes of those NPOCs in recent five years (2013-2017) at an urban site Tsuen Wan (TW) were analyzed by thermal desorption – gas chromatography mass spectrometer (TD-GC/MS). Around 61.8% of four most abundant hopanes, 42.5% lower molecular weight (LMW) C_{21}-C_{26} n-alkanes and 18.4% high molecular weight (HMW) C_{27}-C_{36} n-alkanes were found declined in this period, while the less consistent trend of PAHs implies the complexity of factors on its sources or degradation processes.

Traditional approaches on source appointment were also examined. Both scatter plot and concentration ratio to elemental carbon (EC) among PAHs indicate that the major source was vehicular emission in spring and summer while biomass burning in fall and winter. Seasonal changes due to higher oxidation reactivity in summer was also found from the ratio-ratio plots of PAHs. Meanwhile, the hopane/EC ratio plots indicate the vehicular-dominated emission in Tsuen Wan. Carbon preference index (CPI) value of LMW and HMW n-alkanes were also calculated and both results agree with the n-alkane/EC ratio plots that LMW n-alkanes are mainly emitted from vehicle sources while HMW came from biogenic emissions.

Analysis of Aerosol Nitrogen by Thermal Evolution - Chemiluminescence Based Method

Yao GE, Qian Feng LI, Jian Zhen YU*
Department of Chemistry, Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong;
*Corresponding author: chjianyu@ust.hk

Abstract

We have developed an aerosol nitrogen analyser for analysis of nitrogenous species in aerosol samples collected on a filter substrate. This instrument integrates a combustion-based aerosol carbon analyser and a chemiluminescent NO_x analyser[1] to enable detection of aerosol nitrogen. During the thermal evolution process, nitrogen-bearing compounds are first oxidized to NO_x (nitrogen oxides, $NO+NO_2$) with MnO_2 as catalyst. After that the gas products are transformed to NO in the presence of molybdenum catalyst, and subsequently quantified by a chemiluminescence detector. This system offers relatively fast (30 min per run) and sensitive total nitrogen measurements of a small size (~1 cm^2) of the aerosol sample without any pre-treatment. The temperature program is under investigation with the purpose of differentiating organic and inorganic nitrogen-containing compounds. Such differentiation has been partly achieved through a 5-step temperature program from 150°C to 800°C. Different sets of nitrogenous standards including inorganic salts (e.g. NH_4NO_3, KNO_3, $(NH_4)_2SO_4$, etc.), urea, nitro-aromatic compounds and amino acids have been used to calibration tests and most of them have shown reasonable linear response. The N/C ratio of ambient samples is also examined to seek possible benchmark values for distinct groups of organic matter. Alternatively, the overall ON (organic nitrogen) contents in aerosol samples can be calculated from the difference between TN (total nitrogen) and IN (inorganic nitrogen). The IN is the sum of nitrogen from NH_4^+ and NO_3^- that can be determined by ion chromatography. In summary, this instrument offers a competent and convenient tool for characterization of nitrogen pool in atmospheric aerosols.

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Comparison on decadal trend of biomass burning contribution towards PM2.5 in Pearl River Delta region between satellite data and levoglucosan tracer method

Ka Fung LEUNG, Tong LIU, Bin-Yu KUANG, Jian Zhen YU*
Division of Environment and Sustainability, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong;
*Corresponding author email: jian.yu@ust.hk

Abstract

Biomass burning (BB) is among major sources contributing to fine particulate matter ($PM_{2.5}$) pollution. The BB contribution to ambient $PM_{2.5}$ can be tracked by levoglucosan, an established unique molecular tracer that is a thermal pyrolysis product of BB[1]. On the other hand, intensity of open field burnings can be evaluated by satellite data[2]. There has not been inter-comparison of these two approaches in tracking the BB source. In this work, we analyzed the long-term biomass burning trend in PRD region by comparing these two different assessment methods. Levoglucosan concentrations were measured by high-performance anion-exchange chromatography coupled with pulsed amperometric detection (HPAEC-PAD) for three sampling sites in PRD region (Guangzhou, Nansha and Tsuen Wan) over a ten-year period (2008 to 2017). Satellite data was obtained from NASA's Moderate Resolution Imaging Spectroradiometer (MODIS) C6 Fire Product. The results showed aligned trend with higher BB contribution in winter due to crop residue burning and residential heating. However, there existed some discrepancies, which may be due to undetected burnings by satellite.

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Abundance and Sources of Benzo[*a*]pyrene and Other PAHs in Ambient Air in Hong Kong: A Review of Measurements from 1997 to 2016

Ke Zheng LIAO, Jian Zhen YU*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong;
*Corresponding author email: jian.yu@ust.hk

Abstract

Many compounds in the polycyclic aromatic hydrocarbons (PAHs) family are of environmental concern due to their toxicity, carcinogenicity and mutagenicity, prompting the need of monitoring their long-term trends and research on their potential sources. Three air monitoring programs in Hong Kong have been recording concentrations of ambient PAHs since 1997. In this work, we review all the available measurements in these monitoring programs, with emphasis on the temporal trends of BaP and the other 16 PAHs in the past 19 years. Correlation analysis shows that those PAHs sharing similar structures exhibit highly correlated relationships and virtually identical long-term trends. Almost every measured PAH's concentration in Hong Kong exhibits a decline trend since 1998, with a statistically significant Sen's slope. For instance, BaP has been reduced by 79% at Tsuen Wan site and 77% at Central West station from 1998 to 2016, with a Sen's slope of -0.016 and -0.011 ng/m^3/year, respectively. The correlation of BaP with some major species in respirable suspending particulate (RSP) and three diagnostic ratios of PAHs are employed to explore the source origins of PAHs in Hong Kong. The above analysis reveals that PAHs mainly come from a combination of vehicular emission and biomass/coal combustion. The down-going trends of PAHs are consistent with the abating particulate matter emissions from vehicular exhaust and biomass/coal combustion, as indicated by their respective source tracers.

Acknowledgements

We thank Hong Kong Environmental Protection Department for making the data sets available. This work is partially supported by Environment and Conservation Fund (ECF 99/2017).

Polyphenyls and Phenyl-Polycyclic Aromatic Hydrocarbons in Atmospheric Aerosol Samples

Zhong REN, Yingge MA, Jian Zhen YU*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong;
*Corresponding author E-mail: jian.yu@ust.hk

Abstract

Polycyclic aromatic hydrocarbons (PAHs) are a family of toxic yet highly persistent compounds widely distributed in the atmosphere. Ordinary measurements can only identify and quantify about 30 kinds of PAHs. However, in those measurements, many substituted PAHs are ignored, which would underestimate the amount and health effects of PAHs. Polyphenyls and Phenyl-PAHs are generally overlooked in the previous studies. In this research, Comprehensive two-dimensional gas chromatography coupled with a time-of-flight mass spectrometer (GC×GC-TOF) was used to analyze aerosol samples collected at multiple locations in Shanghai. As a result, 20 polyphenyls or phenyl-PAHs were found in 17 samples. These compounds contain 3 or 4 benzene rings, such as phenyl-naphthalene, terphenyls, phenyl-anthracene, and quterphenyls. Semi-quantitative analysis of polyphenyls and phenyl-PAHs were carried out by comparing the mass spectra responses with parents PAHs. In future work, more efforts would be stressed on more accurate quantitative analysis.

Source Apportionment of $PM_{2.5}$: Impact of measurement time resolution

Shuhui Zhu, Jian Zhen Yu*
Division of Environment and Sustainability, Hong Kong University of Science and Technology, Hong Kong, China;
*Corresponding author: jian.yu@ust.hk

Abstract

Measurements of $PM_{2.5}$ chemical composition measurements, coupled with positive matrix factorization (PMF) model, are commonly used to derive at contributions of sources to $PM_{2.5}$ pollution. To understand time-resolution influence on source apportionment of $PM_{2.5}$, we conducted PMF analysis using chemical speciation datasets with time resolution varying from hourly to daily. Hourly concentration datasets of $PM_{2.5}$ and its major constituents, including 6 inorganic ions, 14 elements, organic carbon, and elemental carbon, were measured from December 2017 to April 2018 at an urban site in Dezhou, Shandong Province in China. Thirty-three additional datasets were generated by averaging the 1-hour (PMF_{1h}) resolution data into 2-hour (PMF_{2h}), 4-hour (PMF_{4h}), 6-hour (PMF_{6h}), 8-hour (PMF_{8h}), 12-hour (PMF_{12h}) and 24-hour (PMF_{daily}) time intervals. A similar set of eight source factors were resolved with all the 34 datasets by PMF analysis, including secondary nitrate and sulfate, vehicular and biomass burning emissions, secondary organic carbon, power plant combustion, industry emissions, residual oil combustion, sea salt and dust. Little difference was observed in PMF_{2h} and PMF_{4h} solutions in terms of source profiles and source contributions, however, noticeable variations were observed starting from PMF_{6h} solutions, especially for secondary sources (e.g., secondary nitrate and sulfate, secondary organic carbon). The modeled contribution to $PM_{2.5}$ by the secondary nitrate and sulfate source decreased from 58% in PMF_{1h} solution to 36% in PMF_{daily} solution, while the contribution from secondary organic carbon source increased from 1.4% to 11%. The results indicate that obvious deterioration exist in source information resolved by PMF when the time resolution shifts from hourly to daily. In another words, using high-time resolution data improves the precision of identifying and quantifying $PM_{2.5}$ sources when compared with the traditional daily filter-based data.

Acknowledgements

This research was supported by Prime Fund Program of China (DQGG0304, DQGG0107). The authors thank State Environmental Protection Key Laboratory of the Formation and Prevention of Urban Air Pollution Complex (Shanghai Academy of Environmental Sciences), Dezhou Municipal Bureau of Ecology and Environment, Dezhou Environmental Protection Monitoring Center for the assistance in online instruments maintenance.

Quantification of DNA Damage Product in Toxicant-Exposed Cells by Liquid Chromatography Tandem Mass Spectrometry with Isotope-Dilution Method

Pui Yin CHUNG[1] and Wan CHAN[*, 1, 2]

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

Email: chanwan@ust.hk

Abstract

Reactive oxygen species (ROS) such as peroxide, superoxide, and hydroxyl radicals are generated intracellularly in cells or when exposed to exogenous toxicants. Results from previous studies have demonstrated that prolonged exposure to excess ROS lead to oxidative stress and induce DNA damages, some of which eventually leading to various human diseases including cancers[1]. One of the major G oxidation products, 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) was quantitated in the genomic DNA and in the extracellular fluid of toxicants exposed cells, using LC-MS/MS method of high sensitivity and selectivity. It may serve as biological dosimeters of exposure to toxicants and for risk assessment, as well as help study the poorly understood chemical toxicology of human exposure to airborne particulate matters, e.g. PM2.5.

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Quantitation DNA Adducts of Aristolochic Acid I in Internal Organs of Rat by LC−MS/MS with Stable Isotope Dilution Method

Liu Yushuo[2] and Wan Chan[1, 2]

[1] Department of Chemistry, [2] Division of Environment & Sustainability, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong.
Email: chanwan@ust.hk

Abstract

Aristolochic acids (AAs) occured naturally in *Aristolochia* herbs are highly carcinogenic, mutagenic, and nephrotoxic phytochemicals. The major ingredient of AA is aristolochic acid I which have shown to bind covalently to DNA. DNA adduct formation is regarded as one of the mechanism of chemical carcinogenesis so the DNA-AAI adduct could be an indicator for tumor or cancer progression detection. We developed in this study a highly sensitive and selective ultra-high performance liquid chromatography-coupled tandem mass spectrometric method to quantiate the DNA-AAI adduct in target (kidney cortex, medulla, liver and stomach) and nontarget organs (small intestine, large intestine, lung, heart and spleen) of AAI-dosed rats. Result showed significantly higher concentration of dA-AAI adduct in target organs than that in the nontarget organs. The study also revealed for the first time that small and large intestine produced the highest concentration of DNA-adduct. These findings suggest that AAI would first attack alimentary system in which stomach is the major target organs while other organs did not present any injury induced by DNA adduct formation. It is also hoping that the mechanism of DNA-AAI adduct formation could be revealed after the analysis and comparison of the signal intensity in different organs.

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Manganese oxides for pseudocapacitive applications under large current

Authors: Alice W.M. Chan[1], Zhuofeng Hu[2,*], Jimmy C. Yu[3,*]

[1] School of Life Science, The Chinese University of Hong Kong; alicecwm@link.cuhk.edu.hk

[2] School of Environmental Science and Engineering, Sun Yat-Sen University; st04hzhf@gmail.com

[3] Department of Chemistry, The Chinese University of Hong Kong; jimyu@cuhk.edu.hk

Abstract

Supercapacitors are attractive due to their high power density. It could be used as complementary power supplies of batteries and power boosting devices for vehicle acceleration. Supercapacitors made of abundant and low-cost materials like manganese oxides have been widely investigated. While capacitance is usually reported in 1 A/g in literatures, applications in larger current are favorable because it results in shorter discharge time (i.e. faster energy supply). However, capacitance is relatively low under large current because the electrolyte is not fast enough to adsorb onto the supercapacitor material. For example, Mn_3O_4/rGO nanosheet is of 223.1 F/g at 5 A/g and 62.5 F/g at 20 A/g while graphene/Mn_3O_4 nanoparticles is of 181.8 F/g at 10 A/g. [1,2]

In this research, Mn_3O_4 particles grown on nickel foam is of 325 F/g at 55A/g, the capacitance is retained at 91% after 1000 cycles. This high performance under large current could be due to fast electron transfer attributed by the high conductivity between the current collector and the active material and the large surface area of the material. Characterizations including XPS and SEM are done before and after GCD stabilization and capacitive measurements.

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Cerium modulated structure disorder in Co_3O_4 nanosheets for electrocatalytic oxygen evolution reaction

Lejing Li, Jimmy C. Yu*
Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

The design and synthesis of high-performance OER (oxygen evolution reaction) electrocatalysts are critical factors for electrochemical energy storage and conversion processes, including regenerative fuel cells, metal-air batteries and water splitting.[1,2] Here, we report the remarkable enhancement for OER activity of electrodeposited Co_3O_4 in alkaline media after constructing composite (Co_3O_4/CeO_2) or introducing cerium into Co_3O_4 ($Co_{3-x}Ce_xO_4$). In particular, the nickel foam supported $Co_{3-x}Ce_xO_4$ electrode (NF-$Co_{3-x}Ce_xO_4$) only requires an overpotential of 220 mV to achieve a current density of 10 mA cm^{-2}, which is 80 mV lower compared with that of Co_3O_4. On the basis of transmission electron microscope (TEM) and selected area electron diffraction (SAED) techniques, we uncover, investigate, and discuss that the introduction of cerium specie result in higher disorder degree of crystallinity, this structure distortion is pivotal to upgrade the electrocatalytic property of Co_3O_4 with more defect and active sites.

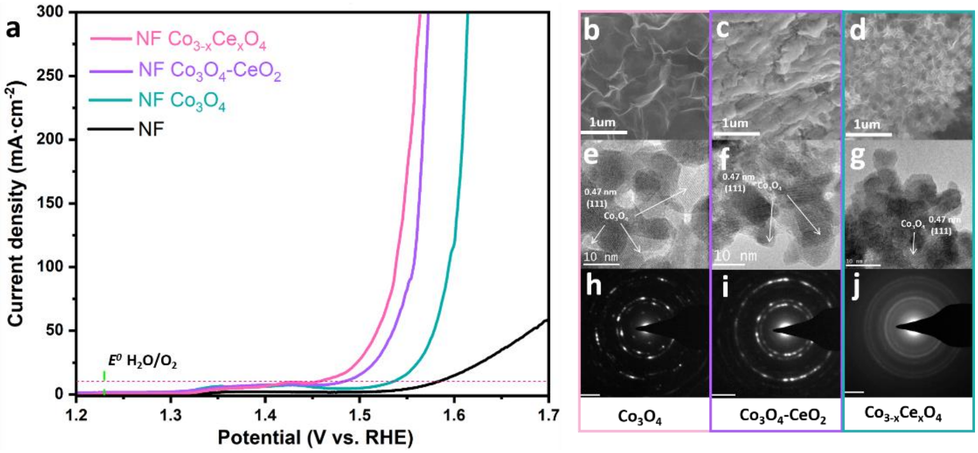

Figure 1 (a) Polarization curves of the as-prepared Co_3O_4, Co_3O_4/CeO_2 and $Co_{3-x}Ce_xO_4$. (b-d) SEM images, (e-f) TEM images and (h-j) SAED of Co_3O_4, Co_3O_4/CeO_2 and $Co_{3-x}Ce_xO_4$, respectively.

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Fe enhanced visible light driven nitrogen fixation on BiOBr nanosheets

Yang Liu, Zhuofeng Hu* and Jimmy Yu*
Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong.
E-mail: jimyu@cuhk.edu.hk

Abstract

Nitrogen reduction is central to the global nitrogen cycle. Photocatalytic nitrogen fixation challenged by many difficulties such as the bind with N_2 on the catalyst surface and the electron transfer to the adsorbed N_2.[1] Inspired by the Fe-protein in the nitrogenase, the Fe doped BiOBr nanosheets (Fe-BiOBr) was demonstrated to convert N_2 to NH_3 in water without any sacrificial reagents driven by visible light. The Fe dopants can promote the formation of oxygen vacancies (OV). The OV-connected Fe serves as the active sites to capture and reduce N_2.[2-3] The N_2 fixation rate of Fe-BiOBr is remarkably enhanced by eight times, compared with BiOBr without dopants. This work provides an insight into the mechanism of the N_2 photo-fixation and the strategies for the catalyst design.

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A long-lived phosphorescence iridium(III) complex as a switch on-off-on probe for live zebrafish monitoring of endogenous sulfide generation

Chung-Nga Ko, Chung-Hang Leung and Dik-Lung Ma

SCT1209B, Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong, China.

Abstract

In this work, we report a novel iridium(III)-based luminescent switch on-off-on probe, for the *in vitro* and *in vivo* detection of sulfide ion. The mechanism of this platform is based on the effective charge transfer quenching of the iridium(III) complex **1** by Fe^{3+}, followed by the restoration of luminescence upon the addition of Na_2S. The probe, hereinafter referred to as **1–Fe**$^{3+}$, exhibited a linear range of detection for Na_2S from 0.01 to 1.5 mM, with a detection limit of 2.9 μM at signal-to-noise ratio (S/N) of 3. We also demonstrate the utility of **1–Fe**$^{3+}$ for cell-based imaging as well as for the detection of enzymatic sulfide generation in living zebrafish

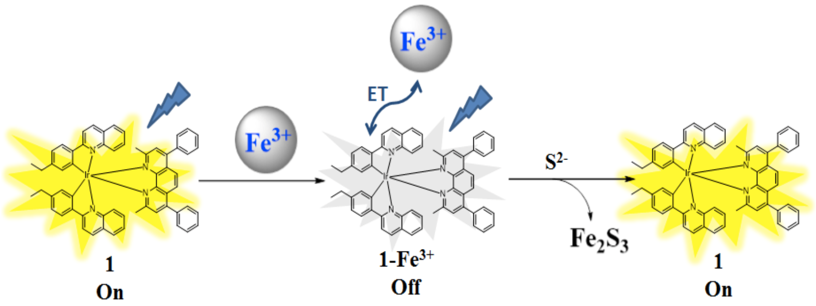

Figure 1: Mechanism for the on-off-on probe **1–Fe**$^{3+}$

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Bimetallic Group 4 Post-Metallocenes Bearing an Aromatic Core Structure: Synthesis, Spectroscopic Characterization and Catalysts for Olefin Copolymerization

Qian Liu, Man-Kit Tse and Michael C. W. Chan*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon.
Email: mcwchan@cityu.edu.hk

The development of chelating [O,N,C(sp^3)] ligands for supporting group 4 post-metallocene catalysts has been reported, and excellent olefin polymerization activities have been achieved.[1,2] In this work, the synthesis of two series of homobimetallic M(IV) (M = Ti, Zr, Hf) complexes bearing different aromatic bridges are described. The new derivatives have been fully characterized by ^1H and ^{13}C spectroscopy, together with [^1H, ^1H]-COSY, [^{13}C, ^1H]-HSQC and DEPT-135 NMR experiments. Studies have been undertaken to assess their olefin polymerization reactivity in conjunction with various cocatalysts. DFT calculations have been performed to investigate the nature of the active species and rationalize the observed catalytic behavior. The Ti_2 catalysts display superior olefin homo- and co-polymerization activities in conjunction with $[Ph_3C][B(C_6F_5)_4]/^iBu_3Al$, and the degrees of comonomer incorporation have been determined by high-temperature ^{13}C NMR spectroscopy.

This work was supported by the Research Grants Council of the Hong Kong SAR, China (CityU 11300414).

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Synthesis, Characterization and Study of Luminescent Ir(III) Complexes with Bidentate Pyridyldiaminocarbene Ligand

Jingqi Han, Kin-Man Tang, Shun-Cheung Cheng, Chi-On Ng, Shek-Man Yiu, Man-Kit Tse, Vellaisamy A. L. Roy, Chi-Chiu Ko*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong (China); vinccko@cityu.edu.hk

Abstract

Transition metal complexes with N-heterocyclic carbene (NHC) ligands have been rapidly developed over the past two decades. This is due to the unique electronic properties and stability associated with the NHC ligands. We have recently shown that the electronic properties of acyclic carbene ligands are highly sensitive to the change of the micro-environment.[1,2] On the basis of these properties, a new series of bis-cyclometalated Ir(III) complexes with bidentate acyclic diaminocarbene ligands, which display tunable mechanoluminescent behavior, has been designed and successfully synthesized. The structures of some of the targeted cyclometallated Ir(III) carbene complexes have been determined by X-ray crystallography. The electronic absorption, emission properties and their potential chemosensory applications of these cyclometallated Ir(III) complexes have been studied.

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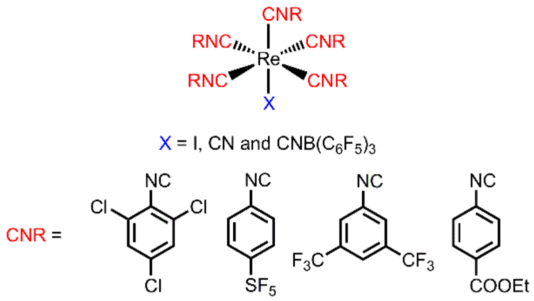
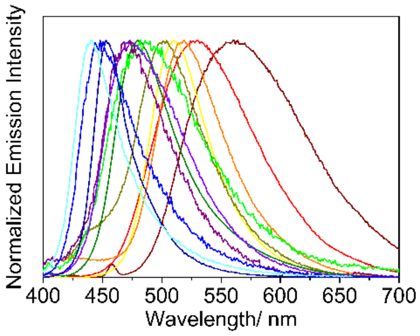
Design of Luminescent Isocyano Rhenium(I) Complexes: Photophysics and Effects of the Ancillary Ligands[1]

Kin-Cheung Chan, Ka-Ming Tong, Shun-Cheung Cheng, Chi-On Ng, Shek-Man Yiu and Chi-Chiu Ko*
Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, China; Email: vinccko@cityu.edu.hk

Abstract

Transitional metal complexes with metal-to-ligand charge transfer excited state have been extensively investigated due to their rich photophysical and photochemical properties. These complexes have been utilized in various areas such as photocatalysts, photosensitizers, luminescent probes and OLEDs. Previously, we have developed readily tunable luminescent isocyano Re(I) diimine complexes.[1] Although these complexes exhibit both MLCT [dπ(Re) → π*(diimine)] and MLCT [dπ(Re) → π*(CNR)] transitions, their emission is originated from the lower-lying ^{3}MLCT [dπ(Re) → π*(diimine)] excited state. To extent our study on complexes with emissive ^{3}MLCT [dπ(Re) → π*(CNR)] excited state, we have designed a series of pentaisocyano Re(I) complexes with different ancillary ligands. In contrast to previously reported penta- and hexaisocyano Re(I) complexes, which are non-emissive at room temperature, the newly designed isocyano Re(I) complexes exhibit phosphorescence in solution state at room temperature and 77 K glassy medium. Moreover, their emission properties could also be modified by changing the isocyanide and ancillary ligands.





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Electronic Communication in Luminescent Dicyanorhenate-Bridged Homotrinuclear Rhenium(I) Complexes

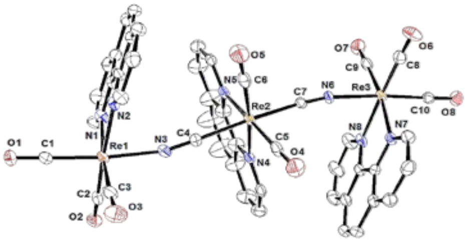
Yelan Xiao,[a] Apple Wai-Yi Cheung,[a] Sze-Wing Lai,[a] Shun-Cheung Cheng,[a] Shek-Man Yiu,[a] Chi-Fai Leung,[b] Chi-Chiu Ko [a,*]

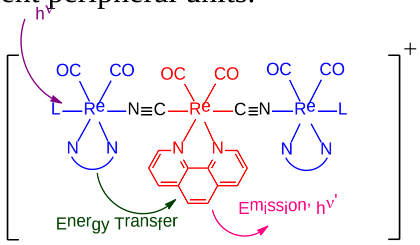
[a]Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, China; Email: vinccko@cityu.edu.hk

[b]Department of Science and Environmental Studies, The Education University of Hong Kong, 10 Lo Ping Road, Tai Po, N. T. Hong Kong, China.

Abstract

A series of cyano-bridged homotrinuclear Re(I) complexes with general formula of {[Re]′[Re][Re]′}$^+$ {[Re]′ = -[Re^I(CO)$_2$(LL)(X)]; [Re] = -[(NC)Re^I(CO)$_2$(phen)(CN)]-; LL = diimine, diphosphine or two carbonyl ligands, X = triphenylphosphine or carbonyl ligand} were synthesized. The structures of most of the trinuclear complexes have been characterized by X-ray crystallography, which show different relative orientations of the peripheral to the central Re(I) units. The photophysical properties of these trinuclear Re(I) complexes have been examined. Except the trinuclear Re(I) complex with Br$_2$phen ligand, all other triads display orange to red photoluminescence derived from the ^{3}MLCT [dπ(Re)→π*(phen)] origin of the central Re(I) unit, suggestive of efficient energy transfer between the peripheral chromophores and the central unit. In addition to the efficient energy transfer processes between the Re(I) chromophores in these trinuclear complexes, the ability of the [NC–Re–CN] bridging ligands for electronic coupling between the rhenium metal centers is evidenced by *ca.* 0.2-0.3 V separation of the two rhenium metal-based oxidation potentials of the chemically equivalent peripheral units.





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Reactivity of a luminescent Osmium nitrido complex

Xin Gu, Jing Xiang, Tai-Chu Lau*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, China. bhtclau@cityu.edu.hk

Abstract

Osmium(VI) nitrido complexes containing polypyridyl ligands are known to exhibit novel electrophilic reactivity towards various nucleophiles via N-C, N-N, N-P, and N-E (E=O, S, Se) bond formation reactions. We have also demonstrated that the highly electrophilic (salen)ruthenium(VI) nitrido complex $[Ru^{VI}(N)(L)(CH_3OH)]^+$ (**RuN**) is capable of reacting with various organic substrates, including alkenes and alkanes at ambient conditions. However, the oxidation of various alcohols by metal nitrido complexes has not been reported. Recently, we have reported a novel luminescent $[Os^{VI}(N)(\mathbf{NO_2\text{-}L})(CN)_3]^-$ (**NO_2-OsN**), which is highly oxidizing/electrophilic upon visible-light irradiation. Herein, the oxidation of various alcohols by **NO_2-OsN** under visible light is presented.

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Visible-light-driven catalytic reduction of CO_2 with a dicobalt complex. Cooperative metals for switching selectivity from CO to $HCOO^-$ upon changing the acid co-substrate

Zhenguo Guo,[‡§] Gui Chen,*[‡†] Claudio Cometto, [‡Ŧ] Hongyan Zhao,[§] Lingjing Chen,[†] Wai-Lun Man,[II] Shek-Man Yiu, [§] Kai-Chung Lau,*[§] Marc Robert*[Ŧ] and Tai-Chu Lau*[§]

[†] School of Environment and Civil Engineering, Dongguan University of Technology, Dongguan, Guangdong, P. R. China. [§] Department of Chemistry, City University of Hong Kong. Tat Chee Avenue, Kowloon Tong, Hong Kong, P. R. China. [II] Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong, P. R. China. [Ŧ] Univ Paris Diderot, Sorbonne Paris Cité, Laboratoire d'Electrochimie Moléculaire, France. Email :bhtclau@cityu.edu.hk

Abstract

Discovering molecular catalysts with controlled selectivity for visible-light-driven CO_2 reduction to fuels is desired. In the design of catalysts employing earth abundant metals, progresses have been made for CO production while generating formate has been more rarely observed. Here we report that a binuclear Co complex bearing a bi-quaterpyridine ligand can reduce selectively CO_2 to $HCOO^-$ or CO upon visible light irradiation. During the catalytic process, the two Co atoms act synergistically for reducing the gas and the reactivity can be steered towards the desired product by simply changing the acid co-substrate. Selective formate production (91-97%) was obtained with turnover number up to 821 in basic acetonitrile solution, using a Ru complex or cheap graphitic carbon nitride as sensitizer. In the presence of a weak acid (phenol), CO_2 reduction affords CO with high selectivity (96-99%) and a maximum turnover number of 829, using either a Ru complex or an organic phenoxazine as sensitizer.

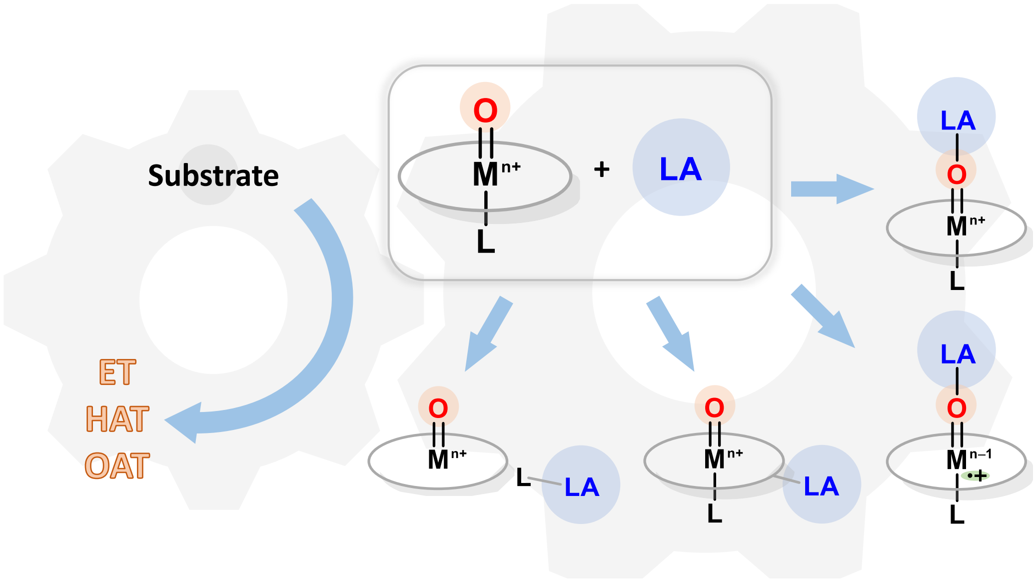
Activation of Metal Oxo and Nitrido Complexes by Lewis Acids

Yingying Liu and Tai-Chu Lau*

Department of Chemistry, City University of Hong Kong, Tat Che Avenue, Kowloon Tong, Hong Kong, China. Email: bhtclau@cityu.edu.hk

Abstract

Metal oxo species (M=O) play key roles as oxidants in chemical and biological systems. Although Brønsted acids have long been known to enhance the oxidizing power of metal oxo complexes, the use of Lewis acids (LAs), such as metal ions, to activate these complexes has received much less attention until recently. The report of the presence of a Mn_4CaO_5 cluster active site in the oxygen-evolving center (OEC) of photosystem II (PS II) in 2004 has stimulated intense interest in understanding the interaction of LAs with M=O. This work analyzes the various modes of activation of M=O by LAs and the pathways for the oxidation of various substrates by LA/M=O systems. The interaction of LAs with metal nitrides will also be involved, although it is much less studied than M=O.[1]



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Reactivity of one electron oxidized Mn(V) Imido Tetraamido Macrocyclic Ligand Complex

Huatian Shi, Shek-Man Yiu, Hung Kay Lee, Tai-Chu Lau*
Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon Tong, Hong Kong. Email: bhtclau@cityu.edu.hk

Abstract

High-valent metal-imido species have been invoked as key intermediates in synthetic oxidative transformation reactions.[1-2] Recently, iron(V) tosylimido tetraamido macrocyclic ligand (TAML) complex[3] and iron(V) tosylimido TAML radical complex[4] have shown their reactivity in N-group transfer and hydrogen atom abstraction reaction. In this poster presentation, we report the synthesis of a new Mn(V) imido TAML complex, its intermolecular N-group transfer to the phenyl ring of TAML and thioanisole and hydrogen atom abstraction with weak C-H substrates after one electron oxidation of Mn(V) imido TAML complex by $(p\text{-BrC}_6\text{H}_5)_3\text{N}^{\cdot+}\text{SbCl}_6$ (**Scheme 1**). Mechanistic studies as well as DFT calculations will be presented.

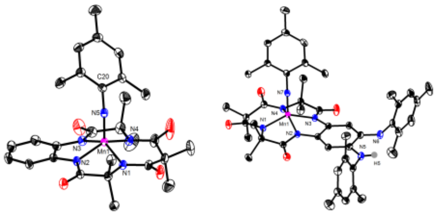
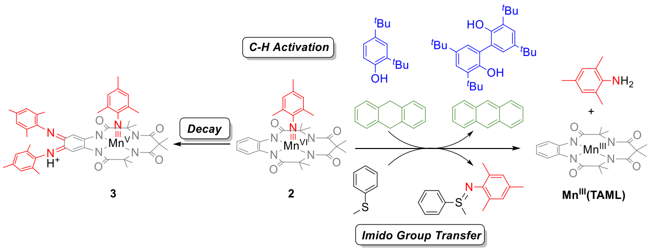


Figure 1 Crystal Structure of Mn(V) imido complexes.



Scheme 1 Reactivity of one electron oxidized Mn(V) imido TAML complex.

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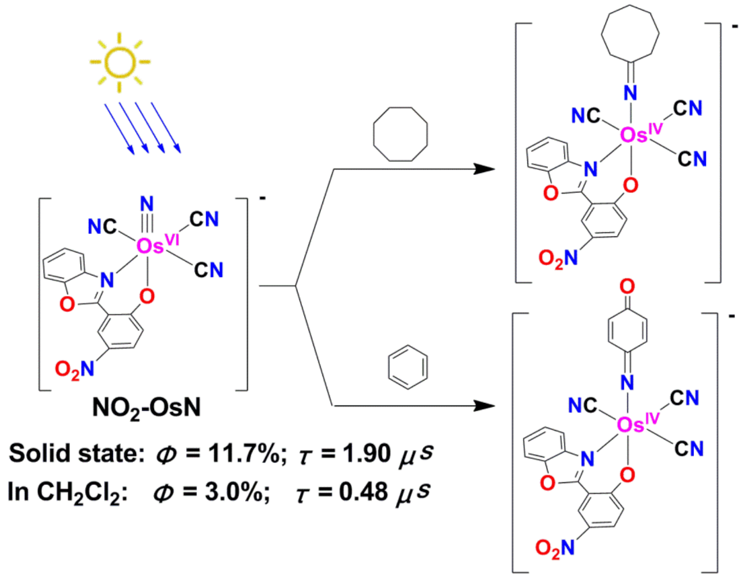
Photochemical nitrogenation of alkanes and arenes by a strongly luminescent osmium(VI) nitrido complex

Jing Xiang and Tai-Chu Lau*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon Tong, Hong Kong. Email: bhtclau@cityu.edu.hk

Abstract

The search for a highly active nitrido complex that can transfer its nitrogen atom to inert organic molecules remains a challenge to chemists. In this regard, the use of solar energy to generate a reactive nitrido species is an appealing strategy to solve this problem. Herein we report the design of a strongly luminescent osmium(VI) nitrido compound, [Os^{VI}(N)(**NO$_2$-L**)(CN)$_3$]$^-$ (**NO$_2$-OsN**). The emission quantum yield (Φ) and life time (τ) are 3.0 % and 0.48 μs, respectively in dichloromethane solution. Upon irradiation with visible light, this complex readily activates the aliphatic C-H bonds of various hydrocarbons, including alkanes. The excited state of **NO$_2$-OsN** can undergo ring-nitrogenation of arenes, including benzene. Photophysical and computational studies suggest that the excited state of **NO$_2$-OsN** arises from O^N ligand to Os≡N charge transfer transitions, as a result it possesses [Os=N$^{\bullet}$] nitridyl character and makes it highly electrophilic.



NO$_2$-OsN

Solid state: Φ = 11.7%; τ = 1.90 μs

In CH$_2$Cl$_2$: Φ = 3.0%; τ = 0.48 μs

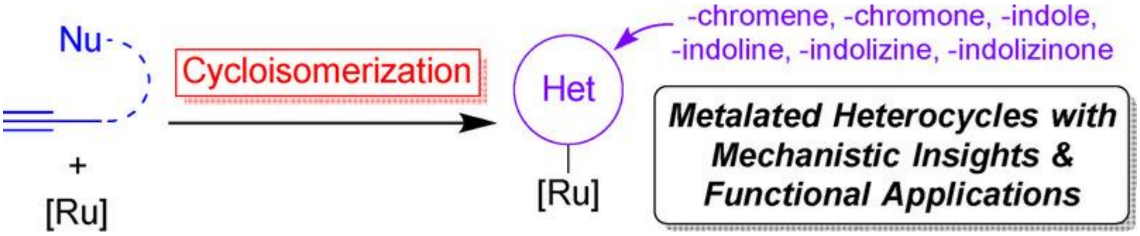
Ruthenium-Induced Alkyne Cycloisomerization: Construction of Metalated Heterocycles, Revelation of Unconventional Reaction Pathways, and Exploration of Functional Applications

Lai-Hon Chung and Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong; lhchung2-c@my.cityu.edu.hk

Abstract

While the fascinating chemistry demonstrated by metalated N-heterocyclic carbene (NHC) complexes highlights the significance of metalated heterocyclic chemistry, the development of other metalated heterocycles is falling behind, presumably because of the sparseness of general synthetic methodologies. In this work, the strategy to prepare metalated heterocyclic complexes by metal-induced cycloisomerization of heteroatom-functionalized alkynes is presented. The isolation of and calculations on novel ruthenium complexes bearing chromene, chromone, indole, indoline, indolizine, and indolizinone moieties prepared from reactions between alkynes and ruthenium complexes are discussed, with emphasis on the mechanistic insights into the ruthenium-induced alkyne transformations and applications in material design and drug discovery.



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Metalated Chromene and Chromone Complexes: pH Switchable Metal–Carbon Bonding Interaction, Photo-Triggerable Chromone Delivery Application, and Antioxidative Activity

Sze-Wing Ng, Lai-Hon Chung, Chi-Fung Yeung, Hoi-Shing Lo, Hau-Lam Shek, Tian-Shu Kang, Chung-Hang Leung, Dik-Lung Ma, and Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong; acywong@cityu.edu.hk

Abstract

The two families of Ru(II)–chromene and –chromone complexes isolated in this work represent the first examples of metalated chromene and chromone complexes synthesized through transition-metal mediated cyclization of phenol-tethered ynone. These unprecedented metalated heterocyclic compounds exhibit remarkable features, such as pH-switchable metal–carbon bonding interactions, photo-triggerable release of organic chromone upon visible-light irradiation, and superior antioxidative property to their organic analog (1,4-benzopyrone). These findings not only offer mechanistic insights into metal-induced activation of functionalized alkynes, but also add a new dimension to rational design of antioxidants and photo-responsive drug delivery systems.

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Ruthenium–Indolizinone Complexes as a New Class of Metalated Heterocyclic Compound: Insight into Unconventional Alkyne Activation Pathway, Revelation of Unexpected Electronic Properties and Exploration of Medicinal Application

Hau-Lam Shek, Lai-Hon Chung, Sze-Wing Ng, Chi-Fung Yeung, Sheung-Ying Tse, Hoi-Shing Lo, Siu-Chung Chan, Man-Kit Tse, Shek-Man Yiu, and Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong; acywong@cityu.edu.hk

Abstract

The two series of ruthenium–indolizinone complexes prepared by Ru-mediated cyclization of pyridine-tethered alkyne represent the first examples of metalated indolizinone complexes. Joint experimental-theoretical investigation suggests an unconventional *5-endo-dig* cyclization pathway as their formation mechanism. They also exhibit moderate cytotoxicity against several human cancer cell lines.

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Synthesis of Ruthenafuran and Osmafuran Prepared by Activation of Ynone in Alcohol

Sheung-Ying Tse, Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong; acywong@cityu.edu.hk

Abstract

Ruthenafuran and osmafuran monocationic complexes have been prepared from reactions between phenyl-ynone HC≡C(CO)Ph and cis-[Ru/Os(dpam)Cl_2] in alcoholic solvents ROH (dpam = Bis(diphenylarsino)methane). The formation of metal–vinylidene intermediate, followed by nucleophilic attack by RO^-, and carbonyl group coordination to the metal center are believed to be the key steps in the formation of these metallafurans.

Multifunctional Nanoplatform for Synergetic Cancer Therapy

Chun Zhang, Li Zhang and Chun-Yuen Wong

Department of Chemistry, City University of Hong Kong; acywong@cityu.edu.hk

Abstract

Photodynamic therapy (PDT) is a promising cancer treatment strategy with little invasiveness and few side effects, with the working principle of generating singlet oxygen from oxygen by light to kill cancer cells. However, cancer hypoxia limits the efficiency of photodynamic therapy. Herein, we report the use of MnO_2 nanoparticles to convert hydrogen peroxide (H_2O_2) in cancer tissue into oxygen, leading to enhanced PDT efficiency. Considering the insufficient therapeutic effects of single therapy modality, photothermal material is also introduced into the nanocarrier to achieve a synergetic effect.

Multifunctional Theranostic Nanoplatform for Cancer-Specific Imaging and Enhanced Therapy

Li Zhang, Chun-Yuen Wong*

Department of Chemistry, City University of Hong Kong; acywong@cityu.edu.hk

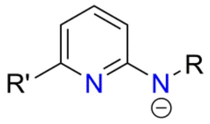
Abstract

Though near-infrared (NIR) light-induced photodynamic therapy (PDT) has attracted much interest in recent years, nonspecific distribution of photosensitizers and intrinsic tumor hypoxic microenvironment still limit the therapeutic efficiency. In this work, we develop a facile and mild method to fabricate a multifunctional cancer specific theranostic nanoplatform which could modulate hypoxia in tumor site to achieve improved PDT effect. Moreover, such theranostic nanoplatform also combines photothermal agent to realize photothermal therapy (PTT), leading to multi-mode imaging guided synergetic PTT/enhanced PDT.

Coordination Chemistry of 2-Pyridyl Amido Ligands with Late 3*d* Metals

Eunice Lok Yan Mau, Hung Kay Lee*
Department of Chemistry, The Chinese University of Hong Kong,
Shatin, New Territories, Hong Kong
hklee@cuhk.edu.hk

2-Pyridyl amido anions of the general formula [N(R)(2-pyridyl)]$^-$ (see figure below) belong to an interesting class of ligands which can bind metal ions in a monodentate, *N*,*N'*-chelating or *N*,*N'*-bridging manner.[1] Earlier, we have reported on the chemistry of a cobalt(II) complex supported by the sterically bulky [N(Si^{t}BuMe$_2$)(2-C$_5$H$_3$N-6-Me)]$^-$ ligand.[2] A few lanthanide(III) amido complexes derived from this ligand have also been synthesised.[3] Recently, we have extended our work to the sterically bulkier [N(C$_6$H$_3$^{i}Pr$_2$–2,6)(2–C$_5$H$_3$N–6–Me)]$^-$ ligand and prepared the corresponding lanthanide(II) complexes.[4] In this poster, we will report on the results of our recent work on the coordination chemistry of *N*-silylated and *N*-arylated 2-pyridyl amido ligands with late 3*d* metals.



R, R' = H, alkyl, aryl or silyl

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Acknowledgements

This work was supported by the Hong Kong Research Grants Council (Project No. CUHK 401407) and The Chinese University of Hong Kong (Direct Grant Project No. 4053324).

Development of Advanced Photodynamic Molecular Beacons with Multiple Controls for Targeted Photodynamic Therapy

Ligang Yu,[1] Roy C. H. Wong,[2] Dennis, K. P. Ng,[2] and Pui-Chi Lo*,[1]

[1] Department of Biomedical Sciences, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, China
[2] Department of Chemistry, The Chinese University of Hong Kong, Shatin, N. T., Hong Kong, China

E-mail address of the corresponding author: gigi.lo@cityu.edu.hk

Abstract

Photodynamic therapy (PDT) has been used in clinic for the treatment of a range of cancers, such as cutaneous, endobronchial, esophageal, and bladder cancers.[1] The therapeutic outcome depends on several interdependent factors, among which the efficacy of photosensitizers is of great importance. While a significant progress has been made over the last two decades, there is much room for further improvement, particularly on the tumor specificity and controlled photoactivity of the photosensitizers.[2] In this presentation, we report a glutathione (GSH) and cathepsin B dual activatable photosensitizer for targeted PDT. The dual activatable photosensitizer consists of two 2,4-dinitrobenzenesulfonyl (DNBS)-substituted phthalocyanine units with a cathepsin B peptide substrate. The photosensitizing properties of this system are significantly inhibited by self-quenching and photoinduced electron transfer to the DNBS groups. After internalization into cancer cells, the peptide sequence is cleaved selectively by the upregulated cathepsin B, separating the two photosensitizing units, while the DNBS moieties are removed by the intracellular GSH. The synthesis, photophysical properties, and in vitro biological activities of this system will be presented.

This work was supported by the Research Grants Council of the Hong Kong Special Administrative Region (Project No. 11303517)

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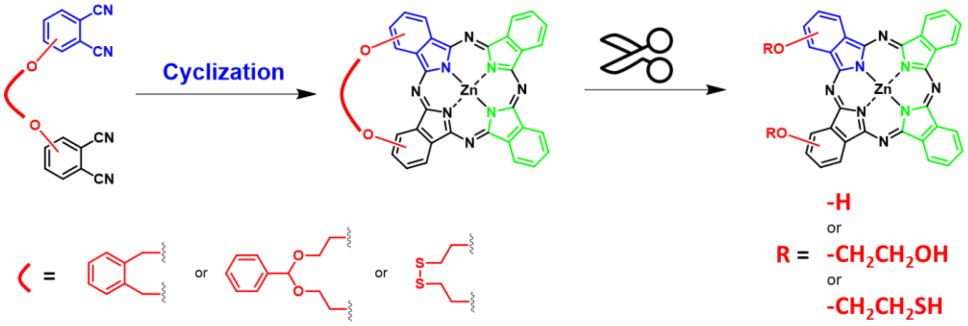
Synthesis of Low-symmetry Phthalocyanines with Cleavable Linkers

Yoonbin Kim and Dennis K. P. Ng*
Department of Chemistry, The Chinese University of Hong Kong,
Shatin, N.T., Hong Kong, China
Email: dkpn@cuhk.edu.hk

Abstract

Low-symmetry phthalocyanines are of particular interest due to their tunable optoelectronic, photophysical, catalytic, and self-assembly properties aroused by the nature and position of the substituents.[1] However, there exist intrinsic difficulties in the preparation of this class of phthalocyanines. For example, for the most common method that employs random cyclization of two or more phthalonitrile precursors, it inevitably results in the formation of a mixture of products, including constitutional isomers that cannot be separated readily.[2] Recently, our group has reported the first ABCD-type phthalocyanine via intramolecular cyclization of the corresponding pre-linked tetrakisphthalonitrile.[3] Although this pre-linked method allows ease control of phthalocyanine synthesis, one of the drawbacks is that the pre-linked positions cannot be further utilized, which constrains the potential applications. We report herein an extension of this study by using cleavable linkers to prepare a series of isomerically pure phthalocyanines with various symmetries (D_{2h}, C_{2h}, C_{2v}, and C_s) in a controlled manner, and the resulting deprotected analogues with free functional groups.



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Photoalkenylation of Iodocarboranes with Unactivated alkenes: Facile Synthesis of Alkenylated-*o*-Carboranes

Hangcheng Ni and Zuowei Xie*
Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong (China); E-mail address: zxie@cuhk.edu.hk

Icosahedral carboranes are boron-carbon molecular clusters which have received much attention in medicine as boron neutron capture\therapy agents,[1] in supramolecular design/nanomaterials as building blocks,[2] and in coordination/organometallic chemistry as ligands.[3] In this connection, a wide variety of methodologies have been developed for the synthesis of functionalized carboranes. Previously, we reported an efficient strategy for the synthesis of aryl-*o*-carboranes and *o*-carborane-fused cyclics through photo-induced C_{cage}-C_{sp2} coupling reactions.[4] Mechanistic study revealed that the reaction proceeded via the radical process, and carbon-cantered carboranyl radical was involved in this reaction. Subsequently, we developed the reaction of iodocarboranes with alkenes for the synthesis of alkenylated carboranes, which further confirmed the versatility of the iodocarboranes as the radical precursor for the functionalization of carboranes.

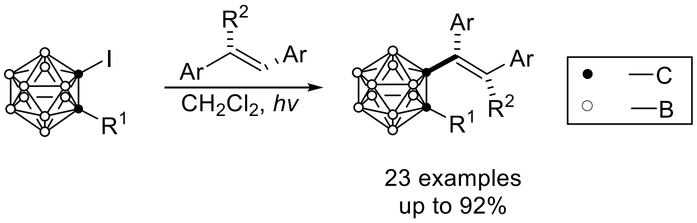

Figure 1. Alkenylation of *o*-carboranes

This work was supported by a grant from the Research Grants Council of HKSAR.

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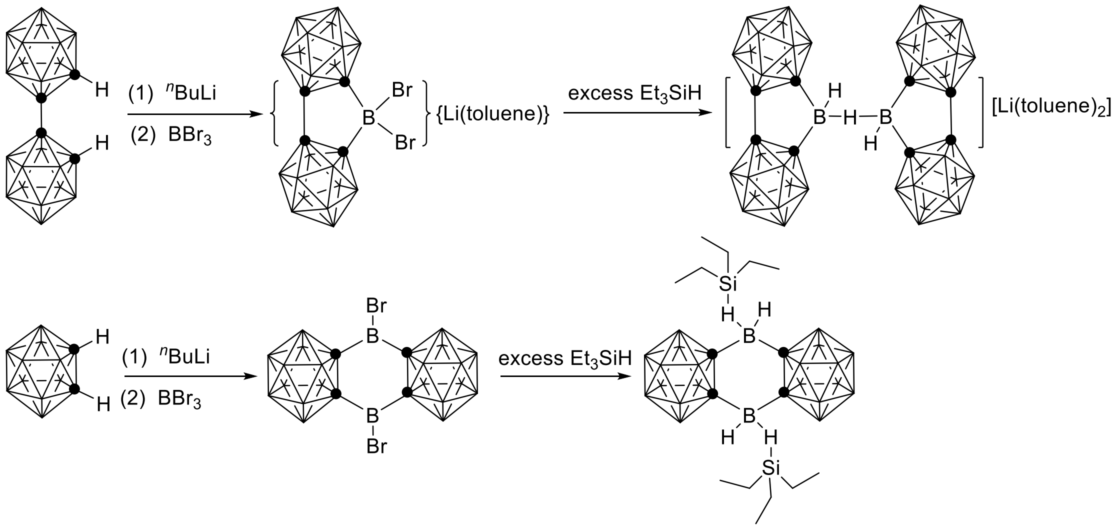
Synthesis and Structural Characterization of Carborane-Fused Boracycles

Hanqiang Wang and Zuowei Xie*

Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China
zxie@cuhk.edu.hk

Boron is one electron less than carbon. Generally, three-coordinate trigonal-planar boron center has a low-lying empty p orbital that can either form π bonding interaction, leading to conjugated systems, or accept the electron pair of Lewis base to afford four-coordinate tetrahedral boron. Such unique properties of organoboranes enable promising applications in optoelectronics and colorimetric chemosensors.[1] We have recently reported that a carborane-fused trigonal-planar azaborole can undergo a fully reversible photothermal isomerization.[2] In this regard, we plan to prepare a new class of carborane-fused boracycles and study their photothermal properties.



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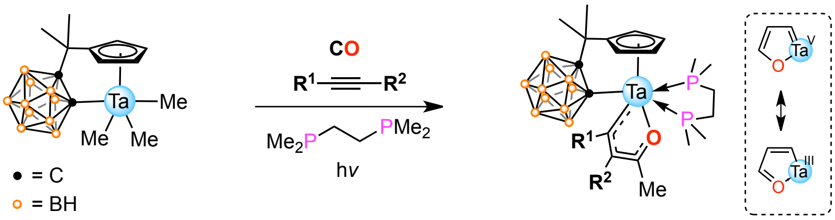
Tantallafuran Supported By A Linked Cyclopentadienyl-Carboranyl Ligand: Synthesis And Structure

Jingting Yang and Zuowei Xie*
Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China
zxie@cuhk.edu.hk

Abstract

Metallafurans are a class of furans in which one CH unit is replaced by isolobal metal fragments.[1] Mostly incorporating late transition metals[2,3] or group 6 transition metals,[4] however, planar group 4 or 5 metallafurans are rarely reported. And for the known examples, the metallacycles are considered to be four-electron π systems rather than six-electron, due to the exhaustion of metal electrons.[5,6]

Herein, we report the synthesis of a planar, six-π-electron α-tantallafuran by a one-pot process. Starting from a tantalum alkyl complex, both CO and alkyne serve as building blocks to construct a planar TaC_3O cycle. X-ray crystallographic analysis indicates a certain degree of bond length equalization over the metallacycle, as an evidence for electron delocalization. DFT study reveals the presence of π-interaction between the metal and the vinyl ketone fragment.



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High coordination number driven rhodamine derivative ring opening – Sensitive and selective lanthanide-ion sensing and biological studies

Fangfang Wei[1], Keith Man-chung Wong[2*], Ka-Leung Wong[1*] ,

[1] Department of Chemistry, Faculty of Science, HongKong Baptist University, Kowloon Tong, Kowloon, Hong Kong. P. R. China.

[2] Department of Chemistry, Faculty of Science, Souhtern University of Science and Technology, No. 1088, Xueyuan Boulevard, Nanshan District, Shenzhen, Guangdong, P. R. China.

Coresponding authors: klwong@hkbu.edu.hk, keithmcwong@sustech.edu.cn,

Abstract

Rhodamine derivatives have been found to selectively sense transition metal ions and related chemosensing behaviors have been extensively studied.[1-2] Drastic color change and emission enhancement were observed as a result of spiroring opening in the metal ion sensing process. In view of the fact that lanthanide ions are well known to have higher coordination number than transition metal ions, utilization of such preference in higher coordination number of lanthanide ions is employed to be a strategy for selective lanthaide ions sensing. Herein, we report the design, synthesis and characterization of two rhodamine derivative-containing compounds (**PYRBH** and **MR1**) which were found to exhibit selective lanthanide chemosensing with high sensitivity but not for various transition metal ions. The proposed sensing mechanisms of **PYRBH** and **MR1** are whown in Figure 1. Their binding constants and detection limits have also been determined.

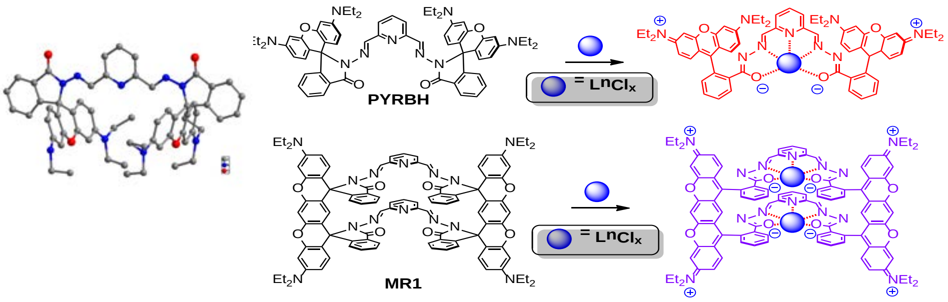

Figure 1

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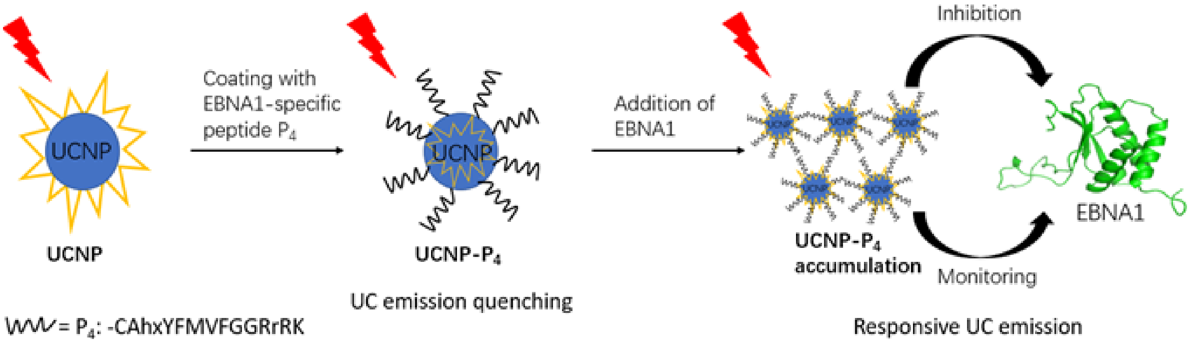
Responsive upconversion nanoprobe for monitoring and inhibition of EBV-associated cancers *via* targeting EBNA1

Shuai Zha, Ka-Leung Wong*
Department of Chemistry, Faculty of Science,
Hong Kong Baptist University, Kowloon Tong, Kowloon, Hong Kong
Email: 16483510@life.hkbu.edu.hk

Abstract

Non-responsive emission enhancement is the disadvantage of upconversion nanomaterials (UCNM) when compared with conventional organic based agents for molecular imaging. We herein show a new strategy by conjugating $NaGdF_4$: Yb^{3+}, Er^{3+}@$NaGdF_4$ (UCNP) with peptides to achieve responsive UC emission enhancement upon binding to a targeted protein – EBNA1. EBNA1 is a well-known viral latent protein for the EBV-associated cancer. Peptide-coating of the functionalized core-shell nanoparticle diminishes upconverted emission intensity drastically. However, the peptide-coated UCNP shows selective and responsive UC emission enhancement via aggregation with the targeted protein. This phenomenon paves a new way for UCNM in molecular imaging.



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Synthesis and Bio-Applications of Luminescent Transition-Metal Complexes

Wang Haitao[†], Zhang Hongyang[†], Zhang Qianling[‡], Zhu Xunjin[*†], Wong Waiyeung[*†§]
[†]Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong, P.R.China; *E-mail: xjzhu@hkbu.edu.hk.
[‡]Department of Chemistry, Shenzhen University, Shenzhen, P.R.China;
[§]Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, P. R. China.
*E-mail: wai-yeung.wong@polyu.edu.hk

Abstract

During the past decade, numerous metal complexes such as platinum[1] and ruthenium[2] complexes have been synthesized to probe bio-molecules and to light up the cells. Iridium complexes have been widely applied in the design and preparation of light-emitting diodes due to their excellent photochemical and photophysical properties[3]. However, Ir(III) complexes are not frequently reported on the DNA binding and other biological applications[4]. Recently, the iridium complexes have shown luminescence in extending oxygen sensing *in vitro* and *in vivo* thus triggered the promising field of bio-applications of irdium complexes[5].

A series of iridium and ruthenium complexes were synthesized and characterized. The mis-matched DNA-binding were acquired from spectra of absorption and photo-luminescence. The HOMO and LUMO energy levels and energy gaps of complexes are obtained. Stokes shifts in those complexes also matched well with the differences of those HOMO and LUMO energy gaps. The bio-application experiments were carried out in cell morphology, proliferation, cytotoxicity, cellular uptake and distribution. The typical characteristics of cell apoptosis were obviously observed by Fluorescence Inverse Microscope (FIM) and confocal laser scanning microscopy (CLSM) under the incubation of those complexes.

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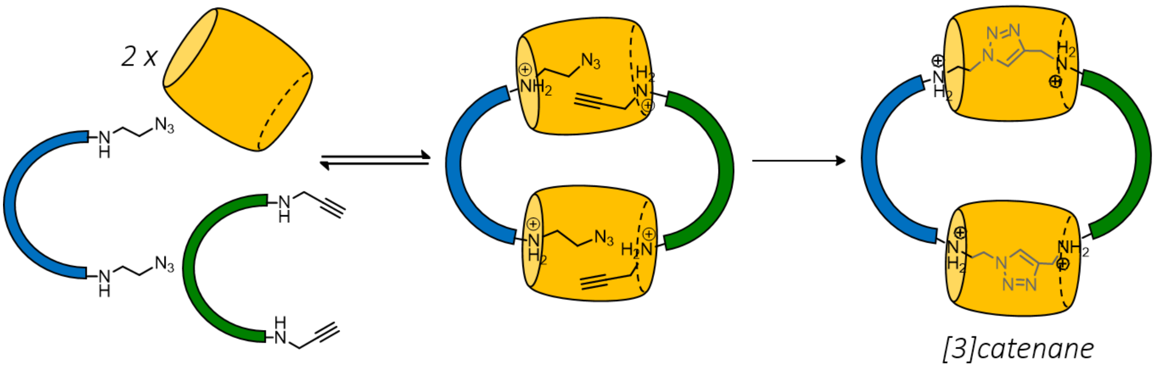
Efficient [3]catenane synthesis by cucurbit[6]uril-mediated azide–alkyne cycloaddition

Antony Wing Hung Ng and Ho Yu Au-Yeung*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong
Email: hoyuay@hku.hk

Abstract

We report here an efficient catenane synthesis by cucurbit[6]uril-mediated azide-alkyne cycloaddition (CBAAC) in which the mechanical bond and covalent bond formations are coupled in a single step.[1-3] Since CB[6] binding is a prerequisite for the covalent ring-closing, interlocking of CB[6] is guaranteed for the exclusive formation of [3]catenane with no other topological isomers. A series of [3]catenanes was obtained in good yield (>85%) with a straightforward purification procedure. The [3]catenanes are characterized by ^{1}H-NMR, ^{13}C-NMR, ESI-MS and MS^2 spectrometry.

*coupled formation of **mechanical** and **covalent** bonds*



[3]catenane

>85%, 10 examples

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N-Heterocyclic Carbene Iron(III) Porphyrin-Catalyzed Intramolecular C(sp^3)–H Amination of Alkyl Azides under Thermal and Microwave-assisted Conditions

Ka-Pan Shing,[a] Yungen Liu,[b] Bei Cao,[a] Xiao-Yong Chang,[a] Tingjie You[b] and Chi-Ming Che[a,b,*]

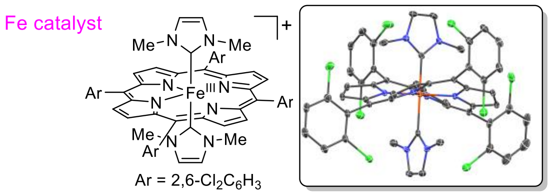
[a] *State Key Laboratory of Synthetic Chemistry and Department of Chemistry, The University of Hong Kong, Hong Kong, China.*

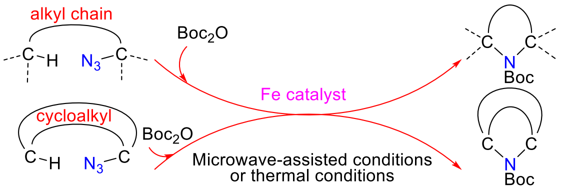
[b] *HKU Shenzhen Institute of Research and Innovation, Shenzhen, China.*

cmche@hku.hk

Abstract

Many bio-active alkaloids are structurally complicated and their syntheses rely heavily on the pre-functionalizations prior to functional group interconversions. Metal-catalyzed alkylnitrene C–H insertion is a powerful tool in streamlining their syntheses. Unlike sulfonyl- and aryl-nitrenes, metal-alkylnitrenoid and free singlet alkylnitrene could undergo facile 1,2-hydride shift to form imines.[1] A breakthrough was achieved using a novel *N*-heterocyclic carbene Fe(III) porphyrin as a catalyst for intramolecular C(sp^3)–H amination of alkyl azides, with broad substrate scope (e.g. primary, secondary and tertiary), up to 95% yield, high regioselectivity (mostly C_4–H selective) and applicability to natural product synthesis (tropane, nicotine, *cis*-octahydroindole and leelamine derivatives).[2] Moreover, we have established a precedent in metal-alkylnitrenoid C–H insertion under microwave-assisted condition which tolerates moisture and O_2 (≥80% yields for 7 out of 10 examples).





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Metal-Metal-to-Ligand Charge Transfer Excited State and Supramolecular Polymerization of Luminescent Pincer Pd(II)-Isocyanide Complexes

Qingyun Wan, Wai-Pong To, Chen Yang, and Chi-Ming Che*

The University of Hong Kong; cmche@hku.hk

Abstract:

Here are described pincer Pd^{II}-isocyanide complexes which display intermolecular interactions and emissive ^{3}MMLCT excited states in aggregation state(s) at room temperature. The intermolecular Pd^{II}-Pd^{II} and ligand-ligand interactions drive these complexes to undergo supramolecular polymerization in a living manner. Comprehensive spectroscopic studies reveal a pathway with a kinetic trap that can be modulated by changing the counter-anion and metal atom. The Pd^{II} supramolecular assemblies comprise two different aggregation forms with only one to be emissive. DFT/TDDFT calculations lend support to the MMLCT absorption and emission of these pincer Pd^{II}-isocyanide aggregates.

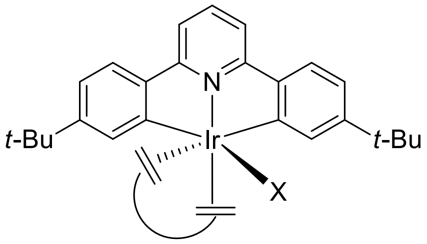
Iridium(III) Complexes with A Dicyclometalated C^N^C Ligand

Wai-Man Cheung, Man-Chun Chong, 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, Hong Kong. E-mail: chleung@ust.hk

Abstract

Metal complexes with dicyclometalated C^N^C ligands (H_2C^N^C = 2,6-diarylpyridine) are of interest owing to their interesting photophysical properties and organometallic reactivity.[1] While the chemistry of Au(III) and Pt(II) C^N^C complexes has been studied extensively, less attention has been paid to the Ir analogues. Herein we describe the synthesis, structure, and reactivity of some Ir complexes with a dicyclometalated C^N^C ligand.



X = Cl, ClHgCl

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Acknowledgement. This work was supported by the Hong Kong Research Grants Council (project no. 16307216).

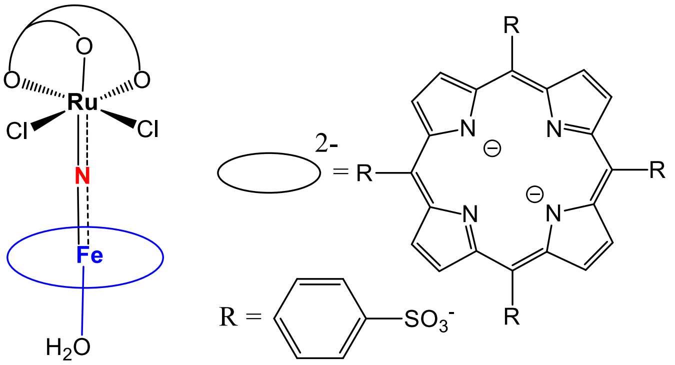
Heterometallic Iron(IV) Nitrido Complexes with Water-Soluble Porphyrins

Rain Ng, Wai-Man Cheung, 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, Hong Kong. E-mail: chleung@ust.hk

Abstract

High-valent iron compounds are of importance due to their involvement as reactive intermediates in enzymatic oxidation. Sorokin and coworkers reported that nitrido-bridged diiron phthalocyanines can catalyze C-H oxidation with peroxides, presumably via high-valent diiron-oxo intermediates.[1] This led us to synthesize heterometallic Fe-N-M complexes and study their oxidation chemistry.[2] Herein we report the synthesis, characterization and redox behavior of heterodinuclear Fe(IV)/Ru(IV) nitrido complexes with water-soluble porphyrins.



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Acknowledgement. This work was supported by the Hong Kong Research Grants Council (project no. 16301815).

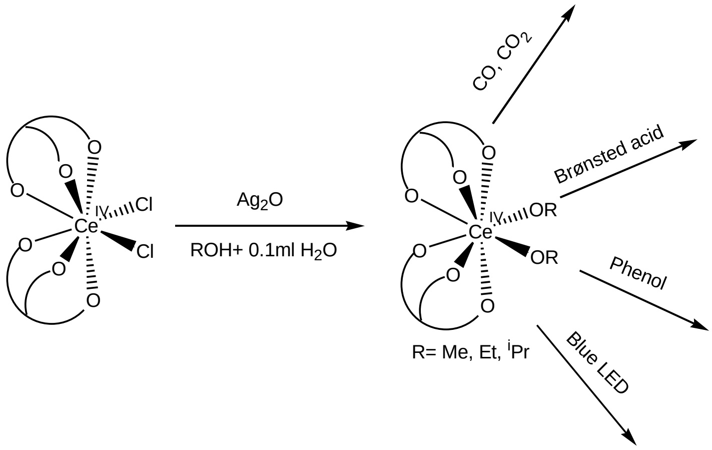
Synthesis, Structure and Reactivity of Cerium(IV) Alkoxide Complexes Supported by A Tripodal Oxygen Ligand

Kai-Hong Wong, 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, Hong Kong. E-mail: chleung@ust.hk

Abstract

Although Ce(IV) alkoxides have been known for a long time, the reactivity of oxidizing Ce(IV) complexes with alkoxide ligands has not been explored. Recently, Zuo and coworkers reported Ce salts can catalyze C-H functionalization of methane in alcohols, presumably via intermediacy of reactive alkoxyl radicals generated by homolysis of Ce(IV) alkoxide species.[1] This prompted us to synthesize Ce(IV) alkoxide complexes and investigate their redox chemistry. Herein, we report the synthesis, crystal structure, and reactivity of Ce(IV) alkoxide complexes supported by the Kläui tripodal ligand.



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Acknowledgement. This work was supported by the Hong Kong Research Grants Council (project no. 16300917)

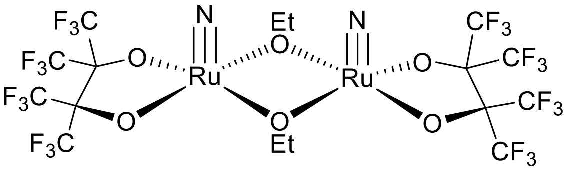
Synthesis and Structure of Ruthenium Perfluoropinacolate Complexes

Wai-Ho Wong, 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, Hong Kong. E-mail: chleung@ust.hk

Abstract

The bidentate O-donor ligand perfluoropinacolate (pin^F) is of interest because it is oxidatively robust and its metal complexes can be easily prepared in water owing to its high acidity. While first-row transition metal pin^F complexes are well documented,[1] there are relatively few second and third row late transition metal complexes with the perfluoropinacolate ligand. Herein, we describe the synthesis and crystal structure of Ru-pin^F complexes.



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Acknowledgement. This work was supported by the Hong Kong Research Grants Council (project no. 16307216)

Chromium(III) for the Premature Aging Disease: Hutchinson-Gilford Progeria Syndrome

Zhenkun Cao,[a] Sheung Kin Ken Wong,[b] ZhongJun Zhou,[b] Hongyan Li,[a] Hongzhe Sun,[a]*

[a]Department of Chemistry, The University of Hong Kong, Pokfulam, Hong Kong

[b]School of Biomedical Sciences, The Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road, Pokfulam, Hong Kong

E-mail: u3005462@hku.hk

Hutchinson-Gilford progeria syndrome (HGPS) is a rare genetic disorder that causes systemic accelerated aging after birth due to a specific mutation in *LMNA* gene.[1] In spite of several fascinating therapeutic strategies being proposed, no effective clinical intervention has been developed so far for HGPS.[2] Multiple beneficial effects of Cr^{3+} have been observed.[3] Here, we prepared a series of chromium(III) complexes and examine their activity on the extension of lifespan of HGPS cells. We found that these complexes can extend up to 50% lifespan of the cells. The mechanism of action of these complexes is under investigation in this laboratory. Our work suggests that chromium(III) complexes may represent a new class of agents for HGPS.

This work is supported by the Research Grants of Hong Kong (RGC), The University of Hong Kong and Norman and Cecelia Yip Foundation.

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Geometry of Bismuth MOFs Adjusted with Polycarboxylate and their Antimicrobial Activity against *Helicobacter pylori*

Xiaojun He[1], Hongyan Li[1], Wei Xia[2]* and Hongzhe Sun[1]*

[1] *The University of Hong Kong, Hong Kong, China*
[2] *Sun Yat-sen University, Guangzhou, China*
E-mail: hsun@hku.hk

A series of bismuth based metal–organic frameworks (Bi-MOFs) were built up by polycarboxylate linker and bismuth nitrate pentahydrate in DMF/H_2O system for three days, and confirmed by crystallography as previously reported bismuth compounds.[1,2] Bi-MOFs materials were strategically fabricated to exploit different linkers to adjust their specific surface areas and geometries.[3] A new Bi-MOFs of composition [Bi(dfp)(bpdc)], denoted as CAU-4-dfp-bpdc, have an exceptionally complicated structure with zigzag Bi-O rods cross-linked by 4,4'-benzophenonedicarboxylic acid (H_2bpdc) ligands. Additionally, [Bi(dfp)(btc)], denoted as CAU-5-dfp-btc, has an 1D structure with chain Bi-O rods cross-linked by 1,3,5-benzenetricarboxylate (H_3btc) ligands. However, [Bi(btb)], denoted as CAU-6-btb, crystal has a 2D typical network shape with different length hexagonal channels, and accessible diameters from 13.49 to 17.85 Å. Importantly, all of bioinspired Bi-MOFs compounds process antibacterial activity against *Helicobacter pylori* (*H. pylori*) with MICs ≥ 2.0 μg/mL, which are comparable to that of bismuth subsalicylate (32 μg/mL). Additionally, these Bi-MOFs compounds exhibit excellent inhibitory effects against *H. pylori* urease activity, implying the potential application of the materials as anti-*H. pylori* drugs.

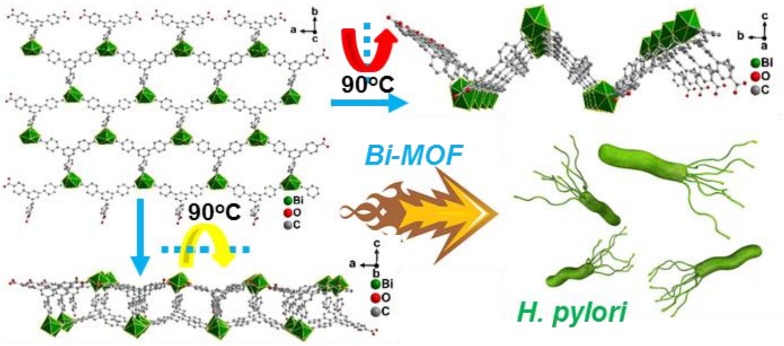

Fig.1 Crystal structure of Bi-MOFs and its application for against *H. pylori*.

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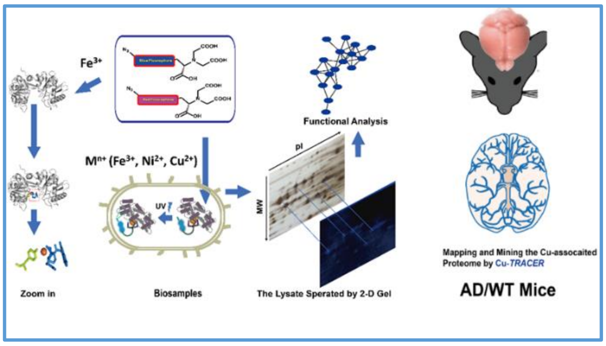
Copper and Cu-associated Proteome in Alzheimer's Disease

Nan Jiang[1], Xiubo Du[2], Tianfan Cheng[3], Lijian Jin[3], Jiazuan Ni[2], Hongyan Li[1] and Hongzhe Sun[1*]

[1] Department of Chemistry, the University of Hong Kong, Pokfulam Road, Hong Kong, P.R. China; [2]College of Life science and Oceanography, Shenzhen University, Shenzhen, P.R. China; [3] Faculty of Dentistry, the University of Hong Kong, 34 Hospital Road, Hong Kong, P.R. China (E-mail: nathan.leo.jiang@gmail.com)

Abstract

In spite of extensive studies on the nexus between Alzheimer's disease (AD) and copper[1], it appears lack of an overview of copper changes due to its labile oxidation stations, various intracellular copper pools and the complicated network of Cu-associated proteome. Both copper and its relevant proteins may play a role in the development of AD and monitering both copper and Cu-proteome are essential. There is no effective chemical tools to identify pathological factors[2]. Herein, we applied ICP-MS to detect endogenous copper content and a reaction-based fluorescent probe to examine intracellular labile Cu(I). These two approaches were then integrated into the Cu-associated proteome which were achieved by the combination of 2-D gel, MALDI-TOF-MS and fluorescent covalent labelling towards Cu-proteins based on a home-made fluorescence probe[3]. The differences of total proteome were demonstrated by label-free LCMS/MS and bioinformatics analysis described the protein-protein interaction network. We observe notable changes of Cu-associated proteomes between AD and wild-type in both cell lines and mice models. Those proteins were subsequently analyzed and validated. The apporach as well as the observation of Cu-proteomes may provide a new horizon to our understanding of the relationship between copper/relevant Cu-proteins and AD development.



*This work was supported by the Research Grants Council of Hong Kong SAR (*HKU17307017P, HKU17333616P*), the University of Hong Kong and the Norman and Cecilia Yip Foundation.*

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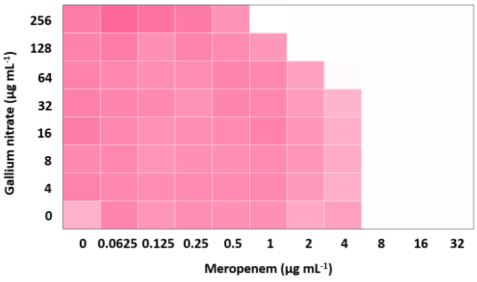
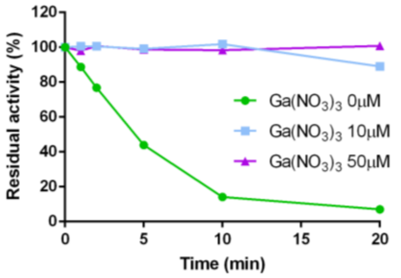
Gallium-Based Agents as Novel Inhibitors of Metallo-β-lactamase

Yuen-Ting Wong[a], *Runming Wang*[a], *Qi Zhang*[a], *Pak-Leung Ho*[b], *Hongyan Li*[a], *Hongzhe Sun*[a]
Department of [a]Chemistry and [b]Microbiology, The University of Hong Kong, Pokfulam Road, Hong Kong, P.R. China, E-mail: hsun@hku.hk

Being the top ten threats to global health in 2019 as enumerated by the World Health Organization (WHO), antimicrobial resistance (AMR) empowers bacteria the ability in confronting existing antimicrobial agents. Metallo-β-lactamase (MBLs), exemplifying with New Delhi metallo-β-lactamase 1 (NDM-1), which is a subclass B1 MBL and able to hydrolyze almost all β-lactam antibiotics, including the last resort carbapenems. Plasmid-encoded *ndm-1* gene is highly transferable across various popular human pathogens and often co-exist with other resistant genes, conferring multiple antimicrobial resistance to bacteria[1].

Combination therapy is regarded as one of the promising approaches in combating AMR. Sun *et.al* (2018) discovered that metallo-agents are potential MBL inhibitors[2]. In this study, we further screened several other metallo-agents for their potential antimicrobial activity and found that gallium-based agents exhibited good antimicrobial activity against MBL-positive bacteria. We show that gallium nitrate had synergistic effect with meropenem (MER), could reduce the minimum inhibitory concentration (MIC) of MER by 8-folds. Co-treatment of Ga-based agents with MER for over 24 hrs could significantly reduce bacterial loads in comparison to single treatment. Enzyme assay experiments show that in the presence of gallium nitrate, over 90% of enzyme activity was retained, in contrast, in the absence of gallium nitrate, nearly all antibiotics could be hydrolyzed, suggesting that gallium nitrate prohibits hydrolysis of antibiotic (e.g. MER). We therefore conclude that gallium-based agents may serve as promising antimicrobial candidates to combat AMR caused by MBL producing bacteria.





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Histone H3 as a target of an organic arsenic anticancer agent ZIO-101 in leukemia cells

Xiaohan Xu, Haibo Wang, Hongyan Li, Hongzhe Sun*

Department of Chemistry, the University of Hong Kong, Hong Kong SAR (E-mail: hsun@ hku.hk)

Metallodrugs often act on multiple protein targets[1]. In order to further unveil the mechanisms of action of arsenic drugs and develop arsenic-based therapeutics, enormous effects have been made towards identification of arsenic binding proteins[2]. S-dimethylarsinoglutathione (ZIO-101) is in phase I/II clinical trials which exhibits significantly improved antileukemia properties and is in a different mechanism of action compared with arsenic trioxide (ATO).

We identify histone 3 (H3) to be a target of ZIO-101 in leukemia cells, using home-made column-type gel electrophoresis coupled with inductively coupled plasma mass spectrometry (GE-ICP-MS)[3]. Whereas no histone H3 can be identified under comparable conditions. MALDI-TOF-MS, CETSA and GE-ICP-MS are further utilized to show that Histone H3 can bind to arsenic both *in vitro* and *in vivo*. Furthermore, our combined biochemical data of reconstituted nucleosomes show that the binding of ZIO-101 to histone H3 leads to destabilize nucleosomes and facilitate the denaturation of nucleosomes, confirming that Histone H3 is a newly identified protein target of ZIO-101.

This work was supported by the Research Grants Council of Hong Kong (17304614P and 17307017P*), and Innovation and Technology Commission of Hong Kong (ITS/085/14)!*

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How to efficiently transport $S_2O_3^{2-}$ by thiosulfate-binding protein CysP

Qi Zhang , Hongyan Li, Hongzhe Sun*

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Pok Fu Lam, Hong Kong, P. R. China; E-mail: hsun@hku.hk

Sulfur, one of major elements, constitutes lots of functional organic molecules *in vivo*[1]. It is transferred into gram-negative bacteria by sulfate/thiosulfate transport system. Thiosulfate transport system has stronger binding affinity with thiosulfate than sulfate. Its unique protein CysP shows highly sequence conservation (>90%) among lots of pathogenic gram-negative bacteria. Thus, CysP has been suggested to be a good candidate of vaccine antigen[2].

Here, we elaborate its exact maturing progress. It presents as a dimer in cytoplasm with a signal peptide and then shows as the trimer in periplasmic space once its signal peptide is deleted. Interestingly, our thermal shift data indicate that, its native substrate $S_2O_3^{2-}$, unlike SO_4^{2-}, doesn't show obvious effect on strengthening the thermal stability of immature CysP although both $S_2O_3^{2-}$ and SO_4^{2-} can enhance mature CysP thermal stability, which may come from different binding affinity as revealed from SPR data which show that the deletion leads to the enhancement in its substrate specificity, i.e. the binding affinity (K_d) is enhanced about 8 times (3.9 and 32.6 nM) between mature CysP and its potential substrate ions, S_2O3^{2-} or SO_4^{2-}, instead of comparable binding (17.43 and 11.1 nM) when the signal peptide is still located at the N-terminal of CysP. Furthermore, we show that the native CysP bind 8-fold $S_2O_3^{2-}$. Our crystallography data further support these arguments, that substrate ion $S_2O_3^{2-}$ is compactly filled into a 7.6Å cavity by interaction with Y_{12}, D_{13}, S_{48}, N_{67}, S_{134}, N_{136}, and F_{196}.

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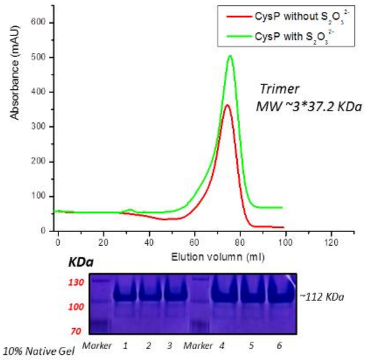

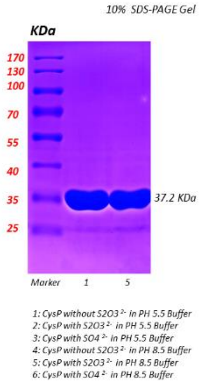

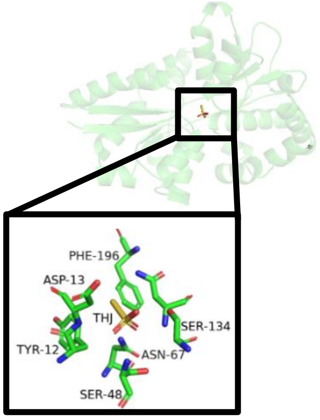

Supramolecular Assemblies of Dinuclear Alkynylplatinum(II) Terpyridine Complexes with Double-Decker Silsesquioxane Nano-Cores: The Role of Isomerism in Constructing Nano-Structures

Ho-Leung Au-Yeung, Sammual Yu-Lut Leung and Vivian Wing-Wah Yam*

Institute of Molecular Functional Materials (Areas of Excellence Scheme, University Grants Committee (Hong Kong)) and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China

E-mail: ayhl@hku.hk; wwyam@hku.hk

Abstract

Analytically pure *cis-/trans-* isomers of double-decker silsesquioxane-functionalized dinuclear alkynylplatinum(II) terpyridine complexes have been isolated, with their isomeric identities being confirmed *via* x-ray crystallographic study. The effects of stereo-configuration on the self-association behavior have been systematically explored. The complexes demonstrate self-association properties *via* the stabilization of hydrophobic–hydrophobic, Pt···Pt and/or π–π stacking interactions. These supramolecular architectures and molecular packings are found to be closely related to the isomeric configurations of the complexes. The difference in aggregation behaviors of the stereoisomers of double-decker silsesquioxanes has provided insights into the assembly properties of this class of stereoisomers. The modulations of Pt···Pt and/or π–π stacking interactions in controlling the aggregation have also been demonstrated through regulating the solvent compositions. Such gradual changes in degree of aggregation have been employed for the construction of helical ribbons and nanotube scaffolds, which have been investigated using various spectroscopic studies.[1]

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Versatile Control of Directed Supramolecular Assembly *via* Subtle Changes of the Rhodium(I) Pincer Building Blocks

Alan Kwun-Wa Chan, Maggie Ng, Kam-Hung Low, and Vivian Wing-Wah Yam*

Institute of Molecular Functional Materials (Areas of Excellence Scheme, University Grants Committee, Hong Kong) and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P.R. China; E-mail: alan7788@hku.hk; mkyng@hku.hk; wwyam@hku.hk

Abstract

Various rhodium(I) pincer complexes with different structural features have been prepared and found to display interesting self-assembly properties due to the extensive Rh(I)···Rh(I) interactions. The incorporation of electron-withdrawing $-CF_3$ substituent has been found to improve the stability of the complexes and also facilitate the directed assembly of complex molecules, providing an opportunity for the systematic investigation of the various noncovalent interactions in their versatile self-assembly behaviors and insights into the structure−property relationship in governing the intermolecular interactions. Density functional theory calculations have been performed to study the effect of $–CF_3$ substituent on the assembly of the complex molecules, and the results reveal the presence of two conformations of comparable energies, with the eclipsed conformation being 1.42 $kJmol^{-1}$ higher in energy than the slightly staggered conformation. An isodesmic growth mechanism is identified for the solvent-induced aggregation process. The complex molecules exhibit intense low-energy absorption bands corresponding to the absorptions of the dimers, trimers, and higher order oligomers upon aggregation, with energies related to the electronic properties of the tridentate *N*-donor ligand. Chiral auxiliaries have also been introduced into the rhodium(I) complexes to build up helical supramolecular assemblies and soft materials.

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Controlling Self-Assembly Mechanisms through Rational Molecular Design in Oligo(*p*-phenyleneethynylene)-Containing Alkynylplatinum(II) 2,6-Bis(*N*-alkylbenz-imidazol-2′-yl)pyridine Amphiphiles

Michael Ho-Yeung Chan, Sammual Yu-Lut Leung, and Vivian Wing-Wah Yam*

Institute of Molecular Functional Materials (Areas of Excellence Scheme, University Grants Committee (Hong Kong)) and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China. Email: mchanhy@hku.hk; wwyam@hku.hk

Abstract

The systematic control over association mechanisms of self-assembled materials has been demonstrated through the rational design and synthesis of a series of amphiphilic dinuclear alkynylplatinum(II) bzimpy (bzimpy = 2,6-bis(*N*-alkylbenz-imidazol-2′-yl)pyridine) complexes containing the shape-persistent oligo(*p*-phenyleneethynylene)s. Multi-stage morphological transformations from plates to fibers and to spherical nanostructures under different solvent compositions have been demonstrated. The subtle balances between multiple noncovalent interactions including Pt···Pt, hydrophobic, hydrophilic, and π–π stacking interactions are found to have profound impact on the supramolecular assembly of the system, in which a change in the association mechanism from isodesmic to cooperative and back to isodesmic growth has been observed upon increasing hydrophilicity of the complexes.[1]

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Directional Self-Assembly and Photoinduced Polymerization of Diacetylene-Containing Platinum(II) Terpyridine Complexes

Shishi Fang,[a] Sammual Yu-Lut Leung,[a] Yongguang Li,[a,b] and Vivian Wing-Wah Yam*[a,b]

[a] *Institute of Molecular Functional Materials [Areas of Excellence Scheme, University Grant Committee (Hong Kong)] and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China*

[b] *Lehn Institute of Functional Materials, School of Chemistry, Sun Yat-Sen University, Guangzhou, P. R. China*

E-mail: ccfang@hku.hk; wwyam@hku.hk

Abstract

A series of newly designed and synthesized diacetylene-containing platinum(II) terpyridine complexes exhibited intriguing self-assembly properties.[1] Facilitated by Pt···Pt, π–π stacking, hydrogen-bonding and hydrophobic–hydrophobic interactions, these complexes are preorganized to readily undergo topochemical polymerization reactions upon photoirradiation.[1] The *in situ* polymerization of the diacetylene units to form polydiacetylene, indicated by the UV–vis spectral changes, gel permeation chromatography and dynamic light scattering, was found to alter their assembly behaviors, as revealed by TEM images.[1] It is envisaged that this work may offer alternative promising candidates for the engineering of functional nanoaggregates with desirable photophysical, photochemical and self-assembly properties.

Reference

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Calixarene-based alkynyl-bridged gold(I) isocyanide and phosphine complexes as building motif for the construction of chemosensors and supramolecular architecture

Franky Ka-Wah Hau, Kai-Leung Cheung, Nianyong Zhu and Vivian Wing-Wah Yam*

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

Email address: haukawah@hku.hk; wwyam@hku.hk

Abstract

A series of calixarene-based alkynyl-bridged Au(I) isocyanide and phosphine complexes has been designed and synthesized. These complexes are found to exhibit intense emission in dichloromethane solution, in the solid state and in the glass state at 298 K and 77 K. The gold(I) isocyanide complexes with triazolyl group as receptor sites have been shown to switch on a low-energy emission band upon addition of Zn^{2+} ion. The new low-energy emission band is ascribed to result from the switching on of the Au···Au interaction upon the binding of the Zn^{2+} ion that gives rise to a reduced HOMO-LUMO energy gap. Furthermore, an interesting supramolecular architecture of tetranuclear gold(I) phosphine stabilized by Au···Au interaction has been isolated. Short Au···Au distances are found in the X-ray crystal structure.

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A Luminescence Turn-On Assay for Acetylcholinesterase Activity and Inhibitor Screening Based on Supramolecular Self-Assembly of Alkynylplatinum(II) Complexes on Coordination Polymer

Angela Sin-Yee Law, Margaret Ching-Lam Yeung, and Vivian Wing-Wah Yam*
Institute of Molecular Functional Materials (Areas of Excellence Scheme, University Grants Committee (Hong Kong)) and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, People's Republic of China
E-mail: lawsy@connect.hku.hk; wwyam@hku.hk

Abstract

A new approach toward acetylcholinesterase (AChE) detection has been demonstrated based on the electrostatic interactions between anionic alkynylplatinum(II) complex molecules and cationic coordination polymer, together with the spectroscopic and emission characteristics of alkynylplatinum(II) complexes upon supramolecular self-assembly. This process involves strengthening of distinct noncovalent Pt(II)···Pt(II) and π–π stacking interactions, which is evidenced by UV–vis absorption, emission, and resonance light scattering results. Such a method has been applied to AChE inhibitor screening, which is important as the demand for AChE inhibitor assays arises along with the drug development for Alzheimer's disease. It affords an emission turn-on response and operates in a continuous and label-free fashion. The low-energy red emission and large Stokes shift of alkynylplatinum(II) complexes are advantageous to biological applications.

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Law A. S.-Y.; Yeung M. C.-L.; Yam V. W.-W. *ACS Appl. Mater. Interfaces*, **2019**, *11*, 4799–4808.

Highly luminescent phosphine oxide-containing bipolar alkynylgold(III) complexes for solution-processable organic light-emitting devices with small efficiency roll-offs

Chin-Ho Lee, Man-Chung Tang, Wai-Lung Cheung, Shiu-Lun Lai, Mei-Yee Chan and Vivian Wing-Wah Yam*

Institute of Molecular Functional Materials (Area of Excellence Scheme, University Grants Committee) and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China

rleech@hku.hk; wwyam@hku.hk

Abstract

We report the synthesis of alkynylgold(III) complexes with electron-transporting phosphine oxide moiety in the tridentate ligand and hole-transporting triarylamine moieties as auxiliary ligands to generate a new class of phosphine oxide-containing bipolar gold(III) complexes for the first time. Such gold(III) complexes feature high photoluminescence quantum yields of over 70 % in MCP thin films with relatively short excited-state lifetimes of less than 3.9 μs at 20 wt% dopant concentration. Highly efficient solution-processable organic light-emitting devices have been prepared with superior current efficiencies of up to 51.6 cd A^{-1} and external quantum efficiency of up to 15.3 %. Notably, triplet-triplet annihilation has been significantly reduced, as exemplified by a very small efficiency roll-off of ~1 % at practical brightness of 500 cd m^{-2}.

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Realization of Thermally Stimulated Delayed Phosphorescence in Arylgold(III) Complexes and Efficient Gold(III) Based Blue-Emitting Organic Light-Emitting Devices

Man-Chung Tang,† Ming-Yi Leung,† Shiu-Lun Lai, Maggie Ng, Mei-Yee Chan,* and Vivian Wing-Wah Yam*

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

Email: u3500702@hku.hk; wwyam@hku.hk

Abstract

To address and overcome the difficulties associated with the increased reactivity and susceptibility of blue emitters to deactivation pathways arising from the high-lying triplet excited states, we have successfully demonstrated an innovative strategy of harvesting triplet emission via the "thermally stimulated delayed phosphorescence" mechanism, where thermal up-conversion of excitons from the lower-energy triplet excited states (T_1) to higher-energy triplet excited states (T_1') are observed to generate blue emission. The lower-lying T_1 excited state could serve as a mediator to populate the emissive T_1' state by up-conversion via reverse internal conversion, which could enhance the photoluminescence quantum yield by over 20-folds. Organic light-emitting devices with respectable external quantum efficiencies of up to 7.7 % and sky-blue emission with CIE coordinates of (0.17, 0.37) have been realized. The operational stability for the device based on complex **1** has also been explored, and the device is found to show fairly respectable lifetime. This work opens up a new avenue to the design and synthesis of blue phosphorescent emitters.

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†M.-C.T. and M.-Y.L. contributed equally to this work.

Strategy Towards Rational Design of Gold(III) Complexes for High Performance Organic Light-Emitting Devices

Lok-Kwan Li,[‡] Man-Chung Tang,[‡] Shiu-Lun Lai, Maggie Ng, Wing-Kei Kwok, Mei-Yee Chan,* Vivian Wing-Wah Yam*

[*] Ms. L.-K. Li, Dr. M.-C. Tang, Dr. S.-L. Lai, Dr. M. Ng, Ms. W.-K. Kwok, Dr. M.-Y. Chan,* Prof. V. W.-W. Yam*
Institute of Molecular Functional Materials [Areas of Excellence Scheme, University Grants Committee (Hong Kong)] and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China
Fax: +(852) 2857-1586; Tel: +(852) 2859-2153
E-mail: natli@hku.hk; wwyam@hku.hk; chanmym@hku.hk

[‡] Both authors contributed equally to this work.

Abstract

Gold(III) complexes are attractive candidates as phosphorescent dopants in organic light-emitting devices for high luminance full-colour displays. However, no data on the stability of such devices have been reported to date. Through rational molecular design and synthesis, we have successfully generated a new class of cyclometalated gold(III) C^C^N complexes with tunable emission colours spanning from sky-blue to red. These complexes exhibit high photoluminescence quantum yields of up to 80 % in solid-state thin films, excellent solubility and high thermal stability. Solution-processable and vacuum-deposited organic light-emitting devices based on these complexes operate with external quantum efficiencies of up to 11.9 % and 21.6 %, respectively, and operational half-lifetimes of up to 83,000 h at 100 cd m^{-2}.

Reference

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Platinum(II)-based Supramolecular Scaffold-Templated Side-by-side Assembly of Gold Nanorods Through Pt···Pt and π–π Interactions

Yip-Sang Wong, Frankie Chi-Ming Leung, Maggie Ng, Heung-Kiu Cheng, Vivian Wing-Wah Yam*

Institute of Molecular Functional Materials (Areas of Excellence Scheme, University Grants Committee (Hong Kong)) and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, People's Republic of China. newman91@hku.hk; wwyam@hku.hk

Abstract

Side-by-side assembly of gold nanorods (GNRs) has been demonstrated to be directed by the supramolecular scaffolds formed by sulfonate-containing alkynylplatium(II) terpyridine complexes. Driven by Pt···Pt and π−π stacking interactions, the Pt(II) complex has demonstrated a high propensity to assemble in water with the plausible head-to-tail stacking arrangement to construct supramolecular scaffolds, in which the sulfonate groups on the terpyridine ligand at the peripheral position preferentially bind to the sides of the GNRs. Interestingly, the plasmonic properties and the extent of the assembly of the GNRs into ladder rung-like nanostructures can be readily modulated by the concentration of the Pt(II) complex. The photophysical and spectroscopic properties of the alkynylplatinum(II) complex and its supramolecular scaffold obtained from Pt···Pt interaction assisted formation as well as the directed side-by-side assembly of GNRs have been investigated by UV−vis absorption spectroscopy, NMR spectroscopy, energy dispersed X-ray (EDX) analysis and surface-enhanced Raman scattering (SERS). This work provides important insights for the construction of higher-ordered nanoassemblies using both Pt···Pt interactions and template-directed approaches.

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Photochromic Benzo[*b*]phosphole Alkynylgold(I) Complexes with Mechanochromic Property to Serve as Multistimuli-Responsive Materials

Nathan Man-Wai Wu, Maggie Ng, and Vivian Wing-Wah Yam*

Institute of Molecular Functional Materials [Areas of Excellence Scheme, University Grant Committee (Hong Kong)] and Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China

E-mail: nathanwu@hku.hk; wwyam@hku.hk

Abstract

A series of novel benzo[*b*]phosphole alkynylgold(I) complexes has been demonstrated to display photochromic and mechanochromic properties upon applying the respective stimuli of light and mechanical force.[1] Promising multistimuli-responsive properties of this series of gold(I) complexes have been successfully achieved through judicious molecular design, which involves incorporation of the photochromic dithienylethene-containing benzo[*b*]phosphole into the triphenylamine-containing arylethynyl ligand that is susceptible to mechanical force-induced color changes *via* gold(I) complexation.[1] With excellent thermal irreversibility and robust fatigue resistance of this series of gold(I) complexes, multicolor states controlled by the photochromism and mechanochromism have been realized.[1] Repeatable photochromic and mechanochromic cycles without apparent loss of reactivity have also been observed under ambient conditions.[1]

Reference

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A Gold Quartet Framework with Reversible Anisotropic Structural Transformation Accompanied by Luminescence Response

Liao-Yuan Yao 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; email: lyyao@hku.hk, wwyam@hku.hk

Abstract

Hierarchy and chirality are the fundamental characteristics of biomolecules. Chemistry on hierarchical self-assembly and spontaneous symmetry breaking helps to uncover the mechanism of living activities and the origin of chirality in nature. Herein is described an unprecedented chiral gold quartet framework (GQF) with C_4-symmetric structure hierarchically aggregated from an achiral anionic $[Au_{10}(dpptrz)_4S_4]^{2-}$ (**dpptrz-Au$_{10}$**), which was acquired via click-reaction-induced and Au(I)···Au(I)-interaction-directed cluster-to-cluster transformation (CCT) from the rationally designed $[(dppa)_6Au_{18}S_8]^{2+}$ (**dppa-Au$_{18}$**). Inter-cluster hydrogen bonding and alkali ion coordination are observed to assist the hierarchical self-assembly and chiral self-organization of the GQF. Upon exposing the crystal to vacuum, the bottom-up constructed GQF shows an anisotropic structural transformation accompanied by a visual luminescence change in a single-crystal-to-single-crystal (SCSC) manner that becomes reversible upon removal of vacuum. This research largely advances the potential of polynuclear gold(I)-sulfido clusters in hierarchical self-assembly and luminescent materials.[1]

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[†] Areas of Excellence Scheme (AoE), University Grants Committee (Hong Kong)

Energy Landscape in Supramolecular Co-Assembly of Platinum(II) Complexes and Block Copolymers

Kaka Zhang, Margaret Ching-Lam Yeung, Sammual Yu-Lut Leung, 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; email: zhangkk@hku.hk, wwyam@hku.hk

Abstract

Establishment of energy landscape has emerged as an efficient pathway for improved understanding and manipulation of both thermodynamic and kinetic behaviors of complicated supramolecular systems. Energy landscapes of supramolecular co-assembly of platinum(II) complexes and block copolymers have been established. Co-assembly at room temperature has been found to only allow the longitudinal growth of platinum(II) complexes and block copolymers into core-shell nanofibers that are the kinetically trapped products. Thermal annealing can switch on the transverse growth of platinum(II) complexes and block copolymers to produce core-shell nanobelts that are the thermodynamically stable nanostructures. Besides, rapid quenching of a hot co-assembly mixture to room temperature can capture intermediate nanobelt-*block*-nanofiber nanostructures that are metastable and capable of converting to nanobelts upon further incubation at room temperature. Moreover, sonication treatment has been found to couple with the energy landscape of the co-assembly system and open a unique energy-driven pathway to activate the kinetically forbidden nanofiber-to-nanobelt morphological transformation at room temperature.

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†Areas of Excellence Scheme (AoE), University Grants Committee (Hong Kong)

Lanthanide Chiral Cyclen Complexes for MRI and CPL Studies

Lixiong Dai, Ga-Lai Law*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong; ga-lai.law@polyu.edu.hk

Abstract

A series of chiral cyclens and their derivatives of chiral DOTA and chiral DO3A lanthanide complexes were synthesized, revealing significant properties that transcend the parent achiral complexes, displaying potential value as a platform for molecular bioimaging applications. Our design strategy was to incorporate symmetrical chiral substituents around the tetraaza ring, imparting enhanced rigidity to the lanthanide chiral DOTA/DO3A complexes. The sterically locking approach involving a bidentate chromophore is adopted to control the formation of one stereoisomer, giving rise to extreme rigidity, high stability, and high emission intensity, which is crucial for circularly polarised luminescence (CPL) applications.[1] The chiral Gd-DOTA complexes are shown to be orders of magnitude more inert to Gd release than Gd-DOTA, making them as safer magnetic resonance imaging (MRI) contrast agents.[2]

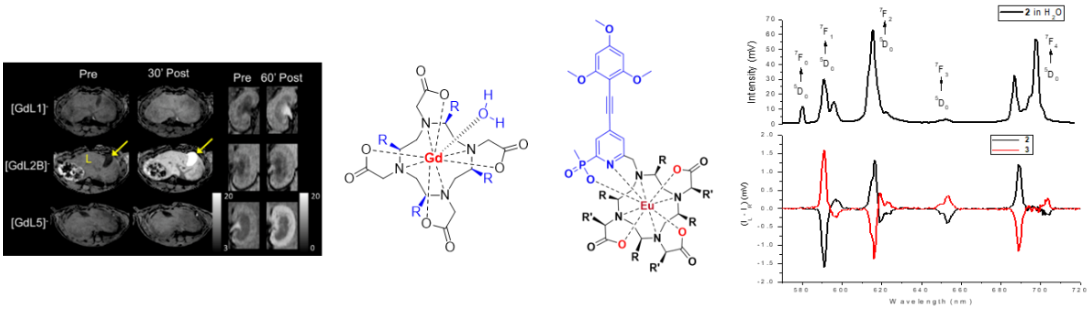

Figure 1. Lanthanide chiral DOTA and chiral DO3A complexes for MRI (left) and CPL studies (right).

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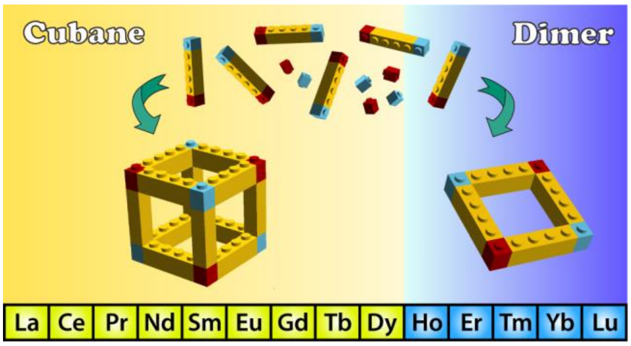
Assembly of lanthanide(III) cubanes and dimers with single-molecule magnetism and photoluminescence

Ho-Yin Wong, Wesley Ting Kwok Chan, Ga-Lai Law*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong

Email: ga-lai.law@polyu.edu.hk

Discrete lanthanide(III) tetranuclear cubane-like clusters seldom occur throughout the Ln^{III} series and behave as single-molecule magnets (SMMs).[1,2] Herein, a series of cubane, $[Ln_4(\mu_3\text{-OH})_4(\mu\text{-tfa})_4(hfa)_4(phen)_4]$ (**1**–**9**, Ln = La–Dy (except Pm), tfa = trifluoroacetate, hfa = hexafluoroacetylacetonate, phen = 1,10-phenanthroline), and dinuclear clusters, $[Ln_2(\mu\text{-OH})_2(hfa)_4(phen)_2]$ (**10**–**16**, Ln = Tb–Lu), were synthesized and characterized. Two types of clusters were formed due to the change of preferred coordination geometry for lighter and heavier Ln^{III} ions which favour nine-coordinated cubane and eight-coordinated dimer respectively. Magnetic study shows that **8**-Tb_4 and **9**-Dy_4 are ferromagnetically coupled and SMM in nature because of the larger Ln…Ln distance compared to other discrete cubanes. The anisotropic barrier, U_{eff}, of **9**-Dy_4 are determined to be 67.0 K. In addition, the photophysical properties of **6**-Eu_4, **8**-Tb_4 and **10**-Tb_2 owing to tfa, hfa and phen sensitization and O–H quenching, are presented.



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Supramolecular Transformation of Helicates and Cages in Chiral C_2-Symmetrical Ligands

King-him Yim, Chi-tung Yeung, Ga-lai Law* and Wing-tak Wong*

Department of Applied Biology and Chemical Technology

The Hong Kong Polytechnic University

Email: ga-lai.law@polyu.edu.hk; w.t.wong@polyu.edu.hk

Abstract

Self-assembly supramolecular architectures have received a lot of attention due to various applications such as catalysis, display materials and luminescent probes. A large number of transition metal self-assembled supramolecular architectures have been reported such as helicates, tetrahedral cages and metal organic frameworks. Controlling the formation of the desired self-assembled supramolecules is important to achieve specific structural properties for specific applications in order to prevent the formation of unwanted cluster or geometries. Recent investigations have demonstrated certain stimuli that can trigger the geometric transformations, for example, by solvent, guest, anion and concentration of the ligand.[1] By contrast to transition metals, lanthanide ions are less commonly used in preparing self-assembly supramolecule due to its labile coordination number and poor stereochemical preferences. From our previous study, the formation of supramolecular architectures is sensitive to the size of lanthanide ion and the flexibility of the ligand.[2] Therefore, the control of the formation of a desired geometric structure still remains a challenge. In this study, two pair of bis(tridentate) ligand with C_2 symmetry was prepared to investigate the transformation between the helicate and tetrahedral cage morphology.

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Zeolite-template 1-D Carbon Nano-chain Synthesis

Kwan Chee LEUNG, Benedict Tsz-woon LO, Kwok-yin WONG

Department of Applied Biological and Chemical Technology, the Hong Kong Polytechnic University, Hong Kong

Ordered nano-size carbon chains with controlled length and shape have received more and more attention recently because of their potential applications in catalysis, energy storage and electrical conduction. The zeolite-template method is one of the promising synthetic methods for the synthesis of controlled and ordered nano-size carbon chains.[1,2] The zeolite pores provide rigid size and shape for the organic precursors to undergo pyrolytic carbonization, forming interconnected carbon frameworks.

Herein, the synthesis of zeolite-template carbon was performed and the characterisations of the synthesised zeolite-template carbon give promising results. STEM image (Fig.1a) and the strong and noticeable peak at 685 mass of the MALDI-TOF-MS (Fig.1b) implied that single-dimension graphene-like carbon chains (Fig.2) were able to be produced.

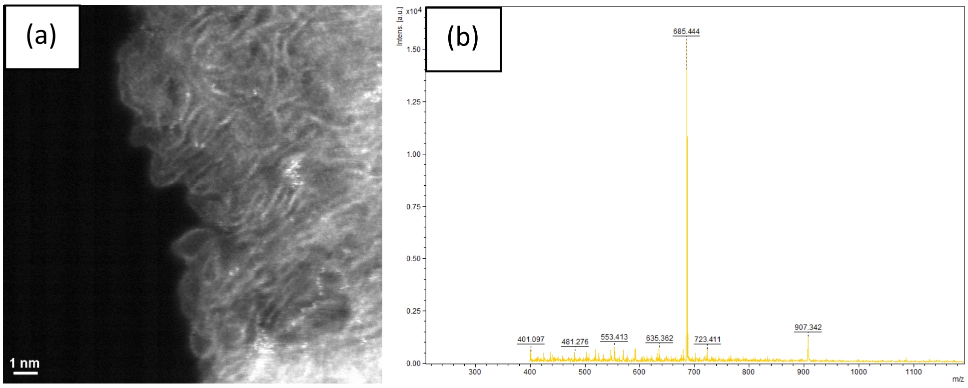

Fig.1 (a) STEM image of the synthesised zeolite-template carbon. (b) The mass peak of MALDI-TOF-MS at 685 mass.

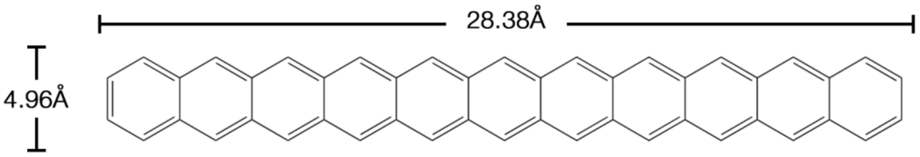

Fig. 2 Target single-dimension graphene-like carbon chain product.

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Precise Assembly of 3d Nano-clusters Inside MOFs

Qi Xue, Tsz Woon Benedict Lo*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, email: qixue.xue@connect.polyu.hk

Single atom catalysts have been emerged as a new kind of catalysts that have potential application in industrial catalysis, bio mimetic enzyme, and photo catalytic reactions, because of its high metal dispersion and maximized metal utilization[1]. But how to control the atom number to adjust its chemical properties, which can enable us to know more detailed mechanism of catalytic reaction and have more efficient catalysts, is immensely challenging.

In our research, we have chosen MIL101[2] as the starting MOF material. Successive metal species were incorporated inside the MOF. Different number of foreign atoms in the MIL101 can be adjusted through Lewis pairs, to realize the control of atom number. Through PXRD, the crystal structures were analyzed. After the coordination of 3 equivalent of Cu species, the parent crystal structure of MIL101 remains (Fig.1). Elemental analysis by ICP-OES also verify that the consecutive addition of Cu species has been successful. Advanced structural characterization at world-class synchrotron facilities, namely, SPring-8 (Japan) and Diamond Light Source, will be performed to determine the crystal structures by Rietveld refinement.

NIR-laser Triggered Nanosystem as a Therapeutic Agent for PA-guided Photothermal Therapy and Chemotherapy against Cancer

Fang XY, Li SY, Lui DKH, Li X, Gu YJ, Wong WT*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University

w.t.wong@polyu.edu.hk

A combination of chemo- and photothermal therapy has emerged as a promising strategy for cancer therapy. However, the predicament of accurate drug delivery and the ability to trigger drug release in specific tumor sites remains a challenging problem. In this study, we designed Au/DOX@SeNPs-iRGD nanosystem as a therapeutic agent for PA-guided photothermal therapy and chemotherapy against cancer. The novel nanosystem could achieve to synergistic thermo-chemotherapy based on the photothermal sensitization property of Au nanocages and antitumor activity of doxorubicin and SeNPs. The functionalized nanosystem was dispersed with highly uniform size and could release the chemical drugs under the radiation of NIR laser due to the photothermal transition. Therefore, it could achieve the goal of double control by precise drug controlled release under acidic conditions and NIR laser and thus reduce side effects on normal tissue as shown in figure 1. This study could provide a new strategy to treat cancer theoretically and clinically.

Keywords: nanosystem, accurate drug delivery, thermo-chemotherapy, cancer therapy

Catalyst Evolution: Design and Synthesis of Re(V) Alkylidyne Catalysts for Alkyne Metathesis Reactions

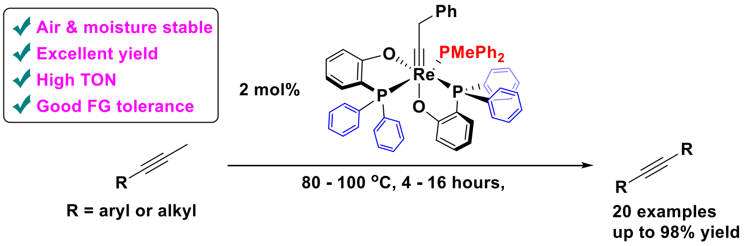
Mingxu Cui, Wei Bai, Herman H. Y. Sung, Ian D. Williams*, Zhenyang Lin* and Guochen Jia*

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

Abstract

Alkyne metathesis, the twin brother of olefin metathesis, has already been developed for over half-century.[1] However, alkyne metathesis has caught far less attention than olefin metathesis. To date, highly efficient alkyne metathesis catalysts are usually based on high valent alkylidyne complexes of Mo(VI) or W(VI). Interestingly, to the best of our knowledge, low valent transition metal alkylidyne catalyzed alkyne metathesis has never been reported. Inspired by the success of low valent Ru olefin metathesis catalysts, we decided to explore a new approach to alkyne metathesis reactions with low valent alkylidyne complexes which are expected to be more robust and simpler to handle.

In this work, we have synthesized a series of Re(V) alkylidyne complexes. Preliminary investigations showed that ligands would significantly influence catalytic activities of Re(V) alkylidynes for alkyne metathesis.[2] With carefully designed ligand systems, low valent Re(V) alkylidynes could promote alkyne metathesis efficiently with good functional group tolerance. Most impressively, Re(V) alkylidyne catalysts are air and moisture stable, and catalytic reactions could proceed well in wet solvents. In this presentation, details will be described.



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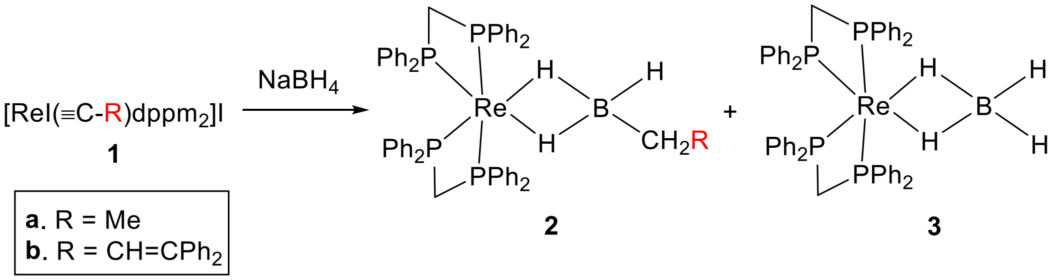
Reactions of Rhenium Carbyne Complexes with Borohydride

LEE, Kui Fun, 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; Email: kfleeaf@connect.ust.hk

Abstract

Reactions of rhenium carbyne complexes with nucleophiles such as alcohols, alkylides, amines, phosphines, and thiocyanates usually give rhenium carbene complexes by addition reactions. It is also reported that $NaBH_4$ attacks regiospecifically on the γ-carbon of the vinylcarbyne ligand of $[ReCp^*(CO)_2\{\equiv C\text{-}CH{=}CMe_2\}]BF_4$ to give $[ReCp^*(CO)_2\{{=}C{=}C(H)CHMe_2\}]$.[1] However, we recently found that reactions of $[ReI\{\equiv C\text{-}R\}dppm_2]I$ (**1**) with $NaBH_4$ produced unexpected η^2-borane rhenium complexes, $[Re\{\eta^2\text{-}H_2BH(CH_2R)\}dppm_2]$. For example, $[ReI\{\equiv C\text{-}R\}dppm_2]I$ (R = Me, vinyl) react with $NaBH_4$ in refluxing THF to yield the complex **2a**, **2b** and **3**.



Scheme 1. Reactions of **1** with $NaBH_4$ in refluxing THF.

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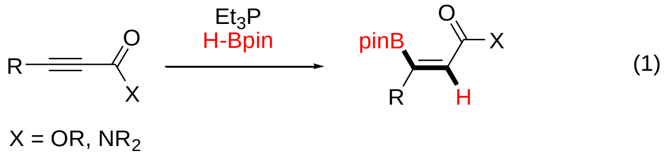
Understanding *trans* Hydroboration of Alkynoate Esters through DFT Calculations

Xueying Guo, Zhenyang Lin*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, PRC
E-mail: chzlin@ust.hk

Abstract

Organoboron compounds are ubiquitous in organic chemistry due to the versatility of C-B bonds in various transformations. Alkenylboronates are excellent substrates for such cross-coupling reactions. Their medicinal applications highlight their significance not only as synthetic intermediates, but also as end products.

As transition metal-free stereoselective *trans* hydroboration synthetic approaches were quite limited. A novel phosphine-catalyzed *trans* hydroboration of alkynoate esters and amides to yield alkenylboronates was achieved and reported by Santos and his coworkers (eq 1).[1] The reaction proceeded under mild conditions with exclusive (*E*)-selectivity to afford (*E*)-β borylacrylates and (*E*)-β borylacrylamides in good to excellent yields. Our theoretical calculations on the mechanism have revealed a phosphonocyclobutene to boronocyclopentene intermediate transformation process, which is the rate-limiting step as well as the stereoselective step of the reaction. In this poster, we will report our DFT results from which *trans*, instead of *cis*, hydroboration is theoretically explained.



Scheme 1. Phosphine-catalyzed *trans* hydroboration of alkynes.

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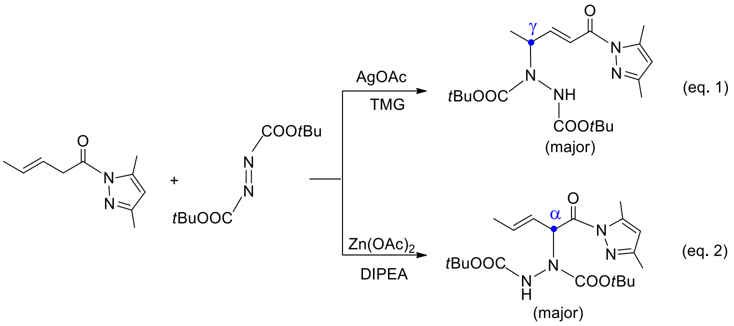
DFT Studies on Metal-Controlled Regioselective Amination of N-acylpyrazoles with Azodicarboxylates

Shujuan Lin and Zhenyang Lin*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, People's Republic of China; E-mail: chzlin@ust.hk

Abstract

Amino-carbonyls are important structural motifs present in many natural, biological and pharmaceutical relevant compounds. Thus, C-N bond construction to synthesize amino-carbonyl compounds has attracted extensive research interest. Recently, Zhang and co-workers reported a metal-controlled regioselective amination of unsaturated N-acylpyrazoles with azodicarboxylates.[1] Under a silver catalyst, the reaction gives γ-amination product with high selectivity (eq. 1). Interestingly, the α-amination product is generated as the major product using a zinc catalyst (eq. 2). The metal-controlled selectivity was believed to be a result of the different coordination preference between silver(I) and zinc(II). In this work, we carried out detailed mechanistic studies with the aid of DFT calculations for the amination reactions shown in eqs. 1 and 2. We hope to gain deep insight into the interesting results observed experimentally and understand how different coordination helps to determine the regioselectivity.



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Principal Interacting Spin Orbital (PISO) Analysis: Beyond the closed-shell bonding interactions

SHEONG Fu Kit, ZHANG Jing-Xuan, LIN Zhenyang*

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

Email: chzlin@ust.hk

Abstract

We have recently developed a principal component analysis (PCA) based bonding analysis method, Principal Interacting Orbital (PIO) analysis,[1] for understanding the fragment interactions in closed-shell chemical systems. The applicability of our method ranges from traditional structure-and-bonding analysis, through the understanding of interactions in cluster compounds, to the analysis of various reactions. Still, a lot of compounds with considerable chemical interests have unpaired electrons, including but not limited to organic radicals or high-spin transition metal complexes. In this work, we will present our attempt to extend the PIO analysis to open-shell species, known as the Principal Interacting Spin Orbital (PISO) analysis, by performing PCA on alpha- and beta-density matrices separately. We found that, in an open-shell system, apart from the bonding/interacting patterns (e.g. covalent bond, donor-acceptor interaction, mutual delocalization, etc.) found in the original PIO analysis, where the analysis results of alpha- and beta-densities are similar, we have also found out other interesting patterns in chemistry using PISO. Other than the expected "alpha-bond" (we follow the convention that there are more alpha- than beta-electrons), we also discovered other interesting patterns like "beta-bond" and "alpha-beta mutual delocalization". These patterns could help us better understand a wide range of chemically relevant open-shell systems that are previously not applicable to original PIO analysis.

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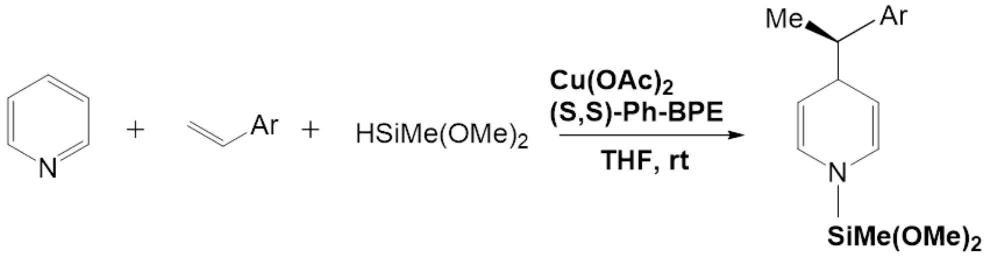
The DFT Studies on Cu-Catalyzed 1,4-Dearomatization of Pyridines

Linlin Wu and Zhenyang Lin*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China
chzlin@ust.hk

Abstract

Dearomatization of pyridines normally requires harsh condition due to the delocalization of π bonds. Furthermore, the selectivity between 1,2- and 1,4-dearomzatization of pyridines is rather challenging. Recently, Buchwald and his co-workers reported asymmetric Cu-catalyzed 1,4-dearomatization of pyridines under mild conditions without requiring pre-activation of pyridine, protecting group manipulations, or preformation of nucleophiles (shown in **Scheme 1**). To understand the experimental observations, we investigated the detailed reaction mechanism with the aid of DFT calculations. In this poster, we will present our findings.



Scheme 1. Asymmetric direct catalytic 1,4- dearomatization.

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Construction of Superatomic Orbitals and GUM-like Orbitals of Gold Clusters Through Orbital Alignment and Localization

Jing-Xuan ZHANG, Fu Kit SHEONG, Zhenyang LIN*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, PRC
Email: chzlin@ust.hk

Abstract

Understanding the electronic structures of gold nanoclusters is of great importance to comprehend their distinctive properties. Many electron-counting rules have been proposed, including the *Jellium model*,[1] which successfully explained a number of spherically shaped gold clusters using superatomic orbitals, and *Grand Unified Model (GUM)*,[2] which decomposes large gold clusters into triangular and tetrahedral units with 3-center-2-electron and 4-center-2-electron bonds, respectively. Molecular orbitals, although hinting these models, are usually too delocalized to correlate with these intuitive models. In this work, we employ the idea used in Natural Orbital of Chemical Valence (NOCV) analysis,[3] align the orbitals of a huge cluster to those of small isolated yet chemical meaning fragments with the jellium electrons not assigned to any fragment, to build an *ab initio* quantum mechanical foundation and achieve an automatic construction and direct visualization of the above electron-counting models. Superatomic orbitals have been obtained with clean shapes, and triangle- and tetrahedron-based 2-electron orbitals can be identified with the aid of traditional Boys or Pipek-Mezey localization schemes.

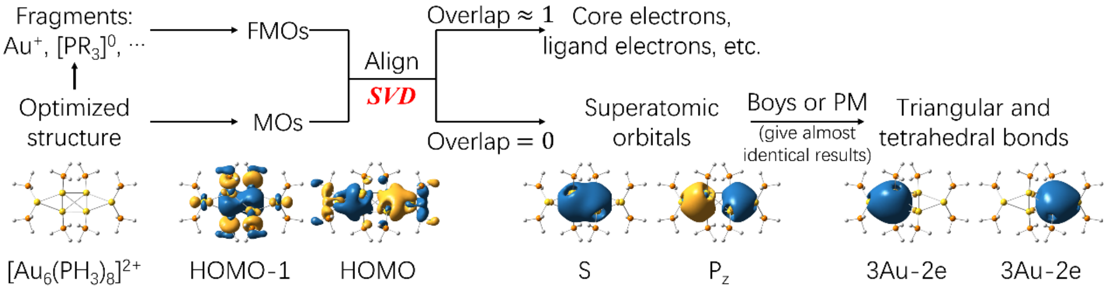

Fig. 1. Workflow for automatic construction of Superatomic orbitals and GUM-like orbitals

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Mechanistic Studies on the Palladium-Catalyzed Cross-Dehydrogenative Coupling of 4-Phenoxy-2-Coumarins: Experimental and Computational Insights

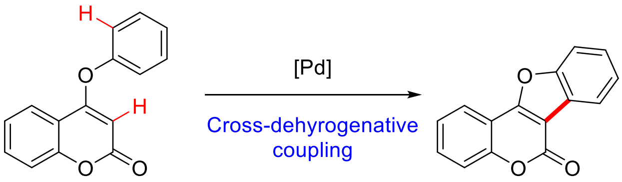
Zhihan Zhang, Zhenyang Lin*

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

Email: chzlin@ust.hk

Abstract

The mechanism of the palladium-catalyzed cross-dehydrogenative coupling of 4-phenoxy-2-coumarins (Scheme 1) has been studied. Density functional theory calculations[1] are supported by isotopic labelling studies and kinetic isotope effects.[1, 2] A double concerted metalation-deprotonation mechanism is proposed.



Scheme 1. Cross-dehydrogenative coupling of 4-phenoxy-2-coumarins and 2-pyrones.

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MOF Isomerism due to Guest Molecules: Three Distinct Forms of [Cd(BzIm)$_2$] All with ABW-Topology

Wentao Zhou, Yan Zhou, Fion T-Y. Yeong, Fanny L-Y. Shek, Herman H-Y. Sung, Lawrence W-Y. Wong and Ian D. Williams*

Department of chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong; chwill@connect.ust.hk

Abstract

ZIFs are a new class of porous material with three-dimentional structures constructed from tetrahedral metal dications (e.g., Cadmium, Zinc and Cobalt) bridged by bent imidazolate type anions. Their frameworks are structurally analogous to SiO_2 and Aluminosilicate zeolites.[1] Unlike SiO_2, the imidazole linkers can be chemically varied. Deliberate control of crystallization processes has produced many materials not known *in* nature.[2]

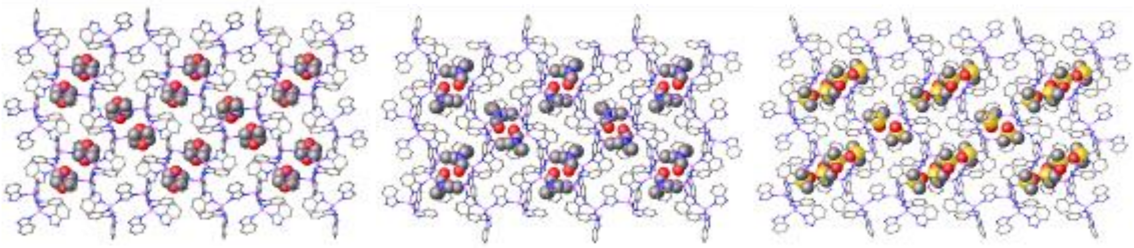

Figure.1. View of plane of (100) of [Cd(BzIm)$_2$]$_n$ •0.25n Solvent (Solvents from left to right: Dioxane, DEF, DMSO)

Three new ZIF phases of [Cd(BzIm)$_2$] were obtained by solvothermal reactions of benzimidazole with Cd^{2+}. These all have the ABW zeolite topology, but with major difference in the porous channels and cavity structure. It illustrates surprisingly that knowledge of the metal, ligand and topology is insufficient to fully define a MOF, which is a quite different case from SiO_2 zeolites.

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Synthesis and Studies on Mixed-Valent Dinuclear Triple Helicates Iron Complexes

Fu-Wai Chan, Shek-Man Yiu, and Hoi-Lun Kwong*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong SAR(China); E-mail: bhhoik@cityu.edu.hk

Abstract

Iron complexes continue to be heavily studied because of their utility as switching centers in potential applications in information technology.1 Most of them are related to the spin states of iron and interaction between iron ions. In general, FeII complexes exist in either a high spin or a low spin state, depending in the nature of the ligand field on the metal ions. The spin-crossover (SCO) compounds, which can switch between a high-spin (HS) and a low-spin (LS) state, can be switched by the external stimuli of temperature, pressure, magnetic field or light.2 The SCO complexes sensitive to changes in ligands with different electron-donating/withdrawing groups and steric hinderance can be synthesized by selecting a ligand with an intermediate ligand field or different substituent. It is proposed that antiferromagnetic-like interactions between FeII ions play important role in the induction of spin transition in the dinuclear FeII complexes. However, most studies focus to change the ligands coordinated on the central iron directly. On the contrary, the insertion of paramagnetic FeIII is rare,3 but is structurally interesting. We have synthesized the mixed valence triple helicate iron complexes and try to investigate the spin state through the NMR studies.

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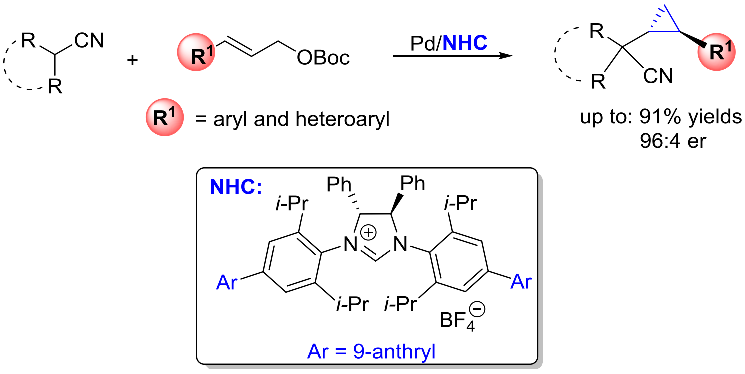
Palladium/*N*-Heterocyclic Carbene-Catalyzed Enantioselective Cyclopropanation Reaction of Nitriles with Mono Substituted Allyl Carbonates

Gao-Peng Zhang, Xue-Long Hou*

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry (SIOC); *Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, SIOC, 345 Lingling Road, Shanghai 200032, China; *xlhou@sioc.ac.cn*

Cyclopropanes are a unique class of structural elements and constitute versatile intermediates for a variety of synthetically useful ring-opening transformations.[1] As the results, there has been an increasing demand for the synthesis of cyclopropanes, especially in enantiopure form. In this regard, Pd-catalyzed asymmetric cyclopropanation of nucleophiles with allyl reagents has emerged as a highly productive methodology for the construction of cyclopropanes.[2] Herein, a novel catalytic system of Pd-catalyzed enantioselective cyclopropanation of nitriles has been developed simply using a monodentate NHC as ligand for the first time. The factors influencing the selectivities of the reaction were also investigated.



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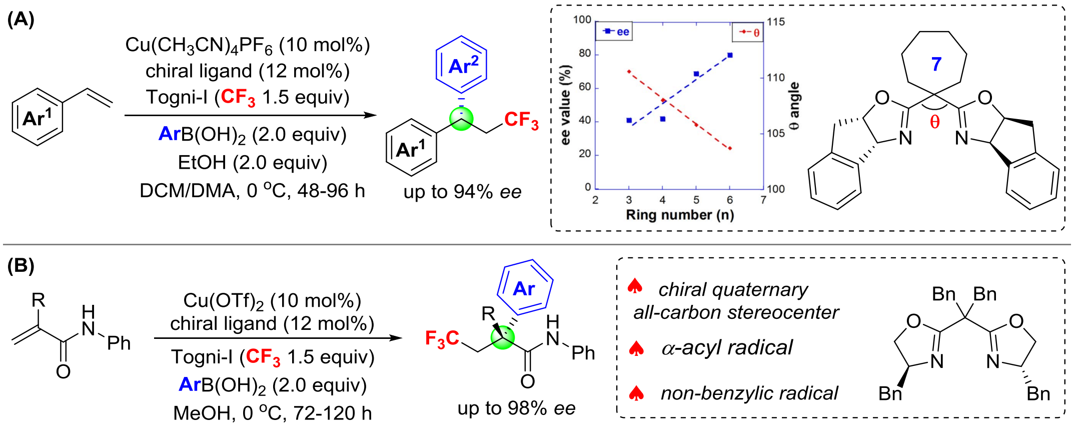
Copper-Catalyzed Asymmetric Arylation of Alkenes via Radical Relay Process

Lianqian Wu, Fei Wang, Xiaolong Wan, Dinghai Wang, Pinhong Chen, Guosheng Liu

Email: *gliu@mail.sioc.ac.cn*

A novel asymmetric radical trifluoromethyl-arylation of alkenes has been developed, which provides an efficient approach to access chiral CF_3-containing 1,1-diarylalkane derivatives with good to excellent enantioselectivity (Scheme 1A).[1] The key to success of this process is the logical design of the chiral ligands and the utility of the method is demonstrated by accessing modified bioactive molecules.

An enantioselective copper-catalyzed arylation of tertiary carbon-centered radicals, leading to quaternary all-carbon stereocenters, has been developed (Scheme 1B).[2] The tertiary carbon-centered radicals, including both benzylic and non-benzylic radicals, were efficiently captured by chiral aryl copper(II) species to give C-Ar bonds with excellent enantioselectivity.[3] Importantly, an acylamidyl (CONHAr) group adjacent to the tertiary carbon radical is essential for the asymmetric radical coupling.



Scheme 1. Copper-catalyzed asymmetric arylation of alkenes via radical process

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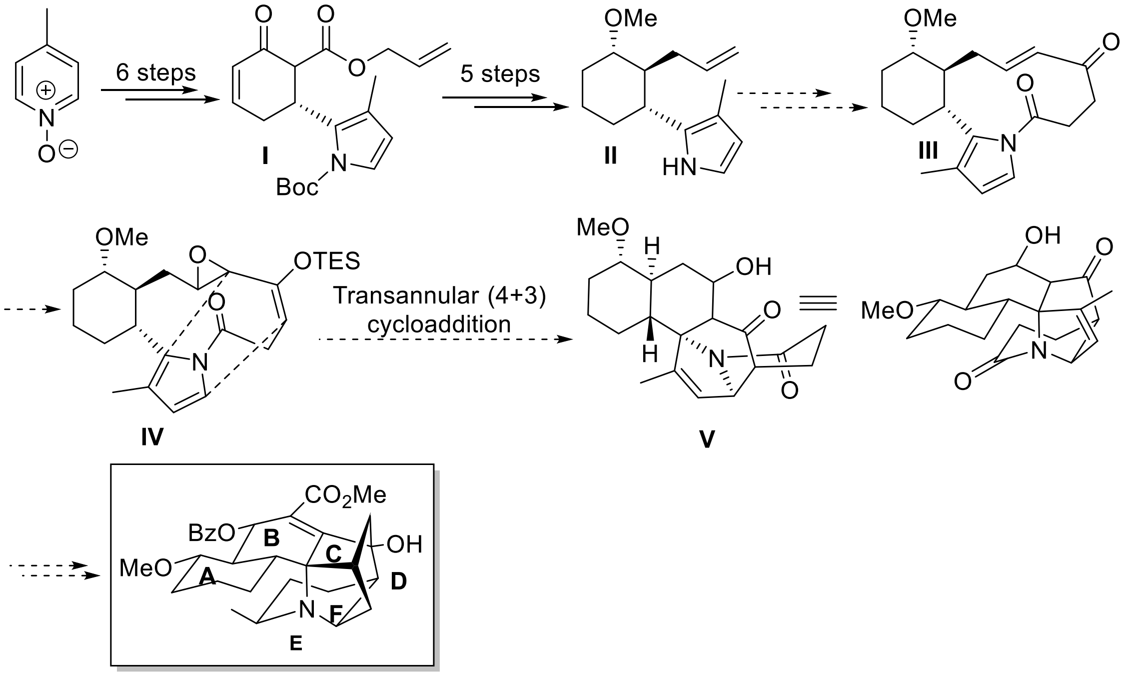
Studies Toward The Total Synthesis Of Himandrine

Yuxuan HE, Pauline Chiu*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong
pchiu@hku.hk

Abstract

Himandrine is a Class II Galbulimima alkaloid which was isolated from the bark of trees of the genus *Galbulimima.* Although there have been many attempts to synthesize the structurally complex alkaloids, only one total synthesis has been reported.[1]

Herein we propose a new approach toward himandrine. We have asymmetrically assembled the A ring in **I** by a modified tandem Michael-Wittig reaction.[2] We plan to assemble **IV** to undergo a pyrrole transannular (4+3) cycloaddition[3] to provide the tropinone skeleton **V**. Our progress in this synthesis will be presented.



(–) Himandrine

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Cooperativity in Shape-Persistent Bis-(Zn-Schiff Base) Catalysts for Highly Efficient Cyclic Carbonate Formation

Yeqing Xia and Michael C. W. Chan*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon.
Email: mcwchan@cityu.edu.hk

Carbon dioxide is a particularly attractive C_1 feedstock because it is sustainable, economical and non-toxic, and many catalyst systems have been developed to mediate its transformation into useful chemicals. We previously adopted a *shape-persistent bimetallic design approach* using two Zn-salphen units bridged by a rigid organic moiety, with the aim of (i) tuning and enhancing the catalytic capabilities of the resultant Zn_2 framework by changing the nature and dimensions of these components, and (ii) potentially creating cooperative reactivity. Importantly, selected bimetallic catalysts displayed excellent activities for cyclic carbonate formation from CO_2 and epoxides, which greatly exceeded those for the corresponding mononuclear analogues.[1]

In this work, a series of conformationally rigid bis-(Zn-Schiff base) complexes linked by a planar bridging unit has been designed and synthesized, and a variety of functionalities have been introduced to investigate substituents effects. The capabilities of these complexes as catalysts for CO_2-epoxide coupling reactions, in conjunction with tetrabutylammonium iodide cocatalysts, have been examined under different conditions. Exceptionally high initial molecular turnover frequencies have been achieved, which are among the best reported to date in the field of organic carbonate synthesis. The possibility of cooperative effects between the metal centers has been investigated using in-situ (ReactIR) spectroscopy, and a plausible reaction mechanism is proposed.

This work was supported by the Research Grants Council of the Hong Kong SAR, China (CityU 11304617).

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Hydrogenolysis of carbon–carbon σ-bonds using water catalysed by semi-rigid diiridium(III) porphyrins

Ching Wai Fong, Ho Yin Yu, Claude P. Gros and Kin Shing Chan*

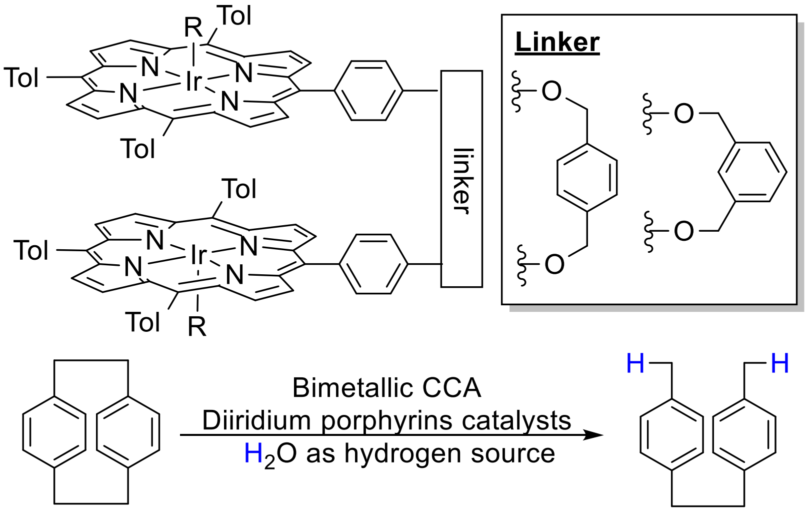
Department of Chemistry, The Chinese University of Hong Kong, Shatin,

New Territories, Hong Kong SAR, People's Republic of China.

E-mail: ksc@cuhk.edu.hk

Abstract

Semi-rigid diiridium(III) porphyrin alkyls with m-xylyl and p-xylyl diether linkers were synthesized. They were found to be catalysts for the carbon–carbon σ-bond hydrogenolysis of [2.2]paracyclophane under neutral conditions using water as the hydrogen source. The ether linkages in semi-rigid diiridium(III) porphyrins are unstable and undergo cleavage during the reaction.



Acknowledgements

The authors are thankful for the financial support from the General Research Fund of Hong Kong (No. 14301717) and the PROCORE France/Hong Kong Joint Research Scheme 2016/17 (F-CUHK 404/16).

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C.W. Fong, H. Y. Yu, C. P. Gros and K. S. Chan. *New J. Chem.*, **2019**, *43*, 3656

Iodine Catalyzed Transfer Hydrogenation of C-C σ-Bond with Water

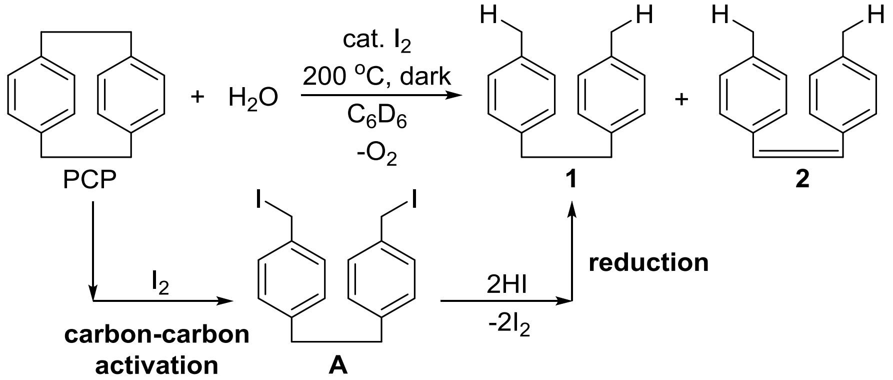
Wu Yang, Ching Tat To and Kin Shing Chan*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, People's Republic of China

E-mail: ksc@cuhk.edu.hk

Abstract

Iodine catalysed the transfer hydrogenation of benzylic C-C bond in [2.2]paracyclophane (PCP) with water to yield 4,4'-dimethylbibenzyl **1**. The C-C σ-bond was first cleaved by the homolytic radical substitution with iodine radical, derived in situ by thermolysis of molecular iodine, to afford the diiodo intermediate **A**. The benzylic C-I bonds in **A** were consecutively reduced by HI, generated in situ from the disproportionation of I_2 with H_2O, to furnish the transfer hydrogenation and regenerate I_2. This transformation demonstrates the isolobal in fragment between iodine radical and rhodium(II) metalloradical for aliphatic carbon-carbon activation, and between hydrogen iodide and rhodium(III) hydride as a hydrogen atom donor.[1,2]



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Catalytic Hydrogenolysis of Cyclooctane with Rhodium Porphyrin Complexes

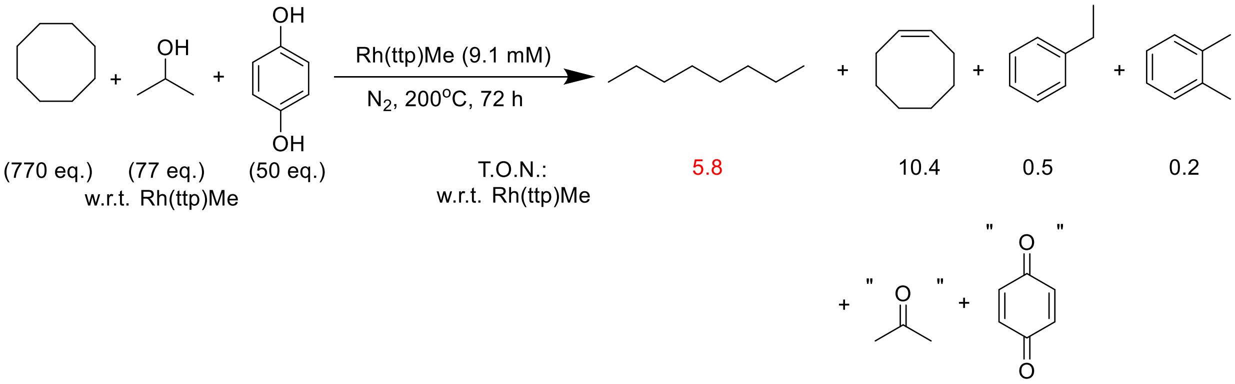
Yu Ho Yin, Kin Shing Chan*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, People's Republic of China

E-mail: ksc@cuhk.edu.hk

Abstract

The Rh^{III}(ttp)Me catalyzed hydrogenolysis of cyclooctane was achieved, although in slow rate. Besides the desired n-octane product, dehydrogenation and isomerization products were also produced, including cyclooctene, ethylbenzene and o-xylene. Phenolic species can promote the transformation. Based on the stoichiometric carbon-carbon bond activation by rhodium porphyrin reported by our group, Rh^{II}(ttp) radical is proposed as the active catalyst.[1] Further optimization and mechanistic study are underway.



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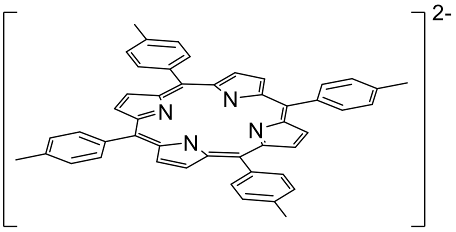

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Copper-mediated 1,2-bis(trifluoromethylation) of Arynes & Trifluoromethylation of Unactivated Alkenes with Me_3SiCF_3 and *NIS*

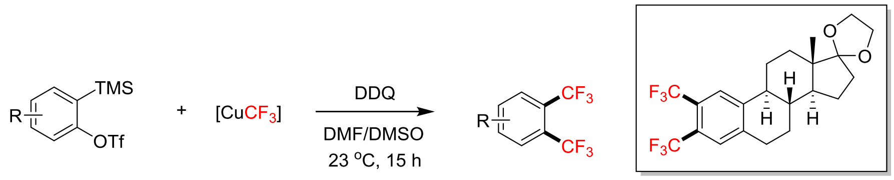
Xinkan Yang, Gavin Chit Tsui*

The Chinese University of Hong Kong, Shatin, N.T., Hong Kong
gctsui@cuhk.edu.hk

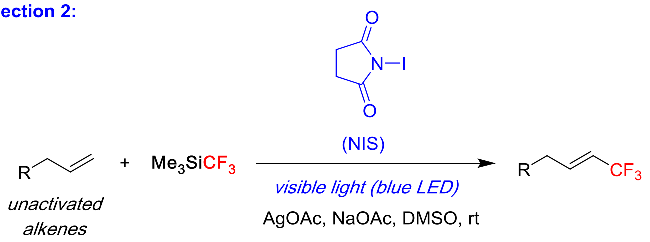
Section one we will describe an unprecedented 1,2-bis(trifluoromethylation) of arynes with $[CuCF_3]$[1] in the presence of an oxidant DDQ[2] The method allows the rapid construction of a new class of 1,2-bis(trifluoromethyl) arenes in one-step from aryne precursors under mild conditions. Its synthetic utility has been demonstrated in the preparation of bis(trifluoromethylated) molecules with potential pharmaceutical and materials science applications. Mechanistic studies indicated the presence of an *o*-trifluoromethyl aryl radical intermediate via CF_3 group transfer from $[CuCF_3]$ to the aryne.

In section two, a novel approach to the trifluoromethylation of unactivated alkenes is presented.[3] This reaction is promoted by *N*-iodosuccinimide (NIS) under visible light irradiation without the need for photocatalysts. The mild conditions allow the direct synthesis of useful trifluoromethylated (*E*)-alkenes from readily available alkene feedstocks with excellent functional group tolerability.

Section 1:



Section 2:



- ◉ no precious metal photocatalyst
- ◉ no gaseous CF_3I
- ◉ no strong oxidant
- ◉ high *E*-selectivity
- ◉ broad FG tolerability

References

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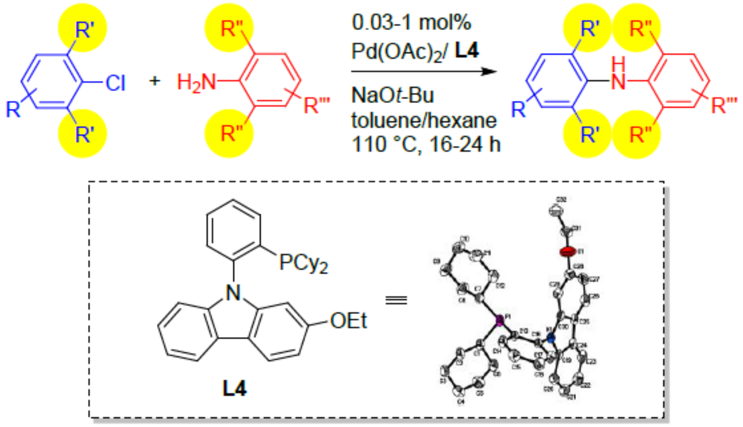
Sterically Hindered Amination of Aryl Chlorides Catalyzed by a New Carbazolyl-Derived P,N-Ligand-Composed Palladium Complex

Wing In Lai, Man Pan Leung, Pui Ying Choy, Fuk Yee Kwong*

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

E-mail: *fykwong@cuhk.edu.hk*

Abstract



A family of benzo[*c*]carbazolyl-based phosphine ligand **L1**-**L4** has been synthesized and their efficacy in promoting the steric hindered Buchwald-Hartwig amination has also been evaluated. In the presence of $Pd(OAc)_2$ (0.03-1.0 mol%) associated with the newly developed carbazolyl-derived phosphine ligand **L4**, the tetra-*ortho*-substituted diarylamines synthesis proceeded smoothly with excellent product yields (up to 99%). Remarkable result was obtained even for the coupling of highly sterically congested 2,4,6-triisopropylaniline and hindered 2-chloro-1,3-diisopropylbenzene (96% isolated yield). A possible decomposition pathway for anthracenyl C-N coupling product is also reported.

Reference

Lai, W. I.; Leung, M. P.; Choy, P. Y.; Kwong, F. Y. *Synthesis*, **2019**, submitted

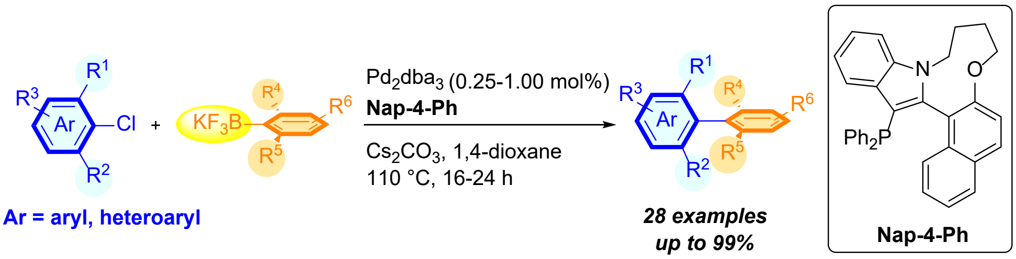
Development of Tunable Linkage Phosphine Ligands for Highly Steric Hindered Tetra-*Ortho*-Substituted Biaryl Synthesis

Man Pan Leung; Pui Ying Choy; Fuk Yee Kwong*

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

E-mail: fykwong@cuhk.edu.hk

Abstract



The first general example of tera-*ortho*-substituted biaryl synthesis *via* Suzuki-coupling of potassium aryltrifluoroborates and (hetero)aryl chlorides is reported. Organotrifluoroborates might act as a better coupling partner than arylboronic acids for Suzuki-coupling due to no association of uncertain amount of boroxine. Its significantly lower activity leads such transformation remains challenging. Herein, a new series of tailor-made indolyl-phosphine ligands bearing a tunable linkage is designed for the challenging tetra-*ortho*-substituted biaryl synthesis. Under the Pd_2dba_3/ **Nap-4-Ph** catalytic system, a wide range of sterically hindered chloroarenes coupled-well with bulky aryltrifluoroborate salts in good-to-excellent yields (up to 99%) with catalyst loading down to 0.25 mol%.

ZnI_2-Catalyzed Regioselective Cascade 1,4-Conjugate Addition/5-*exo-dig* Annulation Pathway for One-pot Access of Heterobiaryl Frameworks

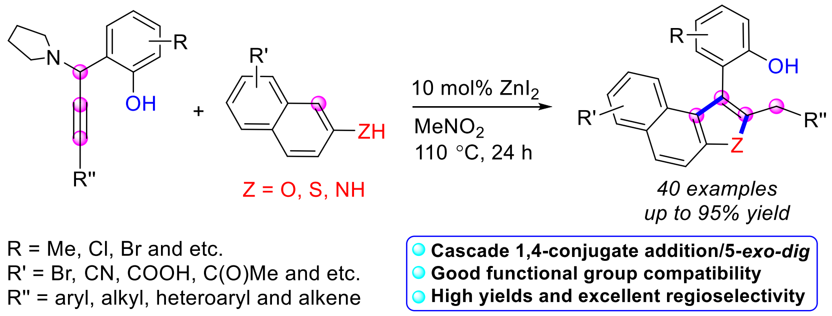
On Ying Yuen, Xinwei He, Fuk Yee Kwong*

Department of Chemistry, The Chinese University of Hong Kong,

Shatin, New Territories, Hong Kong

Email: fykwong@cuhk.edu.hk

A facile access of π-extended heterobiaryl *via* non-cross-coupling strategy has been achieved. In the presence of inexpensive ZnI_2 catalyst and versatile starting materials of propargylamines and *β*-naphthols (or *β*-naphthylamine, *β*-naphthyl mercaptan), a variety of steric hindered heterobiaryl frameworks can be easily achieved. The present catalytic system offers excellent selectivity, good-to-excellent product yield and good functional group tolerance, for instance nitrile, carboxylic acid and ketone moieties, and particularly the –Br and –Cl groups which are not often compatible under conventional coupling reaction conditions. This cyclization process is proposed to proceed through an *in situ* generated alkynyl *o*-quinone methides (*o*-AQMs), following a cascade intermolecular 1,4-conjugate addition/5-*exo-dig* annulation/1,3-H shift pathway.



Related reference:

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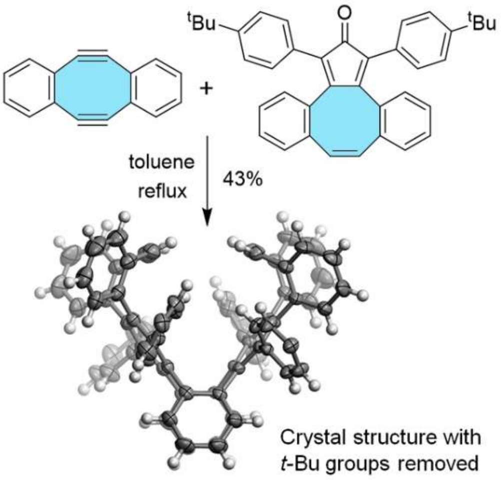
Synthesis of Tribenzo[a,c,e]cyclooctene Oligomers: Toward Negatively Curved Nanocarbons

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

Abstract

Seven- or eight-membered rings embedded in a graphitic network induce negative curvature as displayed by saddle-shaped surfaces in Mackay crystals, which are theoretical three-dimensional carbon allotropes first proposed by Mackay and Terrones in 1991.[1] Negatively curved carbon allotropes are potentially a new frontier of carbon nanoscience after fullerenes, carbon nanotubes and graphene,[2] but are yet to be synthesized.



Herein, we report design and synthesis of tribenzo[a,c,e]cyclooctene oligomers, which are potential precursors for synthesis of negatively curved nanographenes and nanobelts. The key of this synthesis is connecting 1,3-di(4-t-butylphenyl)-dibenzo[e,i]-2Hcyclopentacycloocten- 2-one, dibenzo[3,4:7,8]cycloocta[1,2-c:5,6-c'] difuran and Sondheimer−Wong diyne through Diels-Alder reactions. As revealed by X-ray crystallography, the trimer with a C8-C6-C8-C6- C8 backbone is shaped like a letter C in the crystalline state.

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Halogenated Tetraazapentacenes with Electron Mobility as High as 27.8 cm^2/Vs in Solution-Processed N-channel Organic Thin Film Transistors

Ming Chu, Jian-Xun Fan, Shuaijun Yang, Dan Liu, Chun Fai Ng, Huanli Dong,
Ai-Min Ren,* Qian Miao*

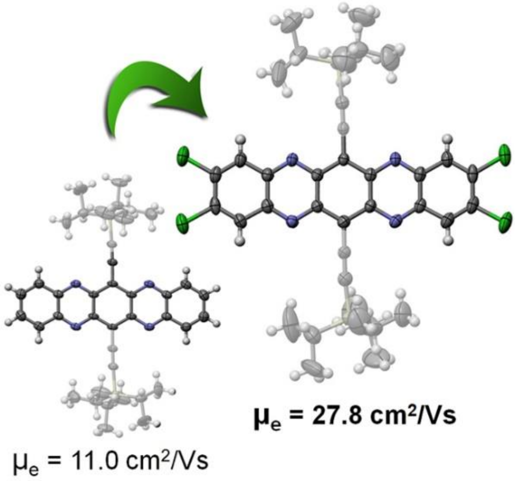
Department of Chemistry, The Chinese University of Hong Kong,

Shatin, New Territories, Hong Kong. P. R. China

E-mail: miaoqian@cuhk.edu.hk

Abstract

Molecular engineering of tetraazapentacene with different number of fluorine and chlorine substituents fine-tunes frontier molecular orbitals, molecular vibrations and π-π stacking for n-type organic semiconductors. Among the six halogenated tetraazapentacenes studied herein, the tetrachloro derivative (4Cl-TAP) in solution-processed thin film transistors exhibits electron mobility of 14.9 ± 4.9 cm^2/Vs with a maximum value of 27.8 cm^2/Vs, which sets a new record for n-channel organic field effect transistors. The computational studies on the basis of crystal structures shed light on the structure-property relationships for organic semiconductors.



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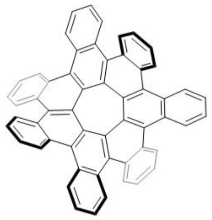
Fully *Ortho*-Benzannulated [n]Circulenes: Synthesis and Remarkable Supramolecular and Solid-State Behavior

Sai Ho Pun, Yujing Wang, Ming Chu, Qian Miao*
Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories,
Hong Kong, China; miaoqian@cuhk.edu.hk

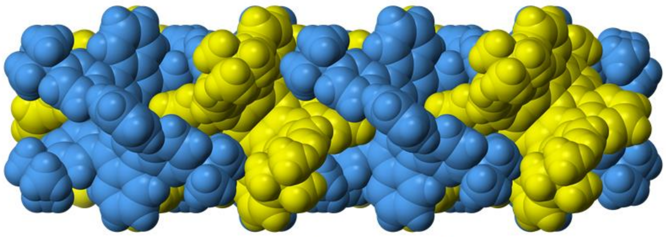
This study puts forth two new members of fully *ortho*-benzannulated [n]circulenes, heptabenzo[7]circulene (**6**) and octabenzo[8]circulene (**7**), which are new negatively curved nanographenes and also represent unprecedented structures of septuple [4]helicene and octuple [4]helicene, respectively. The successful synthesis of them through Scholl reaction in good to excellent yields takes advantage of the reactivity of naphthalene. Quantum chemistry calculations reveal that (**6**) and (**7**) are both flexible π-molecules and adopt saddle-shaped geometry of C_2 and D_{2d} symmetry, respectively, at the global energy minimum in agreement with the single crystal structures. A serendipitous discovery from this study is that tetra(*t*-butyl) octabenzo[8]circulene in the single crystals self-assemble into a supramolecular nanosheet with an unprecedented motif of π-π stacking. Such a new molecular packing mode, in combination with the demonstrated semiconducting property of octabenzo[8]circulene, suggests a new supramolecular two-dimensional material.

Fully *Ortho*-Benzannulated [n]Circulenes



6
Heptabenzo[7]circulene

7a (R = H)
7b (R = ^{t}Bu)
Octabenzo[8]circulene



Unprecedented Two-Dimensional Packing of **7b**

Reference

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Crystal Engineering of Phenylene-Containing Acenes for High-Mobility Organic Semiconductors

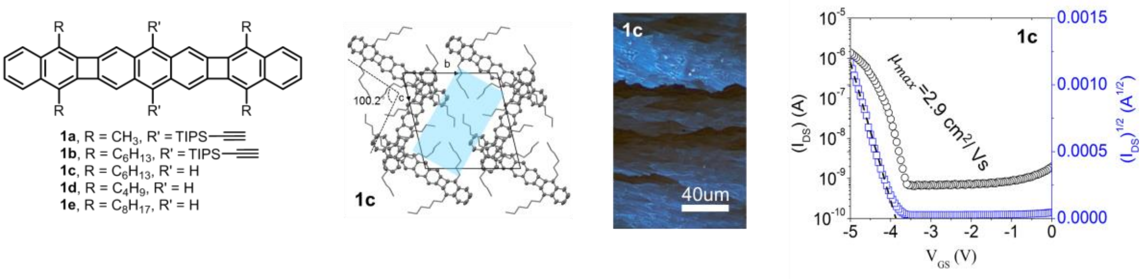
Jinlian Wang[1]*, Ming Chu*[1]*, Jianxun Fan*[2]*, Ai-Min Ren*[2, *]*, Qian Miao*[1, *]

[1] Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

[2] Institute of Theoretical Chemistry, Laboratory of Theoretical and Computational Chemistry, Jilin University, Changchun, 130023, China

E-mail: aimin_ren@yahoo.com, miaoqian@cuhk.edu.hk

Among the polycyclic aromatic hydrocarbons (PAHs), acenes are one of the most important candidates for high-performance organic semiconductors. However, as the length of the acene increases, the reduction of their chemical stability and aromaticity has imposed a limitation on their syntheses and applications in OTFTs.[1] Insertion of four-membered rings into acenes results in phenylenes, with multiple aromatic sextets according to Clar,[2] thus leading to enhanced aromaticity and stability.



Herein we design phenylene-containing acenes **1a-e** with two 4-membered rings and three aromatic sextets, leading to enlongated π-system, without compromising their stability or changing their linear shape.[3] With the compounds **1a-e** in hand, we tested their semiconductor properties using drop-casting method, and **1c** functioned as a p-type semiconductor with a field effect mobility as high as 2.9 cm^2/ Vs. (Figure 1)

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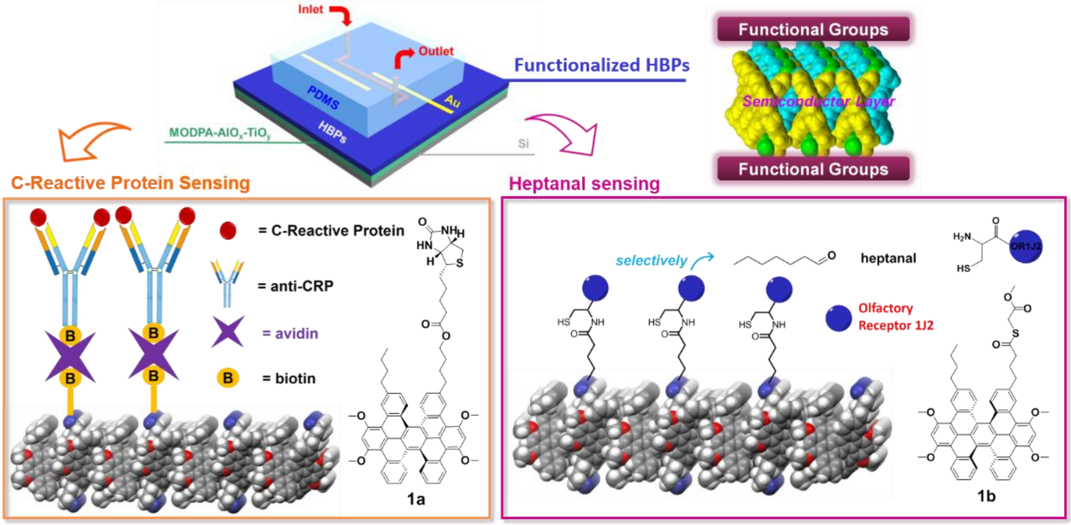
Bioelectronic Sensors Based on Functionalized π-Stacks of Hexabenzoperylenes

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

Our group recently discovered that Hexabenzoperylenes can accommodate a wide variety of functional groups without sacrificing π-π interactions in the solid state, suggested a general platform for OFET sensing by self-assembling into a semiconducting nanosheet. [1] This study demonstrates that this platform allows for the quantitative, in situ, and in real time monitoring of bio-affinity reactions between analytes from solution to the surface-immobilized receptors as a bioelectronic sensor. The examples given include the binding of C-Reactive Protein (CRP) from solution to the anti-CRP antibodies immobilized on the surface of biotin-functionalized HBP (**1a**) which has be modified with avidin. The preliminary results show that this bioelectronic sensor has enabled quantitative and highly sensitive detection of CRP in the 0.05–50 μg mL^{-1} concentration range with an increase of electrical current. The same device containing thioester-functionalized HBP (**1b**) has been demonstrated to selectively detect heptanal, which is the diagnosis of lung cancer down to a concentration of 1×10^{-7} M based on the most powerful ligation method to graft cysteine-functionalized proteins Olfactory receptor 1J2 (OR1J2) on the surface. The bioelectronic sensor is promising to enable the highly sensitive and selective detection of biological species that are important in medical diagnosis.



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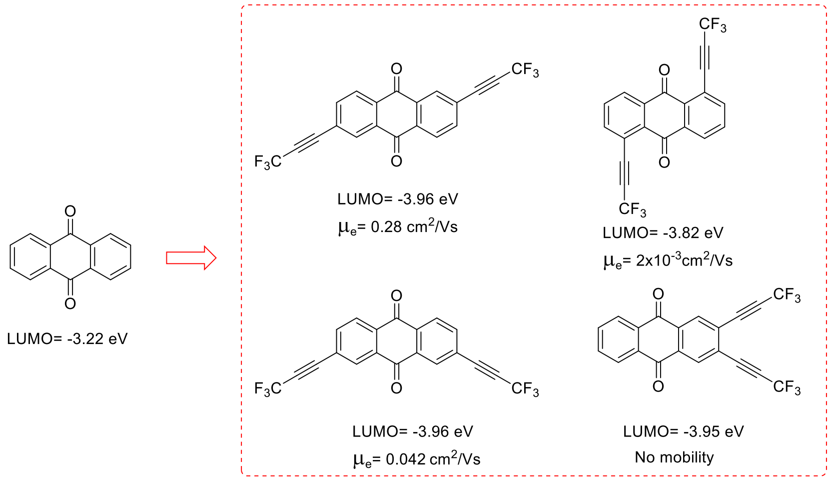
Trifluoromethylethynylated Anthraquinones for n-Type Organic Semiconductors

Mengna Zhao, Xinkai Yang, Gavin Chit Tsui, Qian Miao*
Department of Chemistry, the Chinese University of Hong Kong,
Shatin, New Territories, Hong Kong, China
*Email: miaoqian@cuhk.edu.hk

The ultimate success of high performance OFETs requires organic semiconductors that have high field effect mobility, robust environmental stability and easy processability. Up to now, only a very limited number of electron-deficient building blocks have been developed and utilized in the design of n-type organic semiconductors with high performance. Therefore, more electron-deficient building blocks need to be explored[1]. Quinones, well known as oxidizing reagents in organic synthesis, are one type of promising candidate as organic semiconductors, but have not been extensively studied. Herein, trifluoromethylethynylated anthraquinones have been synthesized using a facile method reported recently[2]. Trifluoromethylethynyl group was first reported to be utilized as an electron-deficient building block for n-type organic semiconductors. It was found that it can dramatically lower the LUMO energy level of anthraquinones to about -3.9 eV. They have been explored as n-type organic semiconductors with the highest electron mobilities of 0.28 cm^2 V^{-1} s^{-1}.



Reference

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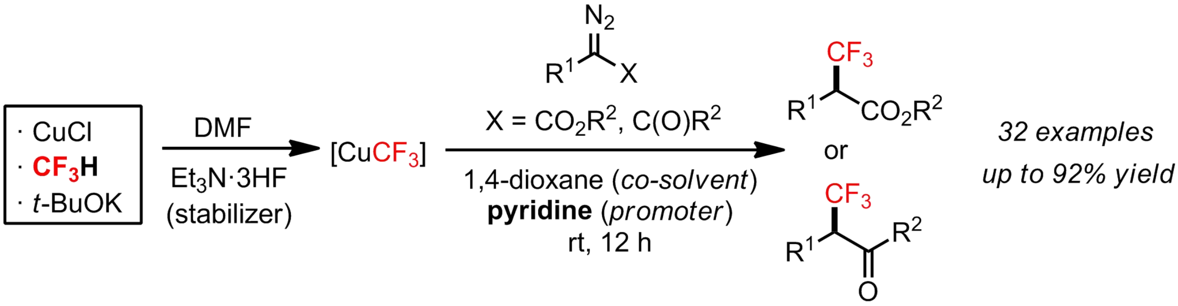
Trifluoromethylation of *α*-Diazoesters and *α*-Diazoketones with Fluoroform-Derived $CuCF_3$: Synergistic Effects of Co-solvent and Pyridine as a Promoter

Qiao Ma and Gavin Chit Tsui*

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

E-mail: gctsui@cuhk.edu.hk

We herein describe a new protocol for copper-mediated trifluoromethylation of *α*-diazoesters and *α*-diazoketones, both using readily available fluoroform-derived $CuCF_3$. The synergistic effect of using 1,4-dioxane as co-solvent and pyridine as promoter is revealed. Reaction conditions are mild and easy to handle, allowing the synthesis of a range of *α*-trifluoromethyl esters and ketones in one-step from *α*-diazo carbonyl compounds. The ultimate CF_3 source is the inexpensive, nontoxic, industrial waste fluoroform.



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Stereospecific Iron-Catalyzed Carbon(sp^2)-Carbon(sp^3) Cross-Coupling with Alkyllithium and Alkenyl Iodides

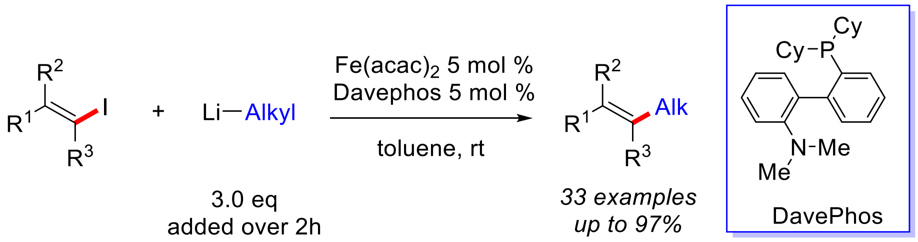
Xiaolin LU, Xiao-Shui PENG*, Henry. N. C. WONG*

Postal address: Department of Chemistry, and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong.

Email: hncwong@cuhk.edu.hk

Abstract

Transition metal-catalyzed cross-coupling reactions for the selective formation of C-C bonds enable the facile preparation of various structurally diverse and complex molecules[1]. The development of an approach to replace Pd/Ni of more economic and environmentally friendly metals is currently in high demand[2]. Herein, an efficient synthetic protocol involving iron-catalyzed cross-coupling reactions between organolithium compounds and alkenyl iodides as key coupling partners was achieved. More than 30 examples were obtained with moderate to good yields and high stereospecificity. Gram-scale and synthetic applications of this procedure are recorded to demonstrate its feasibility and potential utilization.



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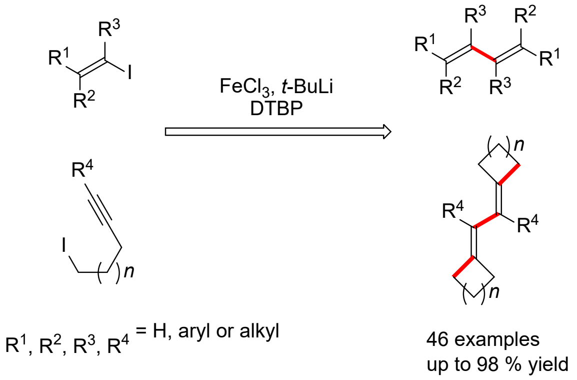
Ligand-Free Iron-Catalyzed Carbon(sp^2)−Carbon(sp^2) Oxidative Homo-Coupling of Alkenyllithiums

Zhuliang Zhong [a], Zhiyong Wang [a], Xiao-Shui Peng [a,b] and Henry N. C. Wong*[a,b]
[a]*Department of Chemistry, State Key Laboratory of Synthetic Chemistry,*
The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China
[b]*Shenzhen Municipal Key Laboratory of Chemical Synthesis of Medicinal Organic Molecules & Shenzhen*
Center of Novel Functional Molecules, Shenzhen Research Institute,
The Chinese University of Hong Kong, No.10. 2nd Yuexing Road, Shenzhen518507, China
Email: hncwong@cuhk.edu.hk

Transition-metal-catalyzed coupling reactions have become cornerstones of many carbon-carbon bond-forming process in recent years.[1] With low cost, high natural abundance, and low toxicity, iron has attracted significant research interests. Here a new strategy was developed for the efficient synthesis of di-, tetra- and hexa-substituted 1,3-butadienes. This one-pot procedure involves lithium-iodine exchange to generate the corresponding vinyllithium intermediates. A subsequent iron-catalyzed ligand-free oxidative homo-coupling eventually led to the formation of 1,3-butadienes in acceptable to excellent isolated yields.[2]



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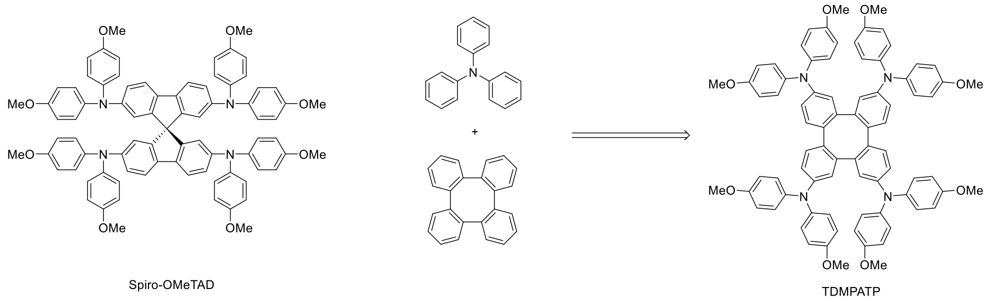
Synthesis and Application of Tetraphenylene Derivatives in Hole-Transport Materials

Xiang Xu, Henry N. C. Wong*

Department of Chemistry, State Key Laboratory on Synthetic Chemistry, State Key Laboratory of Synthetic Chemistry.
The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China
Email: hncwong@cuhk.edu.hk

Abstract

In the past years there has been a surge of interest in perovskite solar cells (PSCs) due to their easy fabrication and superb photoelectric properties since the first report on an all solid state PSC adopting 2,2-7.7-tetrakis (*N,N*'-diparamethoxyphenylamine)-9,9'-spirobifluorene (Spiro-OMeTAD) as the hole transport material (HTM).[1] A typical PSC is constructed using multiple stacked materials, including a glass substrate, an n-type semiconductor fluorine doped tin oxide (FTO) with a gold electrode as an anode, a very thin and compact TiO_2 layer to block holes, a mesoporous TiO_2 scaffold infiltrated with perovskite or just a perovskite layer and a hole-transporting layer with a gold cathode. Among the materials used to fabricate PSC devices, HTMs play a key role in enhancing the solar cell efficiency by inducing efficient hole transport and slowing electron–hole recombination.[2] Triphenylamine (TPA) is a kind of constitutional unit widely used in organic HTMs and tetraphenylene featuring a rigid nonplanar and stable molecule may tend to offer higher glass transition temperature as well as imparting a better thermal and chemical stability. Hence, we then plan to synthesize 2,7,10,15-tetrakis(*N,N'*-diparamethoxyphenylamine)tetraphenylene (TDMPATP), derived from tetraphenylene skeleton and triphenylamine units, attempting to investigate its properties and possible application in HTMs.



Acknowledgement

This work was supported by an Area of Excellence Scheme established under the University Grants Committee of the Hong Kong SAR, China.

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Synthesis and Application of Tetraphenylene-Based Macrocyclic Derivatives

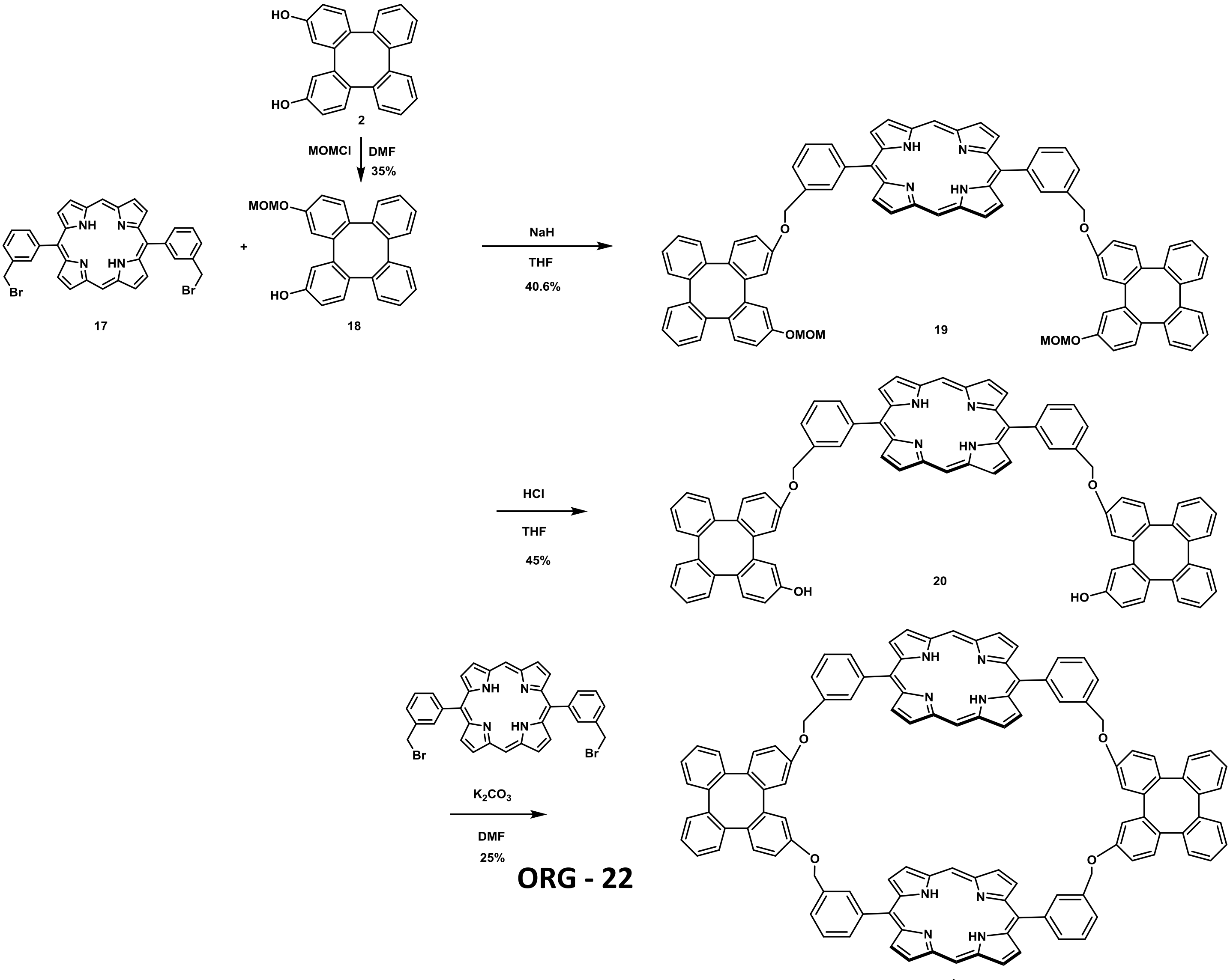
Yang Jiyuan, Deng ChunLin, Xiao-Shui Peng, Henry N. C. Wong*

Department of Chemistry, Center of Novel Functional Molecules and Institute of Molecular Functional Materials[†], State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China
E-mail: hncwong@cuhk.edu.hk

ABSTRACT

The design and synthesis of novel molecular cages are undoubtedly one of the most important research topics in host-guest chemistry and supramolecular chemistry[1]. We have proven that tetraphenylene-based macrocyclic derivatives with porphyrin unit have specific molecular recognition properties attribed to their unique 3D rigid structure.[2].

The synthesis of Tetraphenylene-Based Macrocyclic can be achieved from building block bisphenol **2**, and the details will be presented.

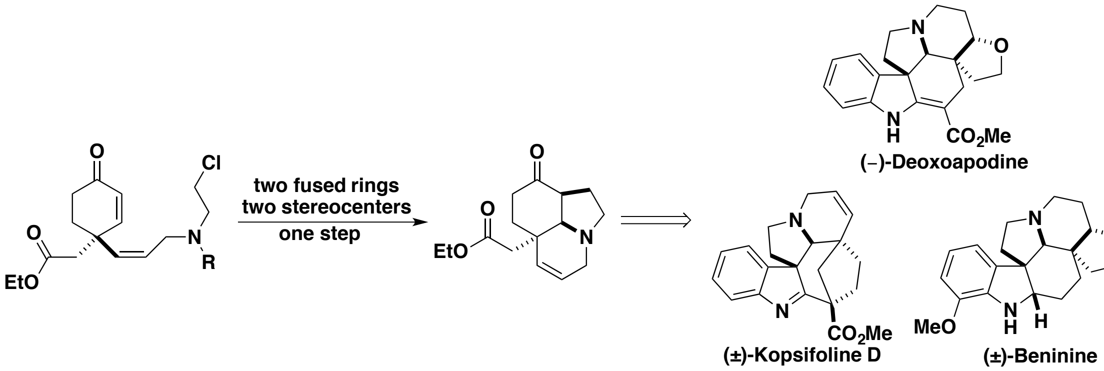


Total Syntheses of (–)-Deoxoapodine, (±)-Kopsifoline D and (±)-Beninine

Yi-Guo Zhou, Xiao-Shui Peng*, Henry N. C. Wong*
Department of Chemistry, and State Key Laboratory of Synthetic Chemistry,
The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China
*E-mail: xspeng@cuhk.edu.hk, hncwong@cuhk.edu.hk

Abstract

Delineated herein are the total syntheses of (−)-deoxoapodine,[1] (±)-kopsifoline D[2] and (±)-beninine.[3] Empowered by a cascade nucleophilic aromatic substitution/Micheal addition/intramolecular substitution protocol, the assembly of the core framework occurring in *Aspidosperma* and *Kopsia* alkaloids was accomplished in a single step with excellent chemo- and stereoselectivity. Corey-Bakshi-Shibata reduction was employed to induce the first chiral center in the early stages of the project. The chirality was further relayed to the backbone by Johnson-Claisen rearrangement. Indole nucleus was assembled by interrupted Fischer indolization. The strategy led to the total syntheses of three structurally diverse alkaloids, and it should be also applicable to the synthesis of some other structurally similar molecules.



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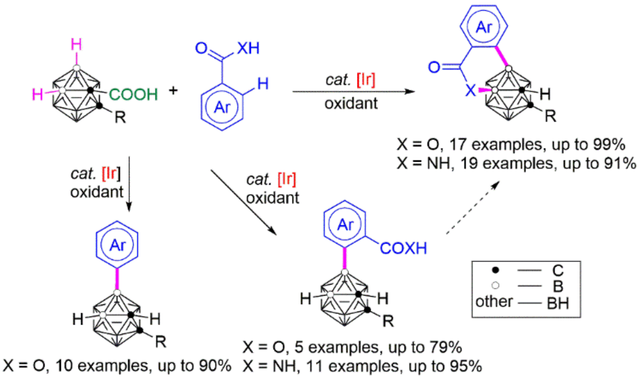
Catalytic Cascade Dehydrogenative Cross-Coupling: A One-Pot Process to Break Two B-H, One C-H, One X-H and Construct New B-C and B-X (X = O, N) Bonds

Yik Ki Au, Yangjian Quan, and Zuowei Xie*
Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The
Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China
E-mail: zxie@cuhk.edu.hk

Abstract

Carboranes, a class of carbon-boron molecular clusters, have many invaluable applications in organometallic chemistry, medicine, and materials science. Recently, by the introduction of directing groups at cage vertices, transition metal-catalyzed B-H activation have been achieved to realize numerous functionalization.[1] On the basis of these achievements and in view of the advantages of dehydrocoupling and cascade reactions, we have developed a straightforward and efficient methodology for the one-pot synthesis of previously unavailable carborano-coumarin or -isoquinolinone derivatives via catalytic cascade B-H/C-H and B-H/X-H (X=O, N) dehydrogenative cross-coupling between benzoic acid or benzamide and carboranyl carboxylic acid. A series of α-carboranyl benzamides, α-carboranyl benzoic acids and aryl carboranes can also be prepared selectively by tuning reaction conditions.



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Copper Catalyzed *o*-Carboranyl B-H Functionalization with Alkynes

Yu Chen, Yik Ki Au, Yangjian Quan,* Zuowei Xie*

Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong (China)

E-mail: yjquan@cuhk.edu.hk; zxie@cuhk.edu.hk

Abstract

Carboranes, a class of polyhedral boron-carbon molecular clusters, are finding a large variety of applications in a wide range of fields. In this connection, the development of methods for efficient and economic cage B-H functionalization is eagerly desired. Although transition metal catalyzed B-H activation has emerged as a viable strategy to functionalize carboranes,[1] base metal catalyzed cage B-H derivatization remains elusive. Herein we report the first example of base metal catalyzed selective cage B-H activation/functionalization.[2] Under the assistance of a bidentate directing group, Cu-catalyzed [4+2] annulation of carboranyl amides with internal alkynes affords unprecedented C,B-substituted carborane-fused-pyridone derivatives, whereas the use of terminal alkynes leads to B-H/C(sp)-H dehydrocoupling.

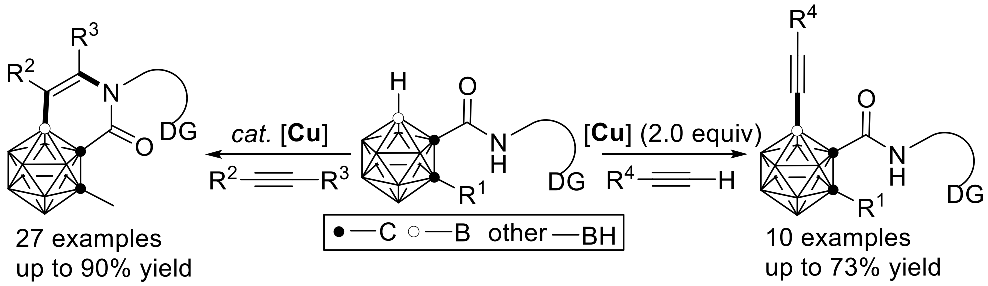

Figure 1: Copper Catalyzed Cage B-H Functionalization.

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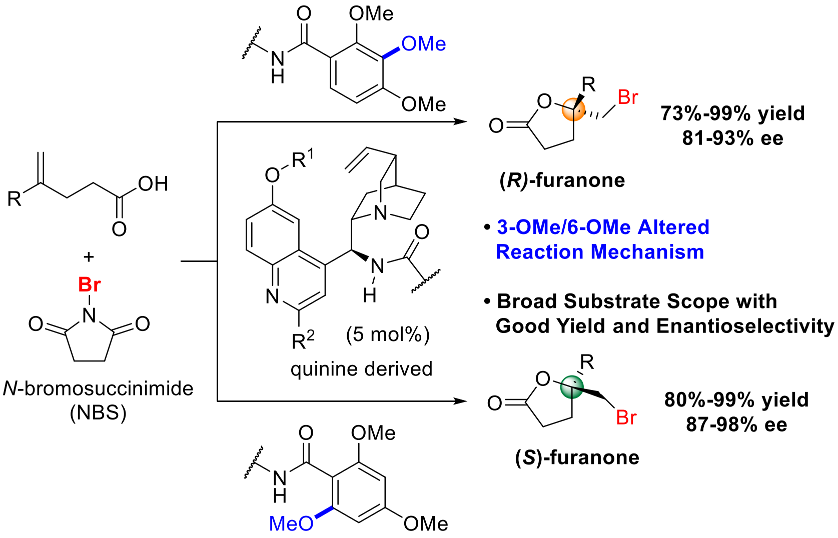
A Catalyst-Control Enantiodivergent Bromolactonization

Yuk-Cheung Chan and Ying-Yeung Yeung*
Department of Chemistry, The Chinese University of Hong Kong, Shatin, Hong Kong
E-mail: yyyeung@cuhk.edu.hk

Asymmetric catalysis allows the preparation of various enantioenriched products for pharmaceuticals. Many chiral catalysts that derived from natural source are not readily available in both antipodes. Enantiodivergent catalysis had been developed in the past decades to address this problem, commonly relied on utilizing different reaction conditions.[1] Simple manipulation on achiral residue of catalyst to switch enantiomeric induction is an attractive but undeveloped approach. Herein, we reported our recent work on enantiodivergent bromolactonization. A simple switch of methoxy substituent from *meta-* to *ortho-* position in benzamide moiety of catalyst leaded to a complete and opposite asymmetric induction. Our mechanistic study suggested 2,3,4- and 2,4,6-trimethoxybenzamide interact with NBS through different pathways.



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Extra π–π Interaction Stabilized Diimine [2]Rotaxanes

Chan Sing Ming and Ken Cham-Fai Leung*

Department of Chemistry, The Hong Kong Baptist University, Kowloon Tong

E-mail: cfleung@hkbu.edu.hk

Abstract

Three rotaxanes **RH-PF$_6$**, **Ph4RH-PF$_6$** and **Ph5RH-PF$_6$** were synthesized by dynamic imine clipping reaction. Except the expected [N$^+$–H···N] hydrogen bond interaction, the X-ray structures indicate that anthracene moiety on axle also has π–π interaction with the marcocycle of the rotaxanes. The π–π interaction stabilizes the formation and allows the isolation of rotaxanes. Dynamic combinatorial experiment indicates that the anthracene axle is more favourable than dimethoxy axle to undergo rotaxane clipping. It shows the potential of using imine clipping reaction *via* one pot synthesis of heterocircuit [*n*]rotaxanes.

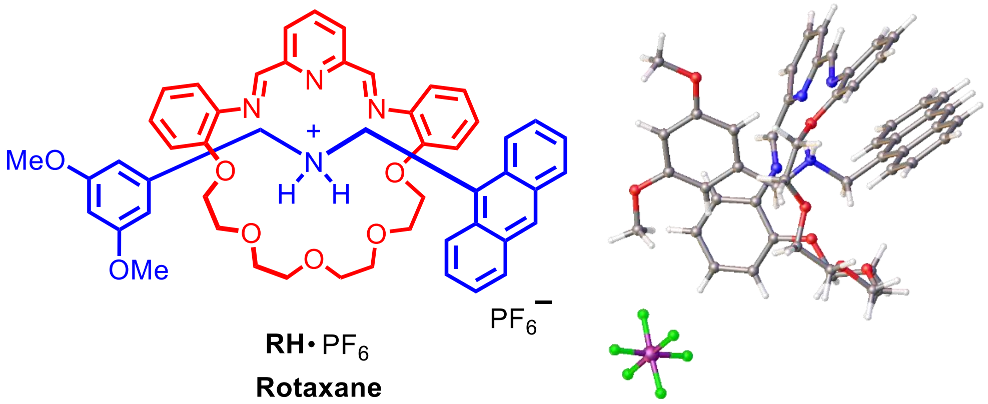

Figure (Left) Structural formula and (Right) solid-state structures of **RH-PF$_6$**.

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Xanthohumol and its Derivatives for Alzheimer's Disease: Inhibitory Effect of Amyloid-β Aggregation and Neuroprotection

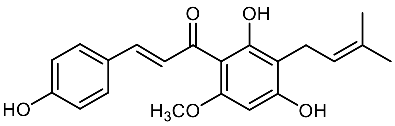
Xueli Wang, See-Lok Ho, Chung-Yan Poon, Ting Yan, Hung-Wing Li and Man Shing Wong*

Department of Chemistry, Hong Kong Baptist University, Hong Kong, SAR China

Corresponding authors: hwli@hkbu.edu.hk; mswong@hkbu.edu.hk

Abstract

Xanthohumol (Xn), a prenylated flavonoid that naturally presents in hop (*Humulus lupulus* L.) and beer. It has been reported that it shows cytoprotection through activation of Nrf2−ARE signaling pathway and capability of scavenging free radicals, suggesting its potential for the prevention of neurodegeneration. However, the bio-incompatibility and BBB impermeability of Xn limited its *in vivo* efficacy potential for treating neurodegeneration diseases such as Alzheimer's disease (AD). Herein, we report a series of novel xanthohumol derivatives that was designed and synthesized to explore their inhibitory effect on amyloid-β (Aβ) oligomerization and fibrillation as well as neuroprotection against Aβ induced toxicities. These derivatives were synthesized by facile base-catalyzed Claisen−Schmidt condensation of a prenylaryl methyl ketone and the corresponding aromatic aldehyde as a key step. Some of these Xn derivatives were found to exhibit a moderate to high inhibitory effect on $A\beta_{1-42}$ oligomerization and fibrillation. Interestingly, those biocompatible Xn derivatives also showed neuroprotection against the Aβ-induced ROS generation and intracellular $[Ca^{2+}]$ influx. Importantly, two of the neuroprotective xanthohumol derivatives were proved to be BBB permeable showing promising potential for treatment of AD.



Xanthohumol

Multidimensional Perovskite for Visible Light Driven Photocatalytic Hydrogen Evolution

Yang Li, Xunjin Zhu *
Hong Kong Baptist University
Email of corresponding author: xjzhu@hkbu.edu.hk

Abstract

For the long alkyl ligand with large size could not be located in the PbI_6 octahedral networks, the traditional three-dimensional perovskite structure was changed into sandwiched layer structure with better humid resistance and photostability. In this work the short methylammonium cations were partly replaced by octadecylamine cations (15% in molar ratio) to combine advantages from both sides. This is so called multidimensional perovskite.

Multidimensional perovskite $OA_{0.15}MA_{0.85}PbI_3$ has been proved very good photocatalysis performance and stability. It can achieve a H2 evolution rate of 960.2umol/(g*h). Also, its crystal structure was investigated by X-ray diffraction and SEM. Its band gap (1.56 eV) was obtained by CV and UV-VIS spectra. Steady state, time-resolved photoluminescence, photocurrent spectra and EIS helped to prove its good charge transportation ability among other ratios. The life time and photocatalysis quantum efficiency are 1.37ns and 1.67% respectively. After the characterization the multidimensional perovskite was confirmed to be essential in the photocatalysis applications.

Panchromatic ternary organic solar cells with porphyrin dimers and absorption-complementary benzodithiophene-based small molecules

Venkatesh Piradi,* Wai-Kwok Wong, Xunjin Zhu

Institute of Molecular Functional Materials, Department of Chemistry and Institute of Advanced Materials, Hong Kong Baptist University, Waterloo Road, Hong Kong, P. R. China.

Email of corresponding author- xjzhu@hkbu.edu.hk

Abstract

Diketopyrrolopyrrole-ethynylene-bridged porphyrin dimers are capped with electron deficient 3-ethylrhodanine (A_2) *via* a π-bridge of phenylene ethynylene, affording two new acceptor-donor-acceptor structural porphyrin dimers (DPP-2TTP and DPP-2TP) with strong absorption in ranges of 400–550 (Soret bands) and 700–900 nm (Q bands). Their intrinsic absorption deficiency between the Soret and Q bands could be perfect compensated by a wide bandgap small molecule DR3TBDTTF with absorption in 500–700 nm. Impressively, the optimal ternary device based on the blend films of DPP-2TPP, DR3TBDTTF (20 wt.%) and $PC_{71}BM$, shows a PCE of 11.15%, while the binary devices based on DPP-2TTP/$PC_{71}BM$ and DPP-2TP/$PC_{71}BM$ blend films exhibit PCEs of 9.30% and 8.23%, respectively. The high compatibility of the low bandgap porphyrin dimers with the wide bandgap small molecule provides a new threesome with $PC_{71}BM$ for highly efficient panchromatic ternary organic solar cells.

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Synthesis and photocatalytic property of a full-spectrum absorption structure porphyrin

SHEN Yue, Xunjin Zhu*
Department of Chemistry, Hong Kong Baptist university, Kowloon Tong, Kowlon, Hong Kong SAR.
E-mail: 17482178@life.hkbu.edu.hk

Previously, our group reported Zn-Tetra naphthalimide conjugated porphyrin(ZnT(p-NI)PP, which showed promising photocatalytic property for H2 production from aqueous solution.

For the optimization of ZnT(p-NI)PP, a full-spectrum absorption structure 5,15-naphthalimide -10,15-BODIPY-porphyrinato Zinc has been designed and synthesized. The luminescence range of BODIPY is from 470 nm to 530 nm, which complements the luminescence range of NI-PP to achieve full-spectrum luminescence. The H_2 production rate (ηH_2) of this structure reach 349 μmol g^{-1} h^{-1}. It's not higher than ZnT(p-NI)PP. The main reason is the poor photo-stability of BODIPY structure. Therefore, our work will focus on the way of developing the photo-stability of BODIPY structure, which further improving the photocatalytic property of the designed structure.

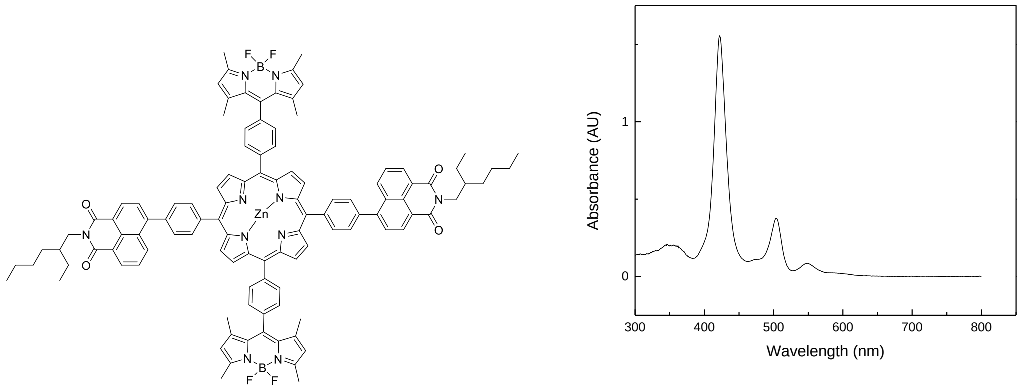

Figure Molecular structure and Absorption of 5,15- naphthalimide -10,15-BODIPY-porphyrinato Zinc

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Rh^{II}-Catalyzed Intermolecular C-H Arylation of Aromatics with Diazo Quinones

Kai Wu, Bei Cao, Cong-Ying Zhou,* and Chi-Ming Che*

Email: **cmc@hku.hk**

The development of efficient methods for the construction of biaryls is very important in organic synthesis, owing to the ubiquity of biaryls in natural products, pharmaceuticals and organic materials.[1] Transition-metal-catalyzed cross couplings between aryl halides (Ar-X) and aryl organometallic reagents (Ar-M) are the most powerful methods for synthesizing biaryls.[2] Although this approach is highly efficient, prefunctionalization of both coupling partners is required, and stoichiometric amounts of organometallic by-products are generated during the coupling. Metal-catalyzed C-H bond activation has recently emerged as a more straightforward and atom-economic method for the construction of biaryls.

We developed an efficient synthesis of biaryls by a dirhodium(II)-catalyzed aromatic C-H arylation with diazo quinones. The new biaryl synthesis can be performed under mild and neutral conditions and without directing group chelation assistance. The reaction tolerates various functionalities and is applicable to a broad range of aromatics. The regioselectivity of the C-H arylation was often high and predictable. The synthetic utility of the method was demonstrated by the late-stage modifications of a series of pharmaceuticals and functional materials as well as a short synthesis of a transthyretin amyloid inhibitor.

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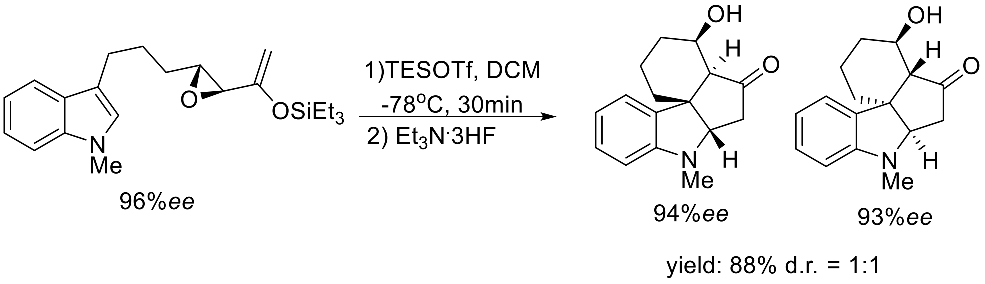
Dearomative Intramolecular (3+2) Cycloaddition Reactions of Indoles with Epoxy and Aziridinyl Enolsilanes

Yueyao Chen, Pauline Chiu*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong
pchiu@hku.hk

Abstract

Our group has developed inter- and intramolecular (4+3) cycloadditions of epoxy and aziridinyl enolsilanes with dienes such as cyclopentadiene and furan, to produce cycloheptanoid cycloadducts in high yields and with good diastereo- and enantiomeric excesses.[1] In contrast to (4+2) cycloadditions of indoles, there have been few reports on dearomative (3+2) cycloadditions of indoles. [2]

Herein, we report a dearomative (3+2) cycloaddition reaction of epoxy and aziridinyl enolsilanes with indoles. This method provides highly functionalized cyclopentaindoline compounds bearing four contiguous stereocenters in good yields and with enantioselectivities in one step (up to 88% yield and 93% ee). Cycloadducts were obtained with retention of *ee* from enantiomerically pure epoxides.



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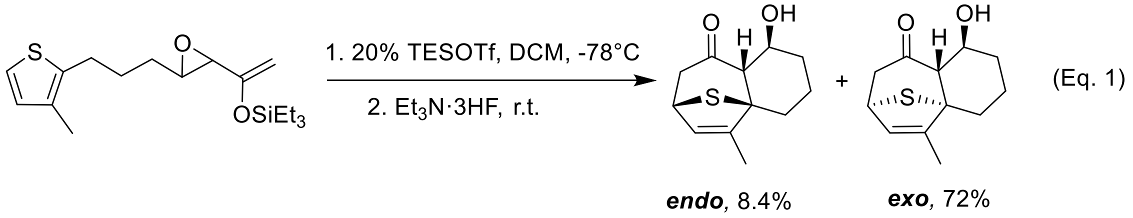
Intramolecular (4+3) Cycloadditions of Thiophenes

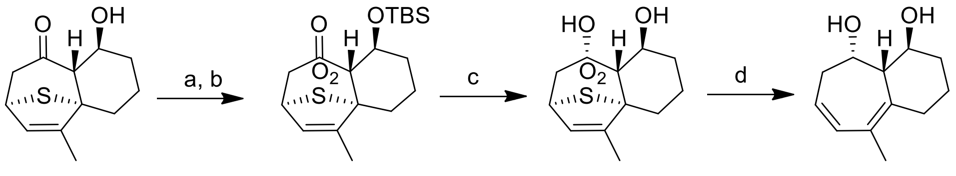
Yufen ZHENG, Pauline Chiu*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong
pchiu@hku.hk

Abstract

In contrast to the rich (4+3) cycloaddition chemistry of furans,[1] only one report of an intermolecular (4+3) cycloaddition of a thiophene has appeared, which occurred with an unknown yield.[2] This paucity of examples is reflective of the high aromaticity of thiophenes that make them generally incompetent as dienes for cycloadditions.

Herein, we report the first series of effective (4+3) cycloadditions of thiophenes which occurred in the intramolecular context. Thiophenes tethered to epoxy or aziridinyl enolsilanes underwent (4+3) cycloadditions under silyl triflate catalysis, to afford *endo* and *exo* cycloadducts in overall yields up to 80% (Eq. **1**). Moreoever, subsequent derivatizations of the cycloadduct afforded functionalized desulfurized diene for organic synthesis applications (Scheme **1**).





Scheme 1: Conditions: a. TBSCl, imidazole, DMF, **95%**; b. mCPBA, **88%**; c. LiAlH$_4$, THF then Δ: **49%** over 2 steps

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Total synthesis of cyclic lipopeptide antibiotic A54145

Hoi Yee Chow†,[1] Delin Chen†,[1] Kathy Hiu Laam Po,[2] Wenjie Ma,[1] Zhenquan Sun,[1] Emily Lok Yee Leung,[1] Sheng Chen*,[2] and Xuechen Li*,[1]
[1]*Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong*
[2]*Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong*
Email: sheng.chen@polyu.edu.hk, xuechenl@hku.hk
†Contributed equally

Abstract

A54145 are a family of cyclic lipopeptide antibiotics produced by *Streptomyces fradiae* that shares high structural similarity with daptomycin, the first-in-class lipopeptide antibiotic approved by FDA in 2003.[1,2] A54145 consists of 13 amino acids, 10 of which forms a lactone ring through the side chain of Thr residue and a 3-amino acid tail linked with a fatty acid chain at the N-terminus.[1] To achieve the total synthesis of A54145, we first obtained the required Fmoc-SPPS compatible building blocks for the three unnatural amino acids present in A54145, namely, 3-methoxyaspartic acid, 3-hydroxyasparigine and 3-methylglutamic acid, by devising novel synthetic routes for the syntheses. Next, we successfully completed the total synthesis of several factors of A54145 family. The bactericidal activity of the synthetic A54145 tested and the NMR spectra were identical to those reported in literature. The establishment of total synthesis of A54145 enables us to investigate structure-activity relationship of A54145 by synthesizing analogues with site-specific modifications in a highly control manner, which may help us better understand their mechanism of action.

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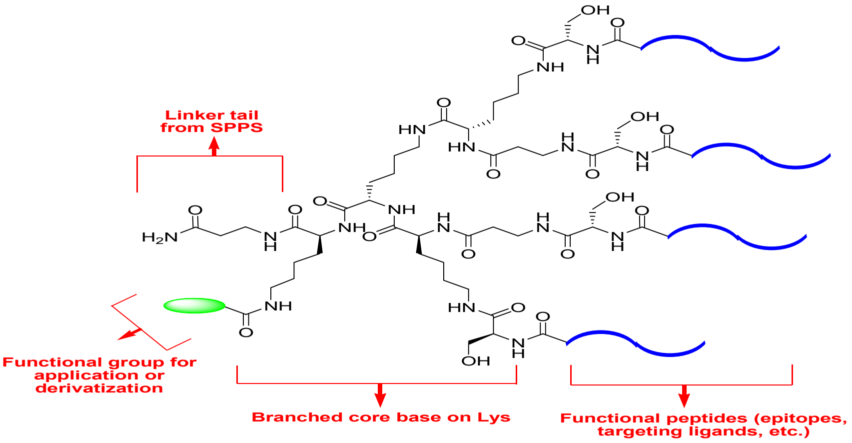
Peptide dendrimer synthesis via serine/threonine ligation

Qiao Guanlin, Li Xuechen*

xuechenl@hku.hk

Abstract

This work applies serine/threonine ligation (STL) method[1] developed by our group to the synthesis of peptide dendrimer. Below is the mode of peptide dendrimer we designed. The poly-L-lysine core structure is biocompatible and can provide multiple linkage sites for peptides and drugs. core branched structure and functional linear peptide are prepared via solid phase peptide synthesis (SPPS) and purified separately. The N-terminal of core branched structure is serine residues, while C-terminal of linear peptides is modified with salicylaldehyde. Though Ser/Thr ligation these two parts will form amine bond in the liquid phase. This convergent synthesis strategy can give a relatively large mass difference between the target product and un-completely reacted products (at least one peptide chain difference), so it's easy for separation and purification. In the core branched structure, the ε-amino of lysine can also be modified with functional groups, thus enable peptide dendrimer to fulfill its' multiple applications.



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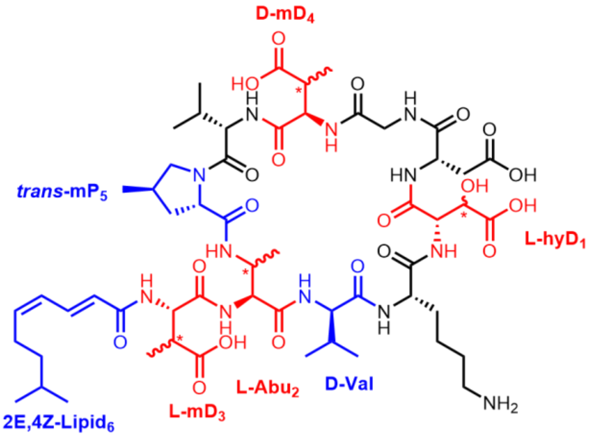
Towards the Synthesis of Malacidin A

Zhenquan Sun, Xuechen Li*
Department of Chemistry, The University of Hong Kong,
Hong Kong, People's Republic of China;
xuechenl@hku.hk.

Abstract

Drug-resistant microorganism has become growing concern of human community since the last decades. Many efforts and techniques are applied for discovering new types of antibiotics to tackle down such problem. In 2018, a novel calcium-dependent cyclic lipopeptide antibiotics called Malacidin A was discovered through culture-independent screening. It has promising potency against the Methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant *Enterococci* (VRE) and is difficult for bacteria to develop relevant resistance under reported conditions. However, the detailed chemical structure was not fully characterized and the further understanding of its mechanism has not been achieved yet. Therefore, it is attractive for us to develop a robust chemical synthesis of Malacidin A and its analogues for these purposes. Proper building blocks and Fmoc-based Solid-Phase Peptide Synthesis strategy have been designed and undertaken now.



10 AAs and 1 lipid tail

● Natural AA residues;

● With well characterization;

●

Prediction:
L-*threo*-(2S,3S)-Abu$_2$
L-*threo*-(2S,3S)-mD$_3$
D-*erythro*-(2R,3S)-mD$_3$

Malacidin A

Reference

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Application of Serine/Threonine Ligation to The Synthesis of Glycosylated Adiponectin

Wu Hongxiang, Li Xuechen*

Post-translational modifications (PTM) account for the structural and functional complexity of proteins. As the most common PTM mode, glycosylation occurs after protein translation on the ribosome. Thus, investigation of the effect of glycosylation on the proteins is the key to understand the relationship between protein structure and function.

Adiponectin, consisting of 244 amino acid residues, shows a variety of bioactivity and is expected to serve as new drug molecule in clinical treatment. However, the effect of glycosylation on the biological activities of adiponectin remains an unknown field and requires further investigation. Hence, we attempt to chemical synthesis of the glycosylated adiponectin in order to further disclose the mechanism of the biological activities of adiponectin.

Our research group has developed a chemoselective Serine/Threonine Ligation (STL) which allows side chain unprotected peptide fragments to be ligated at the Ser/Thr site in good yields. Employing this strategy, we synthesized the adiponectin with variable glycosylation patterns, which will be used in biological research.

Synthesis of Depleted Macrolactone of Amphidinolide C Congeners

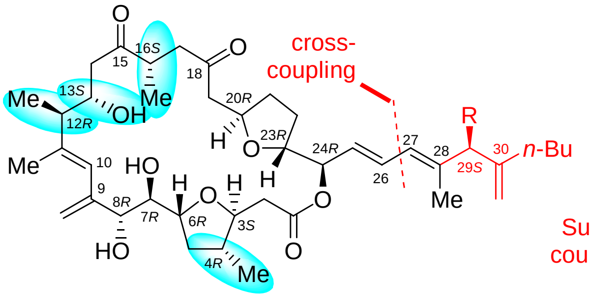
Nanfeng Gao and Wei-Min Dai*

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

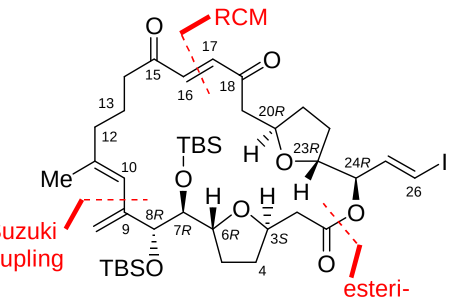
E-mail: chdai@ust.hk

Abstract

As part of our study[1] on synthesis of analogues of amphidinolide C congeners, such as **1**[2a] and **2**,[2b] isolated from the genus *Amphidinium*, we envisioned synthesis of the simplified macrolactone core **3** by depleting four stereogenic centers at C4, C12, C13, and C16.[1b] It was found that the dienyl zincate addition with aldehyde did not work well for the formation of the C8–C9 bond in **3**. We report here on the Suzuki coupling reaction of the vinyl iodide **5** with the vinyl boronate **6** under the Johnson conditions [5 mol % $Pd(PhCN)_2$, 10 mol % Ph_3As, 1.6 equiv Ag_2O, $THF–H_2O$ (8:1), rt; 69%][3] to construct the C7–C11 dienyl diol subunit and the subsequent transformations toward **3**.



1: amphidinolide C1, R = OH
2: amphidinolide C2, R = OAc



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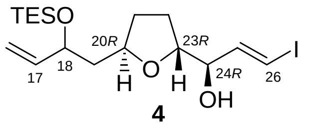

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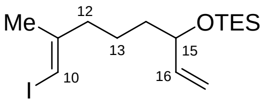
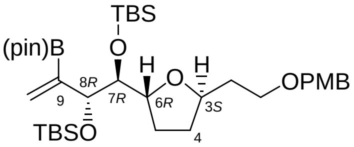


5



6

Acknowledgment. This work is supported by a GRF grant (No. 600913) from RGC of HKSAR and Department of Chemistry, HKUST.

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New Synthesis of the C16–C30 Bis-THF Module of Iriomoteolide-13a

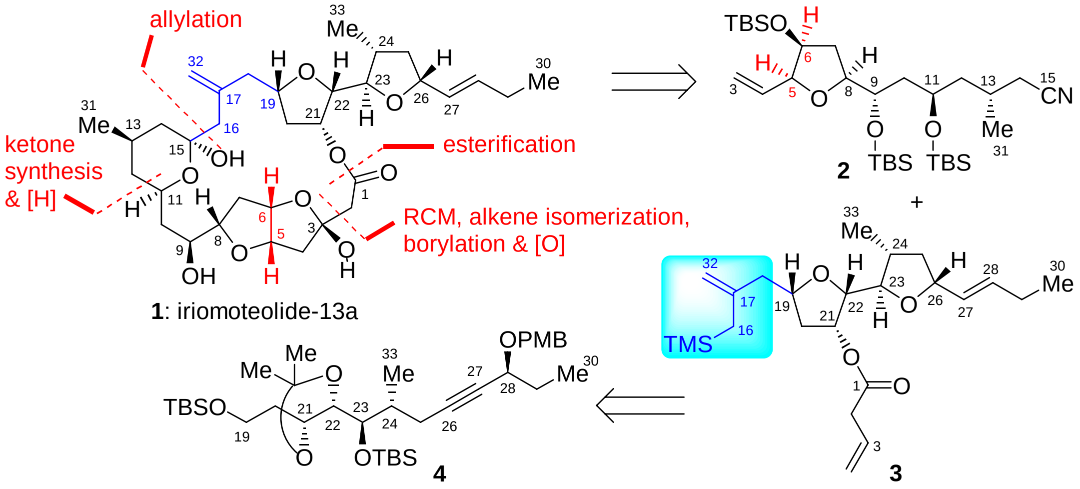
Haichen Ma, Tsz Chun Yip, and Wei-Min Dai*

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

E-mail: chdai@ust.hk

Abstract

In connection with our on-going study on total synthesis of iriomoteolide-13a (**1**) isolated from a benthic dinoflagellate *Amphidinium* sp. (strain KCA09053),[1] we have established synthetic routes toward the C3–C15 aldehyde precursor **2** and the C19–C30 bis-THF subunit.[2] In this presentation, a new route for the synthesis of the fully functionalized C16–C30 module **3** is described. Due to interference of a propargyl group at C19 with the AD reaction of the C21,C22-double bond, the protected C21,C22-diol **4** was used in the current synthesis. After construction of the bis-THF skeleton, the C19-propargyl group was transformed into the allylic silane in **3** via iodoboration (*B*-iodo-9-BBN in AcOH) followed by Pd-catalyzed cross-coupling with TMSCH$_2$MgCl. Reaction of **3** with the aldehyde derived from **2** is in progress.



1: iriomoteolide-13a

2

3

4

Acknowledgment. This work is supported by a GRF grant (No. 16301315) from RGC of HKSAR and the Department of Chemistry, HKUST.

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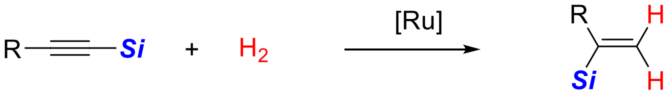
Ru(II)-Catalyzed *Gem*-Hydrogenation of 1-Silyl Alkynes

*Qiang Feng 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

Owing to exquisite control of selectivity by designing substrates and catalysts, the semi-hydrogenation of alkynes to alkenes has been achieved excellent regioselectivity and stereoselectivity using various catalytic systems. The reactions have been demonstrated in the synthesis of various useful complex molecules. However, all the current semi-hydrogenation reactions are vicinal addition, i.e., the two hydrogen atoms are added to the two carbons across the triple bond.[1-4] To the best of our knowledge, semi-hydrogenation of alkynes in a geminal addition mode, i.e. addition of the two hydrogen atoms to the same side of triple bond carbon to form a new double bond after migration of one substituent, remains unknown. Herein, we present the first example of this type. In the presence of a catalytic Ru-based catalyst, the semi-hydrogenation of 1-silyl alkynes proceeded under mild conditions to form the corresponding terminal olefins with efficient silyl migration (see Scheme). The details about this reaction, including reaction conditions, scope, and mechanistic studies will be presented.



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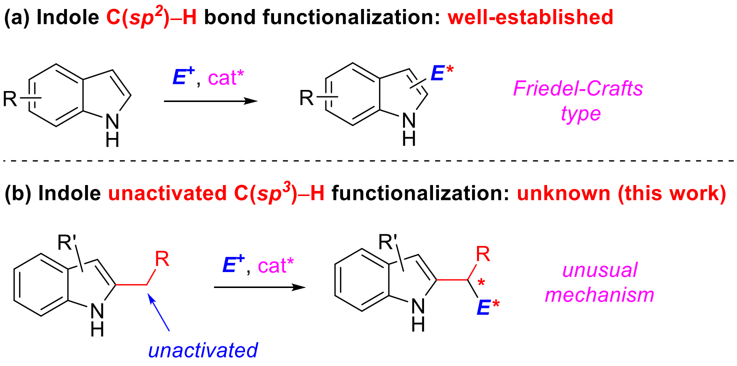
Organocatalytic Enantioselective Functionalization of Unactivated Indole C(sp^3)–H Bonds

*Dengke Ma, Min Chen, 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

Indole is a privileged structural motif widely present in numerous drug molecules, natural products and other biologically important molecules. C–H functionalization of indoles, particularly in a catalytic asymmetric manner, has been a topic of intense investigations in the past few decades owing to the importance of indole as a valuable pharmacophore in chiral drugs. However, almost all the current asymmetric reactions of this type have taken advantage of the π-electron-rich nature of the indole ring to react with an electrophile by a Friedel–Crafts-type mechanism, leading to C(sp^2)–H bond functionalization (Scheme a). In contrast, direct asymmetric functionalization of an unactivated C(sp^3) –H bond at the benzylic position of indoles has been unknown, despite the fact that these reactions provide equally expedient access to functionalized indole-containing chiral molecules. Herein we report the first highly efficient enantioselective example of this type featuring direct asymmetric C–C bond formation at the benzylic position of unactivated 2-alkyl indoles, which proceeds via an unusual mechanism (Scheme b). Details of this reaction will be presented.



Synthesis of 1,2-Dihydroquinolines by Intramolecular Cyclization of Oxetane-Tethered Anilines

Guannan Wang 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

1,2-Dihydroquinolines are useful structural motifs that can lead to various useful biologically important molecules.[1] Therefore, efficient assembly of such structures is an important topic in organic synthesis. On the other hand, oxetane is also a useful unit in organic synthesis and medicinal chemistry.[2] Upon activation, oxetanes can undergo ring-opening reactions with a suitable nucleophile. Although various nucleophiles have been demonstrated to be reactive in oxetane opening reactions, carbon-based nucleophiles have not been well-explored.

A formal intramolecular oxetane ring-opening reaction with an internal carbon-based nucleophile has been designed, leading to the efficient synthesis of 1,2-dihydroquinolines. After careful optimization of the reaction conditions, we observed that in the presence of a suitable Lewis acid, a range of oxetane-tethered aniline derivatives underwent efficient cyclization through an unusual bond reorganization, leading to the synthesis of diversely-substituted 1,2-dihydroquinolines. The reaction may proceed via a mechanism requiring unusual rearrangement steps. The details of this reaction will be presented.

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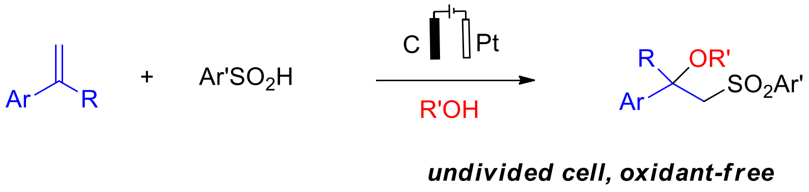
Electrochemical Synthesis of β-Hydroxy-, β-Alkoxy-, and β-Carbonyloxy Sulfones by Vicinal Difunctionalization of Olefins

Zhefan Zhang, Jiyao Yan, Dengke Ma, 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

Vicinal difunctionalization of olefins is a fundamentally important process for the synthesis of various useful molecules from readily available olefin substrates. The addition of a sulfonyl group and oxygen to a double-bond is particularly useful in view of the broad utility of β-oxysulfones, which are not only useful synthetic intermediates in organic chemistry, but also important substructures in a range of biological active molecules. Previously, a stoichiometric amount of oxidant had to be used due to the oxidation nature of this process, which limited the application of this transformation. In this presentation, we will present our recent studies on the use of electrochemical oxidation to achieve the same transformation in the absence of a stoichiometric amount of chemical oxidant. With suitable choice of the conditions, including current, electrodes, and electrolyte, this electrochemical vicinal heterodifunctionalization of olefins reaction proceeded efficiently to form a range of β-oxysulfones in an undivided cell. In addition to the use of external nucleophiles, intramolecular reactions using an internal nucleophile can also work, leading to the synthesis of β-sulfonyl lactones. The detailed scope and mechanism will be presented.



Oxone-KBr-promoted Oxidative Rearrangement of Tetrahydro-*β*-carbolines to Spirooxindoles

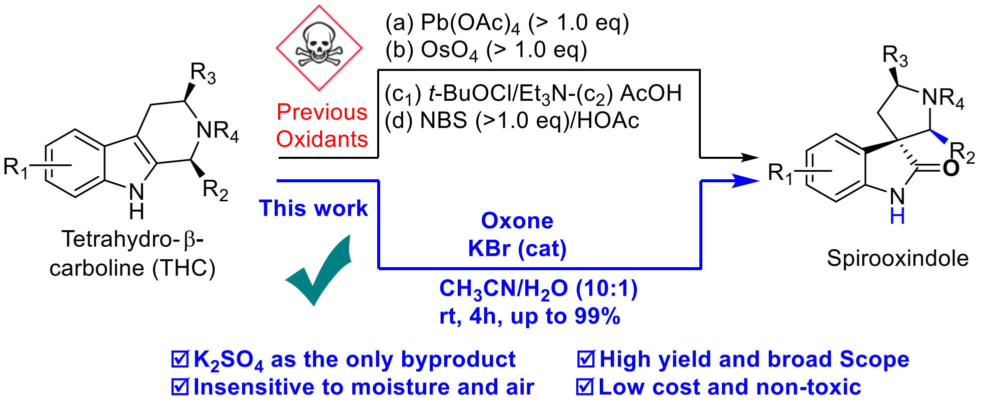
Lixin Liang and Rongbiao Tong*

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

Clearwater Bay, Kowloon, Hong Kong, China; rtong@ust.hk

Abstract

An efficient and environmentally friendly protocol for the oxidative rearrangement of tetrahydro-β-carbolines (THCs) to spirooxindoles was developed, replacing previously reported oxidants with Oxone-KBr(cat), which features (1) generation of K_2SO_4 as the only byproduct from the oxidant, (2) low cost and non-toxic and (3) simple operation with high yield and broad substrate scope.

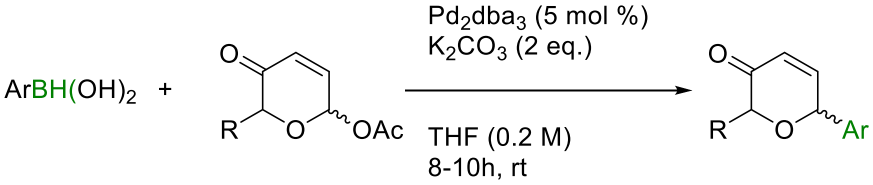


Pd-catalyzed Anomeric Allylic Substitution: Arylation of Pyranulose Acetates with Arylboronic Acids

Ming Wai Liaw, Wai Fung Cheng and Rongbiao Tong*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clearwater Bay, Kowloon, Hong Kong, China; rtong@ust.hk

Abstract

Pd-catalyzed anomeric allylic arylation of dihydropyranosides has been a long-lasting challenge due to low reactivity of Pd-π-allyl complex. Herein we report the first Pd-catalyzed anomeric allylic substitution of pyranulose acetates with aryl boronic acids under mild condition. A variety of 2,6-disubsituted dihydropyrans was efficiently synthesized from the cross coupling of pyranulose acetates reaily accessible from Achmatowicz rearrangement with the commercially available aryl boronic acids.



A 16-Steps Synthesis of Siladenoserinol A

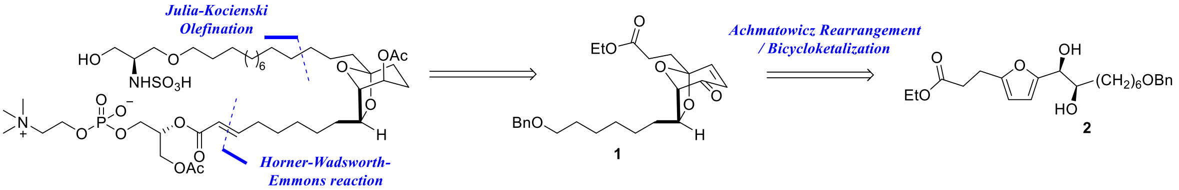
Miguel A. Marquez-Cadena; Jingyun Ren and Rongbiao Tong*
Department of Chemistry, The Hong Kong University of Science and Technology,
Clearwater Bay, Kowloon, Hong Kong, China; rtong@ust.hk

Abstract

Siladenoserinol A, was isolated from the extract of a tunicate in 2013 by Tsukamoto and co-workers;[1] this compound exhibited a strong inhibition of p53–Hdm2 interaction (IC_{50}=2.0μM) and it is characterized for possessing a glycerophosphocholine (GPC) moiety.

One of the main features in the structure of Siladenoserinol A is the 6,8-DOBCO core, a structural motif shared by a wide number of natural products; different synthetic strategies have been employed for the construction of this important motif.[2]

With our synthetic approach we could obtain Siladenoserinol A, highlighting the construction of the 6,8-DOBCO framework, which was successfully obtained in 3 steps through an Achmatowicz rearrangement/bicycloketalization reaction (AR/BCK).



Siladenoserinol A **1** **2**

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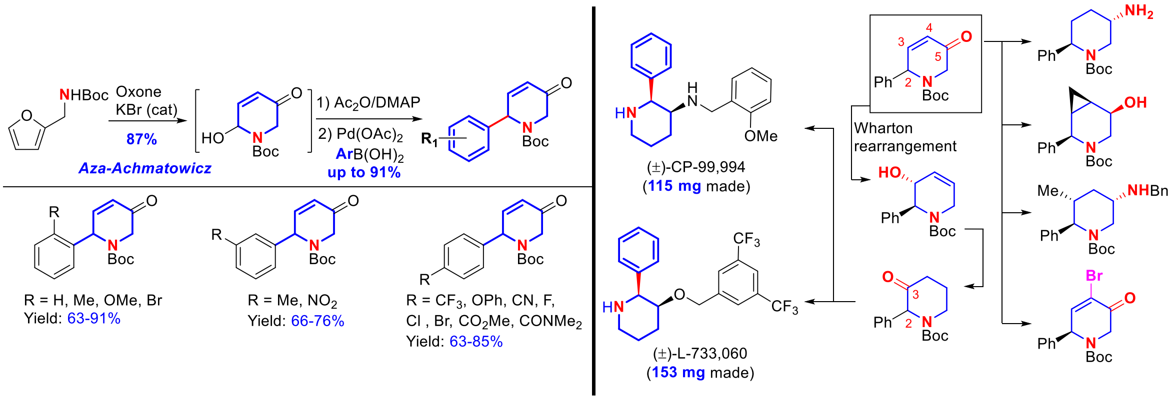
Synthesis of Functionalized 2-Arylpiperidines by Pd-catalyzed Arylation of Aza-Achmatowicz Rearrangement Products with Arylboronic Acids

Xin Xu, Guodong Zhao and Rongbiao Tong*

Department of Chemistry, The Hong Kong University of Science and Technology, Clearwater Bay, Kowloon, Hong Kong, China; rtong@ust.hk

Abstract

A new de novo synthetic method for 2-aryldihydropyridinones, featuring Aza-Achmatowicz rearrangement and palladium-catalyzed arylation with arylboronic acids was established with 22 examples. After Michael addition, Simmons-Smith cyclopropanation, reductive amination, and Wharton rearrangement, a small library of functionalized 2-arylpiperidines were built, including two NK_1 receptor antagonists CP-999,94 and L-733,060.



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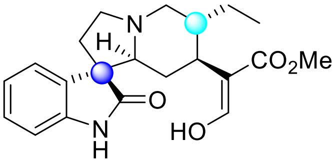
Total synthesis of Rhynchophylline, Isorhynchophylline, Corynoxine B, Corynoxine, Corynoxeine B and Corynoxeine

Zhihong Zhang and Rongbiao Tong*

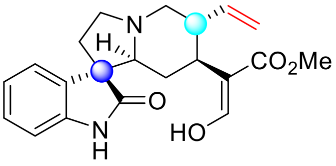
Department of Chemistry, The Hong Kong University of Science and Technology,
Clearwater Bay, Kowloon, Hong Kong, China; rtong@ust.hk

Abstract

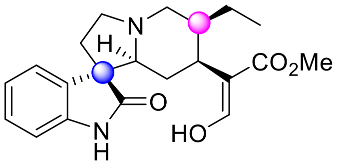
The spiral tetracyclic oxindole skeleton is a basic building block in various natural products such as rhynchophylline, isorhynchophylline, corynoxeine, isocorynoxeine, corynoxine B and corynoxine.[1] These natural products show interesting bioactivity profiles, especially their potential use for the treatment of cardiovascular and central nervous system diseases.[2] Here we designed a divergent synthetic route which could achieve the total synthesis of all these natural products. Rhynchophylline, isorhynchophylline, corynoxeine and isocorynoxeine have been achieved, the total synthesis of corynoxine B and corynoxine are under exploration.



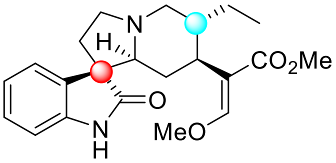
rhynchophylline



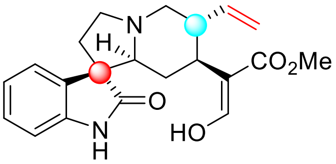
corynoxeine



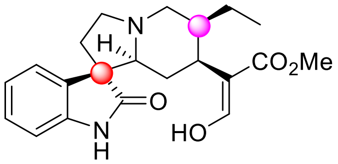
corynoxine B



isorhynchophylline



isocorynoxeine



corynoxine

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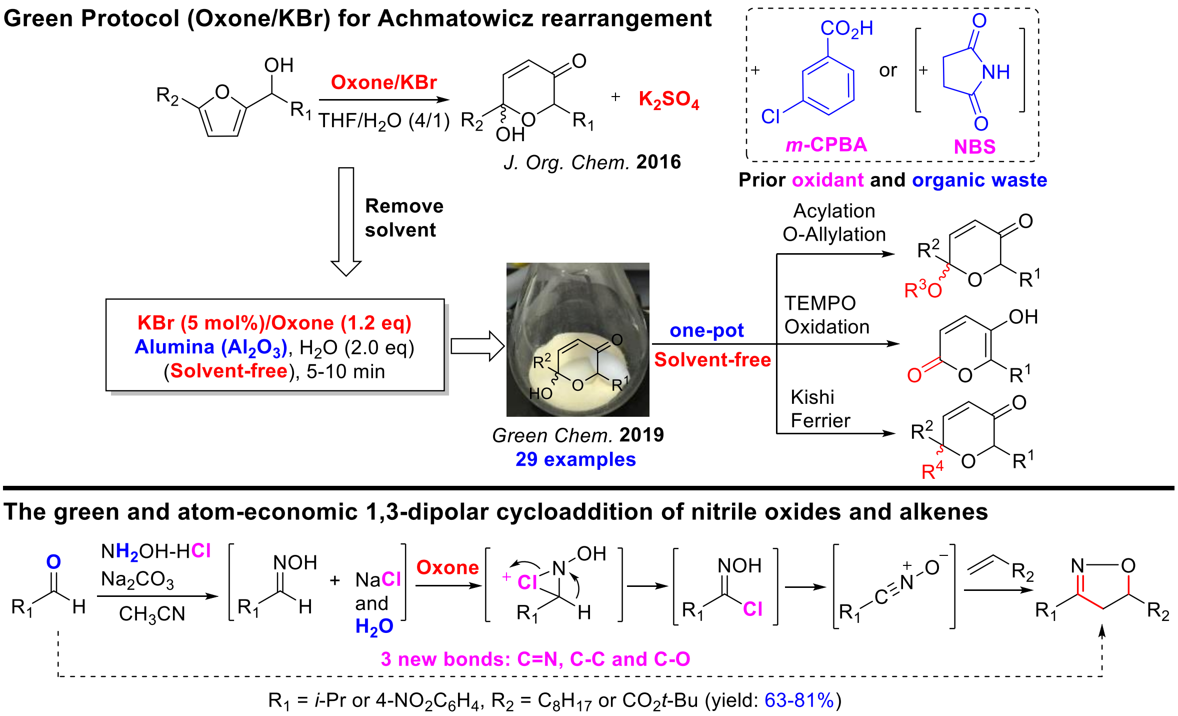
Green Protocol (Oxone/Halide) for Achmatowicz Rearrangement and 1,3-Dipolar Cycloaddition

Guodong Zhao and Rongbiao Tong*

Department of Chemistry, The Hong Kong University of Science and Technology, Clearwater Bay, Kowloon, Hong Kong, China; rtong@ust.hk

Abstract

An environmentally friendly catalytic (oxone/KBr or NaCl) protocol for the Achmatowicz rearrangement (AchR) and 1,3-dipolar cycloaddition was established, featuring the minimal environmental impacts and sequential one-pot reaction.



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Fluorescent Probe for Carbapenemase Detection

Chi-Wang MA, Dan YANG

Morningside Laboratory for Chemical Biology

The University of Hong Kong

Department of Chemistry

Pokfulam Road, Hong Kong

Email address of corresponding author: yangdan@hku.hk

Abstract

β-Lactam antibiotics have been used for almost a century. Their misuse has led to outbreak of antibiotic resistance and created a serious global threat. β-Lactamases, one family of enzymes produced by bacteria, can destroy and hydrolyze β-lactam antibiotics and cause resistance. Carbapenem antibiotics were developed in the past decades and could resist hydrolysis by a wide range of β-lactamases. Although carbapenem antibiotics are known to be one of the "last resort antibiotics", a number of β-lactamases have been reported to hydrolyze carbapenem antibiotics and they are classified as carbapenemases. Traditional methods for carbapenemase detection may take several days, which is definitely too long for critically ill patients[2]. Here, we present our work on a rational design of highly sensitive and selective fluorescent probe for rapid detection of carbapenemases. Our fluorescent probes can also differentiate carbapenemase-producing bacteria from non-carbapenemase-producing bacteria in clinical samples in a rapid manner.

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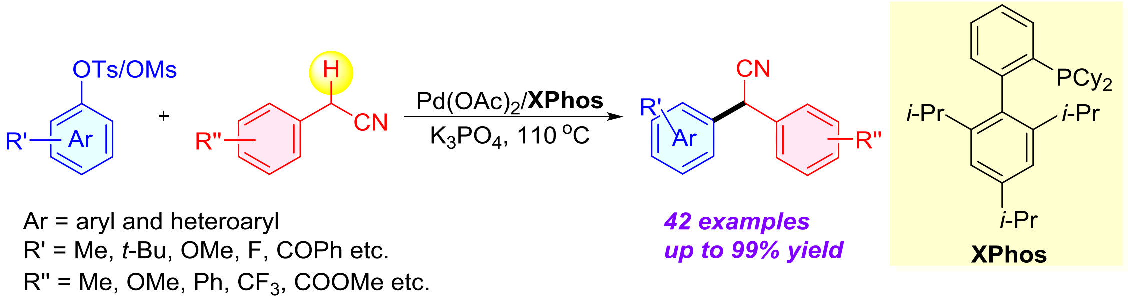
Synthesis of α-Diaryl Nitriles through Palladium-Catalyzed α-Arylation of Benzyl Cyanide Derivatives with Versatile (Hetero)Aryl Sulfonates

Zicong Chen, Xiangmeng Chen, Chau Ming So*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong.

Email: *chau.ming.so@polyu.edu.hk*

The first general examples of palladium-catalyzed α-arylation of benzyl cyanide derivatives with aryl/heteroaryl sulfonates are reported. $Pd(OAc)_2$ associated with XPhos serves as the effective catalyst to facilitate this reaction. A broad range of electron-rich, -neutral, -deficient, and sterically hindered aryl/heteroaryl tosylates and mesylates are coupled with benzyl cyanides bearing different substituents to give the corresponding products in good-to-excellent yields successfully. The catalyst loading down to 0.5 mol% Pd can be achieved. Particularly noteworthy is that 20 unprecedented compounds are synthesized out of 42 demonstrated examples using this protocol.



Ar = aryl and heteroaryl
R' = Me, *t*-Bu, OMe, F, COPh etc.
R'' = Me, OMe, Ph, CF_3, COOMe etc.

42 examples
up to 99% yield

Reference:

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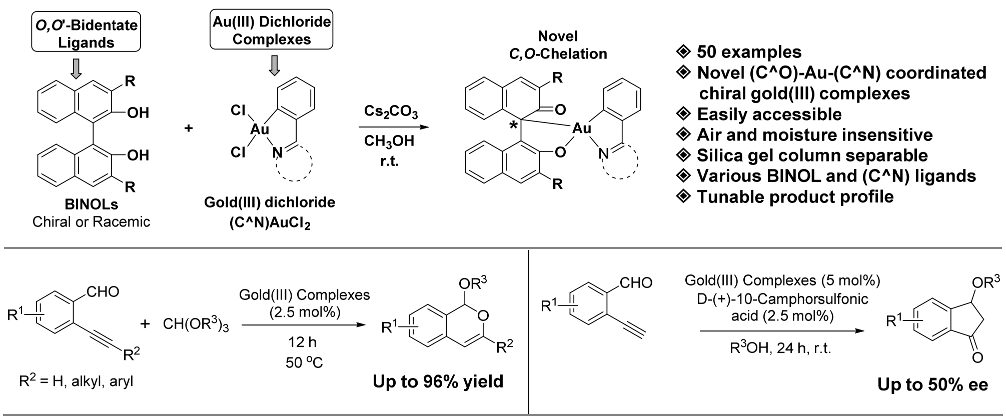
C,O-Chelated BINOL-Gold(III) Complexes: Synthesis and Catalysis with Tunable Product Profiles

Jia-Jun Jiang, Jian-Fang Cui, Hok-Ming Ko, Ka-Pan Shing, Jie-Ren Deng, Nathanael Chun-Him Lai, and Man-Kin Wong*

State Key Laboratory of Chemical Biology and Drug Discovery and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong. mankin.wong@polyu.edu.hk

Abstract

Although the reactivity of gold in homogeneous catalysis has been underestimated in the last century, the past decade has witnessed significant progress in gold catalysis. Gold catalysts present distinguished reactivity, excellent selectivity and high functional group compatibility in diverse organic transformations. Gold(I)-catalyzed organic reactions with good stereoselectivity are well demonstrated; yet, asymmetric gold(III) catalysis remains largely unexplored. Here we introduce unprecedented stable BINOL-gold(III) complexes with easy accessibility and novel C,O-chelation mode. These gold(III) complexes were able to catalyze the cycloisomerization and carboalkoxylation of ortho-alkynylbenzaldehydes with trialkyl orthoformates.



◈ 50 examples
◈ Novel (C^O)-Au-(C^N) coordinated chiral gold(III) complexes
◈ Easily accessible
◈ Air and moisture insensitive
◈ Silica gel column separable
◈ Various BINOL and (C^N) ligands
◈ Tunable product profile

Reference:

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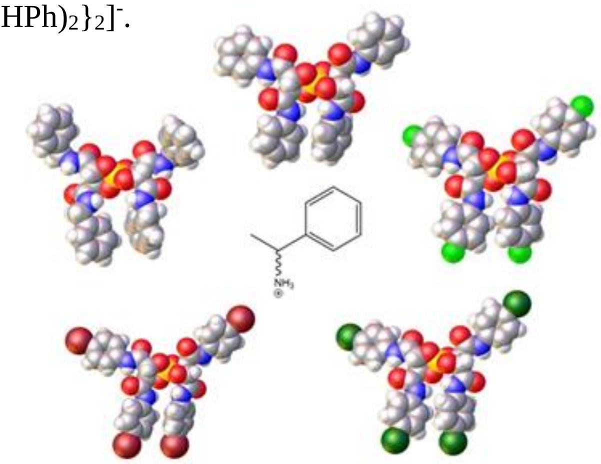
Crystal Engineering the Resolution of a Chiral Amine using A Family of Spiroborate Anions

Xiaoyan Chen, Lawrence W-Y. Wong, Herman H-Y. Sung & Ian D. Williams*
Department of Chemistry, HKUST, Clear Water Bay, Hong Kong, China. Email: xchenbu@connect.ust.hk

The application of the parent ion of this family $[B\{L\text{-}Tar(NHPh)_2\}_2]^-$ to chiral resolutions via diastereomeric salt formation was initially explored for five challenging cases, which could be resolved in facile one-pot reactions with enantiomeric excesses of 34%-94%.[1] Encouraged by this, we then extended the use to further aryltartramide spiroborate anions (-NHAr/-$NHCH_2Ar$, Ar = Ph, 4FPh,4-ClPh and 4-BrPh) to optimize resolution in one of the five examples: *rac*-1-phenylethylamine as a typical test system. This is challenging since there is a single chiral centre with strong shape similarity between enantiomers of the racemic pair and both CH/Me and re-pyramidalization can occur to disorder the cation site. We have found some structural similarity of the resulting salts with preserved packing motifs, including an NH_3R binding site and a short 5.5Å axis. Importantly modification of the cation pockets in these related crystalline salts can lead to successful optimization of the R/S selectivity, with effective enantiopurity in at least two cases, improving on the 76% ee found for the salt from the parent $[B\{L\text{-}Tar(NHPh)_2\}_2]^-$.



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Solvate Structures of the Pharmaceutical Wogonin

Ruel Valerio R. de Grano, Madiha Nisar, Herman H-Y. Sung, and Ian D. Williams*
Department of Chemistry, Hong Kong University of Science and Technology
rvrdegrano@connect.ust.hk

Abstract

Wogonin (8-methoxychrysin) $C_{16}H_{12}O_5$ is a natural flavonoid isolated from S. baicalensis.[1] It has been found to be a potent anti-tumor agent.[2] Two crystal structures of Wogonin were reported to contain water[3] or methanol[4]. Crystal structure is one of the factors which contributes to the solubility and bioavailability of the active compound. This project aims to verify the role of the solvents in the crystal framework of this compound, explore the stability and improve the property of wogonin for more efficient pharmaceutical formulation. In this study, wogonin crystals screening was performed from different solvents both at room temperature and solvothermal condition. The resulting solid forms were examined by P-XRD and SC-XRD. Three different wogonin crystal will be reported, an orthorhombic crystal and a monoclinic hydrate crystal and a monoclinic acetate solvated wogonin. Each showed distinct crystal packing and H-bond interaction with their respective solvents. This study revealed how these solvents control the crystal formation of wogonin, preferring one stable packing over the other in a certain condition.

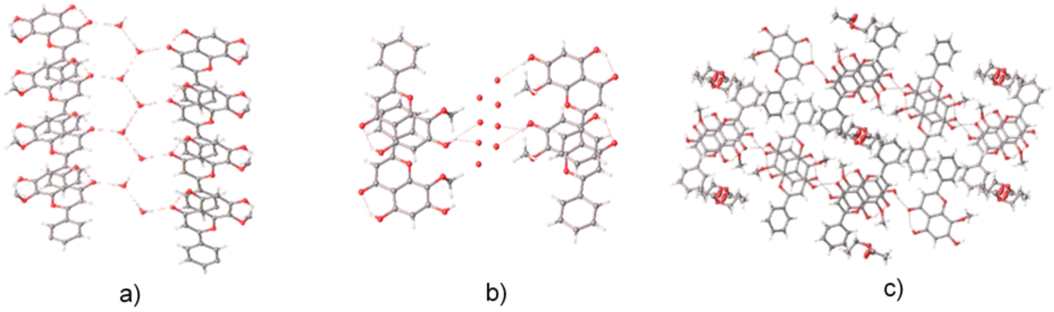

Figure.1. Different Crystal packing of wogonin from various solvents a) ethanol b) methanol/DCM c) ethyl acetate

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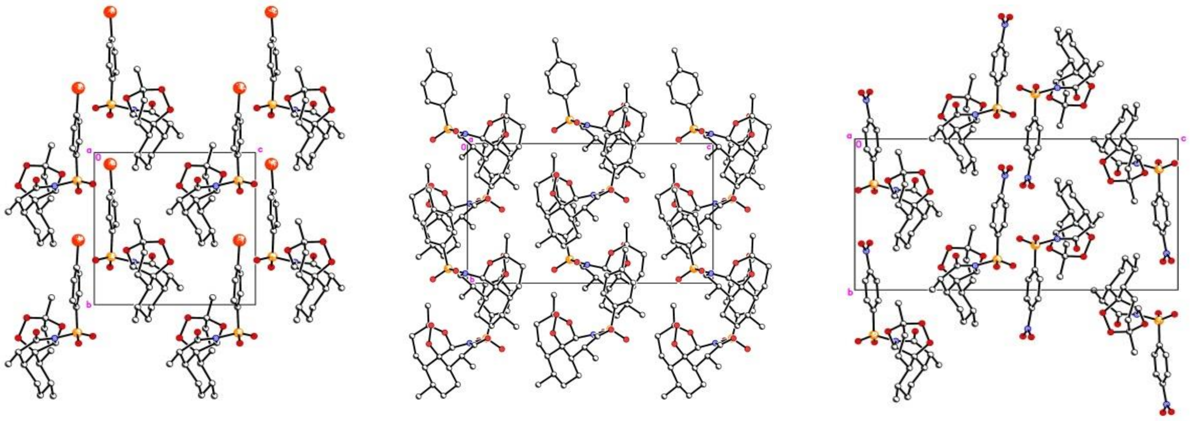
Quasi-Polymorphs of 11-Azaartemisinin Derivatives Grown via Seeds of Molecular Analogues

Madiha Nisar*, Herman H-Y. Sung and, Ian D. Williams
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Hong Kong, China; mnisar@connect.ust.hk

Abstract

11-Azaartemisinin and its derivatives are known for their remarkable activities against drug-resistant malarial parasites.[1,2] Among the active derivatives are N-sulfonyl compounds. Those bearing an aryl group may be readily varied by changing substituents on the Ph ring. Many of these compounds do not make isostructural phases with either the parent Ph compound or each other, despite only minor change in molecular formula.

In this paper we present our study of what may be termed 'quasi-polymorphs' in this series of compounds, explaining how and why their structures are different. We also report on attempts to use hetero-crystal seeding to grow real polymorphs for some of these compounds. These principles could be applied as an approach to otherwise inaccessible solid state forms of many drugs, or indeed organic compounds in general.



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Cocrystallization of Curcumin with Benzenediols and Benzenetriols

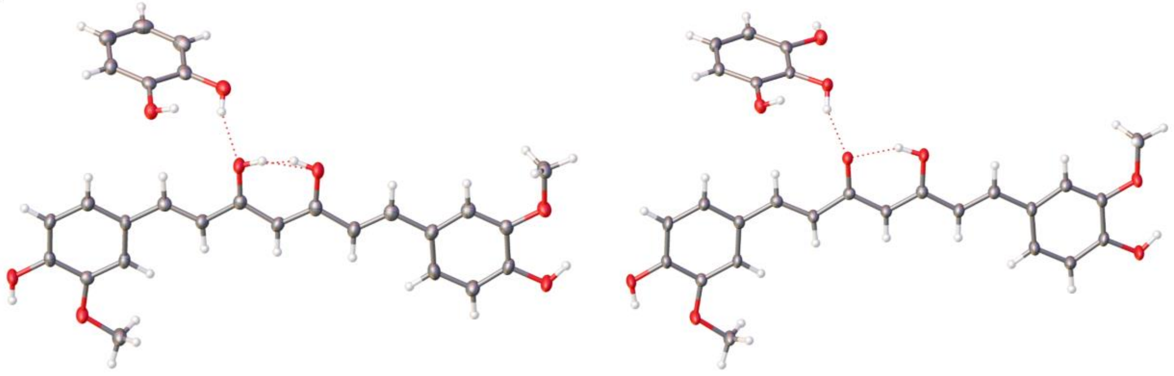
Roy, Monalisa[1]; Wong, Lawrence W-Y.[1]; Williams. Ian D.[1]; Chow, Shing Fung[2]

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

[2]*Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam, Hong Kong SAR, China*

Abstract

The dietary spice, Turmeric or *Curcuma longa*, has been extensively used in traditional medicine in India and China. Ongoing research on the active component curcumin a polyphenol, reports the presence of potent anti-inflammatory, antioxidant, antimicrobial, antispasmodic, lipid powering, and hepato-protective properties besides others.[1] Along with its pharmacotherapeutic capabilities, its safety, almost negligible toxicity and abundancy favours curcumin-based drugs. However, the extremely low bioavailability and aqueous solubility of curcumin [2] hinders its immediate usage as an effective commercial therapeutic compound. One solution to this is cocrystallization [3], [4] of curcumin with benzenediols and benzenetriols, known to have antiseptic and anti-inflammatory properties, to form stable cocrystals [5] that increase the bioavailability and efficacy without interfering with curcumin's inherent features. Single crystal structure determinations on the cocrystals of curcumin with various polyphenols will be presented, some based on small microcrystals obtained by rotary evaporation and isostructural similarities within the family are explored.



(a) (b)

Figure.1: (a) Curcumin-catechol and (b) Curcumin-pyrogallol cocrystals show isostructural.

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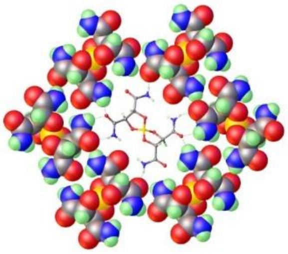
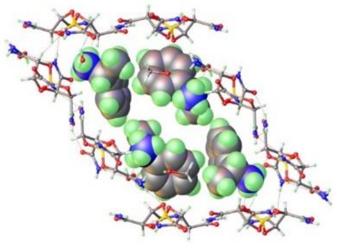
Crystal Engineering of Chiral Space from Spiroborates based on Tartamide [B(L-TarNH$_2$)$_2$]

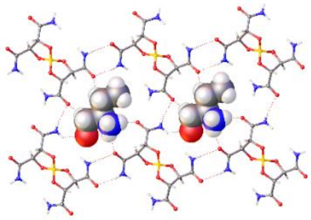
Aristyo Soecipto, Lawrence W-Y. Wong, Herman H-Y. Sung and Ian D. Williams*
Department of Chemistry, HKUST, Clear Water Bay, Hong Kong, China. E-mail: asoecipto@ust.hk

Abstract

Recently we prepared a spiroborate anion bis(mandelato)borate [B(Man)$_2$][1,2] and bis(N,N'-diphenyltartramido)borate [B(L-Tar(NHPh)$_2$)$_2$][3] for the efficient resolution of a variety of chiral cations with excess of 90%ee in the first isolation step. In seeking to extend to a family of spiroborate anions with application to resolution, we have found novel anionic assemblies using [B(L-TarNH$_2$)$_2$], where chiral layers, channels or cavities for both cations and neutral solvent formed by its H-bond which can offer prospects for the dual resolution of both cations *and / or* neutral solvent. Wide array of structure types can be found which are dependent on counter cation, solvent and crystallization conditions such as temperature and time.







In structures of around 75 salt phases studied to-date about 25 contain the sheet on the left. Self-aggregation of inter-amide NH---O=C $R^2_2(8)$ synthons are found between [B(L-TarNH$_2$)$_2$] to encapsulate cations and solvent in regular channels with chiral walls, such as the example shown on the middle with R-NH$_3$CHMePh cations. Another interesting structure where [B(L-TarNH$_2$)$_2$] provides channels for cations within the layer.

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High-level *ab Initio* predictions for the ionization energy, bond dissociation energy, and heats of formation of vanadium methylidyne radical and its cations (VCH/VCH^+)

Chow-Shing Lam, Kai-chung Lau

Department of Chemistry, City University of Hong Kong, Hong Kong SAR;

kaichung@cityu.edu.hk

Abstract

The ionization energy (IE) of VCH, the 0 K V−CH/VC−H bond dissociation energies (D_0's) and the heats of formation at 0 K ($\Delta H°_{f0}$) and 298 K ($\Delta H°_{f298}$) for VCH/VCH^+ are predicted by the wave-function-based CCSDTQ/CBS approach. The CCSDTQ/CBS calculations involve the approximation to the complete basis set (CBS) limit at the coupled cluster level up to full quadruple excitations along with the zero-point vibrational energy (ZPVE), high-order correlation (HOC), core-valence (CV) electronic and spin-orbit (SO) coupling and scalar relativistic (SR) corrections. The present calculations yield IE(VCH) = 6.797 eV and are in good agreement with the experimental IE value of 6.7747 ± 0.0001 eV determined in a two-color laser-pulsed field ionization-photoelectron (PFI-PE) study.[1] The CCSDTQ/CBS calculations give the predictions of $D_0(V^+{-}CH) - D_0(V{-}CH) = -0.024$ eV and $D_0(VC^+{-}H) - D_0(VC{-}H) = 0.334$ eV which are also consistent with the experimental determination of −0.0284 ± 0.000 1 eV and 0.3559 ± 0.0001 eV respectively. This work together with the previous experimental and theoretical investigations supports the conclusion that the CCSDTQ/CBS approach is capable of providing reliable IE and D_0 predictions for VCH/VCH^+ with error limits less than or equal to 20 meV. The present study has demonstrated that, the CCSDTQ/CBS protocol can be readily extended to investigate triatomic molecules containing of 3*d*-metals.

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A combined FTIR and DFT study for the structures and interaction properties of 1-(2’-hydroxylethyl)-3-methylimidazolium tetrafluoroborate and water mixture

Yan Zhen Zheng and Kai Chung Lau*
Department of Chemistry, City University of Hong Kong
Email: kaichung@cityu.edu.hk

Abstract

Water is a ubiquitous constituent of ionic liquids (ILs) and can significantly affect the structure as well as the interionic interactions between anion and cation of ILs. In this work, with the combination of FTIR and DFT calculation, the structure and interaction properties between water and 1-(2’-hydroxylethyl)-3-methylimidazolium tetrafluoroborate ([C2OHMIM][BF_4]) were studied. Excess infrared absorption spectroscopy has been found to be suitable for enhancing spectral resolution[1-2] and was used to analyze the original IR spectra. The O−D stretching vibrational region of water is especially focused as it is sensitive to the change of environment.

It is found that hydrogen-bonding interaction is the main cause that induces the original IR spectra change of v(O−D) and water form relative stable hydrogen-bonding association complex in the mixtures. The hydrogen-bonds between water and ILs are the closed shell interaction, electrostatic dominant and weak strength. A number of species in the TSILs−water mixtures were identified from the deconvolution results, namely ion clusters−water, ion pair–water, anion−water, water cage hexamer, water cyclic tetramer, and water cyclic trimer. The association species changes were also analyzed in the studied concentration range. To better understand the transformation process, a schematic diagram is proposed in Figure 1.

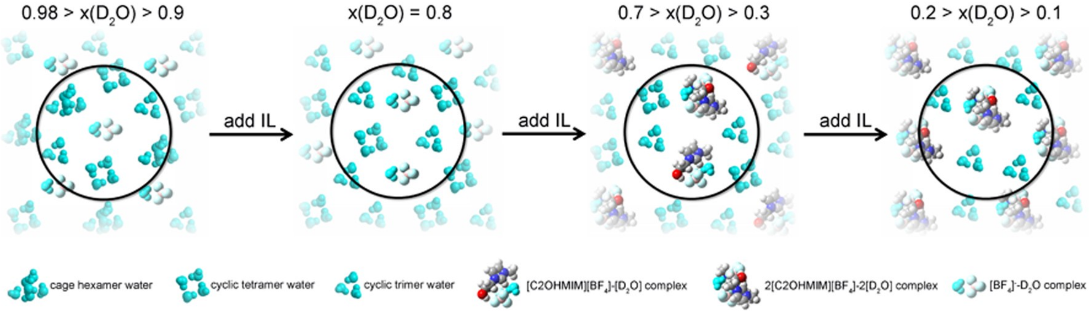

Figure 1. Schematic models for the transformation of the species in the dilution process.

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Reactivity of Hydrated Monovalent Cobalt (I) Toward Nitrous Oxide in the Gas Phase

Ephrem G. Demissie, Wai Kit Tang, Chi-Kit Siu

Department of Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong, China; chiksiu@cityu.edu.hk

Abstract

Cobalt ions solvated in nanoscale water droplets in the phase provides the media for the investigation of the chemistry of cobalt metal in rarely occurred +1 oxidation state. The successive hydration of Co^+ in water clusters and the redox reaction of $Co^+(H_2O)_n$ with N_2O have been studied theoretically using M06/DFT methods with 6-311++g(d,p) basis set. The $3d^8$-electron configuration allow Co^+ to possess different electronic states, with the triplet state being over 100 kJ/mol lower-lying than the singlet and quintet states for all cluster sizes studied ($n \leq 12$). The core structure and coordination number for the ground state hydrated cobalt complexes, $Co^+(H_2O)_n$ (n = 2–12), have been examined. We observed that the monovalent Co^+ is directly bound with four water molecules for cluster sizes n = 4 – 9. However, for larger clusters, n = 10–12, the lowest energy isomer has six coordinated structure and the remaining water molecules occupied the second solvation shell, which forms two or more hydrogen bonds with the first solvation shell. N_2O can react with the Co^+ center either through N- or O-coordination, forming $ONNCo^+(H_2O)_n$ or $NNOCo^+(H_2O)_n$, respectively. The former is preferentially formed for clusters containing up to eight water, while the latter formed larger n. In agreement with a previous experimental result[1], we found that the redox reaction between $Co^+(H_2O)_n$ and N_2O followed by the formation of $[CoOH]^+(H_2O)_n$ and $[CoO]^+(H_2O)_n$ is size dependent and the reaction takes place in the cobalt water clusters containing at least five water molecules.

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Dissociation of N-terminal C_α-C_β bond induced by electron transfer between N-terminus and tyrosine side chain in molecular peptide radical cation

Tang, Wai Kit,[1] Mu, X. Y.;[2] Chu, I. K.;[2] Siu, Chi-Kit*,[1]

1. Department of Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong, China; chiksiu@cityu.edu.hk
2. Department of Chemistry, The University of Hong Kong, Pokfulam, Hong Kong, China

Abstract

Dissociation of molecular radical cationic peptides displays rich gas-phase ion chemistry, providing useful structural information for protein sequencing.[1,2] Low-energy collision-induced dissociation (CID) of tyrosine-containing peptide molecular radical cations $[M]^{\bullet+}$ led to dissociation of C_α-C_β bond at the side chain of the N-terminal phenylalanine residue forming $[M - 91]^+$ associated with a loss of odd-electron neutral benzyl side chain (91 Da).[2] Herein, we demonstrate that the dissociation of N-terminal C_α–C_β bond of $[FYGG]^{\bullet+}$ induced by electron transfer from N-terminus to the tyrosine residue electron hole. Interestingly, infrared multiple-photon dissociation (IRMPD) action spectroscopy of $[FYGG]^{\bullet+}$ shows a characteristic band at 1573 cm^{-1} assigned to the bending of a $NH_2^{\bullet+}$ moiety resulting from the n-π interaction between the non-bonding electron of the N-terminal NH_2 and the π-cationic radical of tyrosine residue. This electron transfer also exhibits distance dependency; increasing the number of spacer (glycine residue) between N-terminal phenylalanine and tyrosine will decrease the abundance of $[M - 91]^+$.

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Quasi-loops Facilitate the Formation of DNA Minidumbbells with Pentaloops

Cheuk Kit Ngai, Sik Lok Lam*

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

Abstract

Three DNA minidumbbell (MDB) structures have been reported to form with two TTTA, CCTG and CTTG tetraloops.[1-2] Recently, our results show that an MDB can also be formed with two CTTTG pentaloops. In the CTTTG MDB, the fourth loop residues (L4 and L4') were found to locate in the major groove, showing no base-base stackings to the loop-closing base pairs. We speculated that a quasi-loop, which contains a discontinuous site along the phosphodiester backbone, may stabilize the MDB by providing backbone flexibility to allow L4/L4' stack well with the loop-closing base pair residues (L5/L5'). In this study, we performed high-resolution nuclear magnetic resonance (NMR) spectroscopy on four sequences with backbone discontinuous sites immediately before L2', L3', L4' and L5', respectively. Our NMR results reveal that a backbone discontinuous site before the L4' position stabilizes the MDB the most, allowing us to better design stable MDBs for DNA nanotechnology applications. This work is supported by Direct Grant (4053270) from The Chinese University of Hong Kong.

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Enhancing DNA Minidumbbell Stability by an Abasic Site

Liqi Wan and Sik Lok Lam*

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

Abstract

Minidumbbell (MDB)[1] is a new form of native DNA structure and exhibits potential applications in DNA nanotechnology.[2] Sequences containing two TTTA, CCTG and CTTG[3] repeats have been reported to adopt MDB structures at neutral pH, and the CTTG MDB remains the most thermodynamically stable one. The solution structure of the CTTG MDB reveals non-ideal geometries for the C-G loop-closing base pairs and the minor groove T·T mispair, which are probably due to constrained backbone geometry in a highly compact structure. In this study, we introduced an abasic site residue (X) between two CTTG repeats to provide backbone flexibilities and studied its structure and stability using high-resolution nuclear magnetic resonance (NMR) spectroscopy and optical melting experiments. The newly designed MDB showed improved base pair geometries and its thermodynamic stability was increased significantly. The results of this study provide deeper insights into the stabilizing forces in MDBs, expanding their applications DNA nanotechnology. This work is supported by Direct Grant (4053194) from The Chinese University of Hong Kong.

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Particle Tracking Microrheology of cytoplasm with Total Internal Reflection Microscope (TIRM)

YANG Gang, NGAI To*
Department of Chemistry, The Chinese University of Hong Kong, Shatin, N. T. Hong Kong
**Email: tongai@cuhk.edu.hk*

Abstract

Cytoplasm is a dynamic network of protein filaments, organelles and macromolecules, spanning the entire cell body and bathed in cytosol. It maintains the shape of cell and a number of cellular and subcellular behaviors also depend on the mechanical functions of cytoplasm. However, study the mechanical properties of cytoplasm is challenging since live cell is a system far from equilibrium. In this work, we attempt to use total internal reflection microscopy (TIRM) to study the viscoelastic properties of cytoplasm and to examine the mechanical properties of cytoplasm correlating to the cellular and subcellular phenomena. TIRM often serves as an ultrasensitive optical technique for measuring the interactions between a probe particle and a flat surface. Because it focuses on monitoring the motion of probe particle within the levitation range of 50 to 400 nm, it is likely to be a suitable tool for studying of the micromechanics of the basal part of cell. We first embedded micron-sized polystyrene (PS) particles in the cytoplasm of NIH-3T3 cells and tracked their movement in the horizontal plane, which was further quantified in x and y on Cartesian coordinate plane. The mean squared displacement (MSD) was different in x and y direction, reflecting the anisotropy of cytoplasm. Of the particles we tracked, the magnitude of MSD and the moving behavior of particles also varied due to the heterogeneity of cytoplasm. The slope of ensemble-averaged MSD against time was close to one, indicating Newtonian-liquid-like cytoplasm, which was

One-step fabrication of Pickering double emulsions and their controlled release properties

ZHANG Tong, NGAI To*

*Department of Chemistry, The Chinese University of Hong Kong, Shatin, N. T. Hong Kong. *Email: tongai@cuhk.edu.hk*

Abstract

Pickering double emulsions combined the high stability of Pickering emulsions with the potentials of double emulsions have attracted significant interest due to their applications in pharmaceutics, cosmetics, and food industries. In this work, we first synthesized a series of poly(*N*-isopropylacrylamide) (PNIPAM)-related microgels and showed that they could be used to stabilize water-in-hydroxy terminated poly(dimethysiloxane) (WSC-209)-in-water (W/O/W) double emulsions by one-step emulsification process. We examined the roles of 1-vinylimidazoe (VIM), 1,4-dibromobutane (DBB), and *N*, *N'*-methylenebisacrylamide (MBA) as co-monomers on the emulsifying ability of Pickering double emulsion. Our results show that the introduction of VIM into the microgels can effectively lead to the formation of double emulsions. At the same time, a combination of DBB and MBA in the presence of VIM endowed the microgels with better emulsifying ability, resulting in double emulsions of higher quality. However, replacing VIM with methacrylic acid (MAA), which gave negatively charged microgels, led to formation of single emulsions. We also investigate the effects of microgel concentration and the water/oil ratio on the emulsion formulation. It was found that relatively high microgel concentrations and water/oil ratios were necessary for the formation of double emulsions. Finally, the release profiles of methylene blue from the inner aqueous phase were studied to demonstrate possible applications of the double emulsions as delivery systems for sensitive ingredients.

Patchy Particles at the Fluid-Fluid Interface

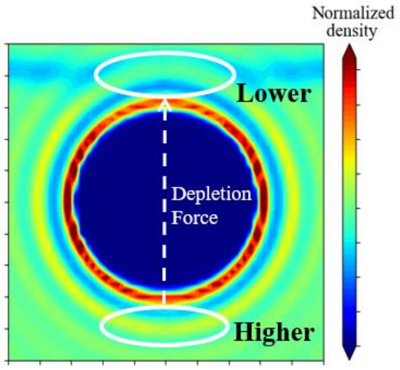
Chung Chi Chio, Ying-Lung Steve Tse*

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

*E-mail: stevetse@cuhk.edu.hk

Abstract

Patchy particles are colloidal particles with two or more physically or chemically distinctive regions. Canonical (*NVT*) Monte Carlo simulations are performed to investigate the stability and dynamics of smooth and rough patchy particles near or at the fluid-fluid interface. We show how the stability of a Janus particle can be controlled by adjusting the surface area ratio of the two faces and how roughness can affect the stability and the orientation of a particle in terms of free energy. Moreover, position-dependent diffusion constants in directions parallel and perpendicular to the interface are calculated for the particles as a function of distance from the interface. We report drastic slowdowns in the parallel and perpendicular diffusivity for all the particles when they are near the fluid-fluid interface. We provide evidence for the hindered diffusion in terms of discrepancy in the fluid density around the particles that leads to depletion forces.



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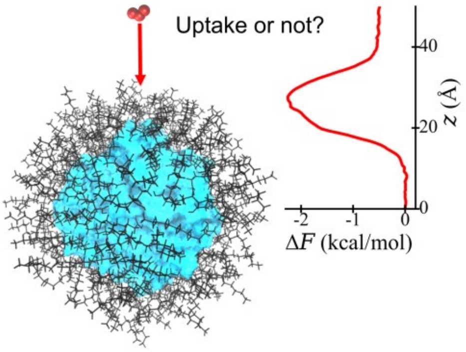
Gas Uptake of Common Atmospheric Gases by Organic-Coated Water Droplets

Wentao Li, Chi Yuen Pak, and Ying-Lung Steve Tse*
Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China.
*E-mail: stevetse@cuhk.edu.hk

Abstract

Organic matters are commonly found in the atmosphere.[1] They can coat on the surfaces of water droplets and have important but nontrivial effects on both physical and chemical properties of the droplets. To shed light on the roles of organic coatings in the gas uptake processes, we studied the uptake of three common atmospheric gases (H_2O, O_3, and SO_2) by a benzoic acid (BA) or lauric acid (LA) coated water droplet in both equilibrium and nonequilibrium molecular dynamics (MD) simulations. Free energy ΔF profiles for gas uptake by coated systems were obtained from equilibrium simulations and compared with the uncoated results in our previous work.[2] By analyzing the intermolecular interactions, we found the change in Coulomb energy dominates the change in potential energy ΔU in the BA-coated systems, while the change in Lennard-Jones energy is crucial in the LA-coated systems. We also found a strong correlation between the entropic contribution $T\Delta S$ and the mobility of water and organic atoms. In the nonequilibrium simulations, we studied the dynamics and kinetics by investigating the influences of organic coatings on the mass accommodation coefficient α. We found a general explanation for the change in α in terms of the relative position of ΔF minimum.



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Title: Coalescence of Organic-Coated Water Droplets

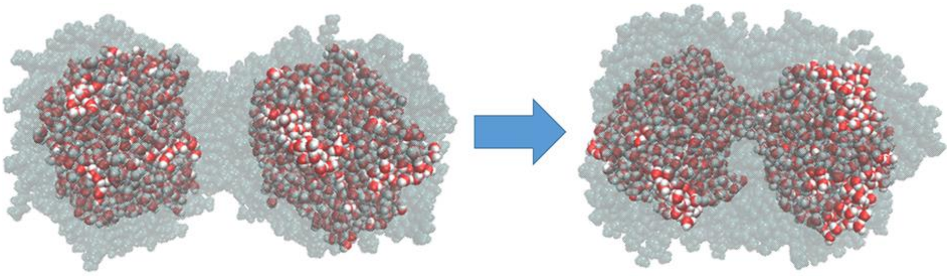
Authors' Names: Chi Yuen Pak, Wentao Li, and Ying-Lung Steve Tse

Postal address: Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China.

*Email: stevetse@cuhk.edu.hk

Abstract

The effect of organic matters on droplet coalescence has been a major concern due to its complexity and important role in cloud droplet growth.[1] In this work, equilibrium and nonequilibrium Molecular Dynamics (MD) simulations were performed to study the free energy profiles ΔF and dynamics of coalescence of organic-coated water droplets respectively. We showed that the changes in water-water interactions and organic-organic interactions resemble to the changes in potential energy ΔU while water-organic interactions oppose to the changes in ΔU. Furthermore, we observed a positive correlation between the change in entropic contribution $T\Delta S$ and the mobility of water and organic atoms. To analyze the dynamics, we systematically studied the outcomes of two colliding droplets as a function of impact speed and impact parameter. We found the stretching separation and shattering of droplets occurred in a slower impact speed, when compared with the pure water droplet collision.[2] For the coalescence cases, we observed the time for complete coalescence is longer for organic-coated droplets due to the migration of organic matters from bulk to interface.



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Computational Study on Zwitterion Catalyzed Esterification Reactions

Xinyan Wang, Steve Ying-Lung Tse*

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

*E-mail: stevetse@cuhk.edu.hk

Abstract

In the previously studied esterification reactions, the mechanisms usually start with the nucleophilic attack of an alcohol at an activated carboxylic acid in presence of a strong acid catalyst.[1-3] Very recently, zwitterions have been found to be good alternative catalysts for esterification without a strong acid. With density functional theory calculations, we discovered a plausible mechanism in which both the negative and positive parts of a zwitterion are involved in an energetically favorable pathway to reach the ester product. The negative part first catches a proton to initiate the reaction and the positive part stabilizes the overall reaction complex. By first understanding how the charge distribution of a zwitterion lowers the energy barrier, we proposed a modified zwitterion catalyst and showed it to be potentially more efficient than existing experimentally made zwitterion catalysts in calculations.

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Effect Chain Length, and Solvent in the Structure of Cellulose tris(3,5-dimethylphenylcarbamate): A Computational Study

Waygen Thor,[a] Lok Wan Ng,[b] Yuen-Kit Cheng[c]
[a] 17482186@life.hkbu.edu.hk, [b] 18439683@life.hkbu.edu.hk, [c] ykcheng@hkbu.edu.hk
Chemistry Department, Hong Kong Baptist University, Hong Kong SAR

Abstract

Cellulose tris(3,5-dimethylphenylcarbamate) (CDMPC) is among the most common stationary phases used in chiral separation column. Currently, there is no reported crystal structure of CDMPC found. Modelling studies of CDMPC so far have been done in reference to the parameterized structure based on the dry crystalline structure of cellulose tris(phenylcarbamate) (CTPC) found in late 80s.[1] Solvent effect was not considered explicitly in those studies. In this work, the structures of CDMPC were studied computationally in the presence of explicit solvent. In 2016, Okada *et al.* reported that the number of monomeric unit of CDMPC would affect the structure of the CSP, and hence the chiral recognition ability. However, most of the previous studies only considered CDMPC with at most nine residues. Thus, the effect of the number of residues on CDMPC is investigated specifically. The modelling of CDMPC with 9, 18, and 26 residues respectively using simulated annealing and molecular dynamics (MD) in explicit solvent were performed. The conformations of the systems were compared and studied in order to find the optimized structure of CDMPC.

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Time-resolved Transient Absorption Spectroscopy for Investigation of Ibuprofen in Solvent-dependent Photochemistry

Bai, Xueqin; Yan, Zhiping; Du, Lili*; Phillips, David Lee*

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

Postal address: phillips@hku.hk

Abstract:

The decarboxylation photochemistry of the common nonsteroidal anti-inflammatory drug Ibuprofen (IBP) is investigated using the ultrafast laser facility, which enables time-resolved transient absorption measurement in the femtosecond time (10-15s) domain. The decarboxylation energy has been demonstrated as being an important factor for photobiological activity. However, it is still unclear whether the triplet state or singlet state mediates the decarboxylation reaction in aqueous solutions[1]. In this work, femtosecond transient absorption spectra reveal that triplet state dominates the decarboxylation process for both neutral form IBP and anion form IBP^- where the time-efficient decarboxylation reaction facilitates the intersystem crossing from an excited singlet to its excited triplet state. Ibuprofen in neutral solutions with 50% water was studied with the detected intermediate exhibiting a lifetime up to 2 nano-second. This excited state has provided some new insight into the potential of using this kind of platform for phototrigger applications[2]. Whereas, in alkali solutions generate dissociated Ibuprofen, whose ultrafast photoreaction behaves very differently according to the femtosecond transient absorption spectra. Therefore, an incremental pH change of the solutions can be utilized to investigate solvent-dependent photochemistry of Ibuprofen.

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Spectroscopic and DFT Studies on the Dibenzene Oxepin Molecule and its Large Stokes Shifted Fluorescence

Li, Yuanchun[1]; Li, Songbo[1] and Phillips, David Lee[1]

[1]Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, China; phillips8hk@gmail.com

Abstract

Dibenz[b,f]oxepin can exhibit bent-to-planar structural change from ground state to the low excited state[2], which is a rare case resulting from out-of-plane bending of a multi-ring system containing aromatic rings[3]. Besides, the reaction mechanisms behind the significantly Stokes-shifted fluorescence of the [n]cycloparaphenylenes and xanthene like molecules are still not clear[4]. To identify the intermediates involved in the structural change and reveal the driving force and mechanism of the process, a combined spectroscopic method involving time-resolved femtosecond transient absorption(fs-TA), time-resolved nanosecond transient absorption(ns-TA), time-resolved transient femtosecond fluorescence (fs-TRF), and nanosecond time-resolved raman(ns- TR^3) is integrated and thoroughly analyzed for studying Dibenz[b,f]oxepin in various solutions in this work. DFT calculation is also used to help reveal the process. The cause of structural/conformational change and redistribution of charges were elucidated from ns-TR^3 spectra as a finger print proof. The Raman band that can be assigned to the stretching vibration of C-C double bond suddenly disappears in the excited states spectra of DBO, which suggests more significant delocalization of the electrons and the formation of the 8π-electrons system in the seven-membered oxepin ring as a result of geometry variation for the bent ground state to the planar excited states.

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Unveiling the Photophysical and Photochemical Reaction Process of Naproxen Via Ultrafast Femtosecond to Nanosecond Laser Flash Photolysis

Liang, Runhui[1]; Li, Ming-De[2*] and Phillips, David Lee[1*]

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

[2] Department of Chemistry and Key Laboratory for Preparation and Application of Ordered Structural Materials of Guangdong Province, Shantou University, Shantou 515063, China.

Email: [1]phillips@hku.hk and [2]mdli@stu.edu.cn

Abstract:

Naproxen is a nonsteroidal anti-inflammatory drug that exhibits phototoxic side effects in humans, but its mechanism of phototoxicity is ambiguous. To uncover photophysical and photochemical reaction processes of naproxen, femtosecond to nanosecond transient absorption spectroscopies were employed to directly detect excited and transient states of naproxen upon UV irradiation in pure acetonitrile, acetonitrile:water 1:1, and acetonitrile:PBS 1:1 solutions. Femtosecond transient absorption results demonstrated that naproxen has two different photochemical pathways at the early delay time before the formation of final products in various solutions. In a pure acetonitrile solvent, naproxen undergoes charge transfer to solvent to generate a radical cation intermediate[1], which decarboxylates to generate a radical intermediate. While in an acetonitrile:PBS 1:1 solution, naproxen predominantly deprotonates first and is promoted to the singlet exited state (^{1}NPX$^-$), which undergoes intersystem crossing to give rise to the lowest-lying triplet states (T_1).[2] T_1 then undergoes decarboxylation reaction and produces a radical species. Kinetic characterization of these processes reveals that the decarboxylation reaction in an acetonitrile:PBS 1:1 solution is faster than that in a pure acetonitrile solvent.

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Copper Phosphide Enhanced Lower Charge Trapping Occurrence in Graphitic-C_3N_4 for Efficient Noble-Metal-Free Photocatalytic H_2 Evolution

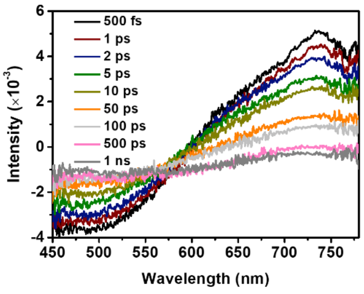
Wenchao Wang,[†,‡] Guisheng Li,[*,‡] David Lee Phillips[*,†]

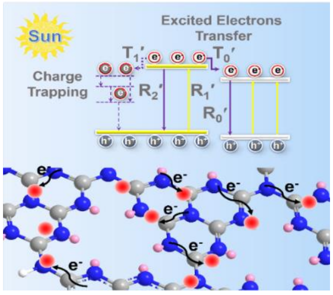
[†] Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong

[‡] Education Ministry Key and International Joint Lab of Resource Chemistry, Shanghai Key Lab of Rare Earth Functional Materials, Shanghai Normal University, Shanghai 200234, China

Abstract

Graphitic carbon nitride (g-C_3N_4) fundamental photo-physical processes show a high frequency of charge trapping due to physicochemical defects.[1, 2] Cu_3P, as an electron acceptor, efficiently captures the photogenerated electrons and drastically improved the charge separation rate Moreover, the robust and intimate chemical interactions between Cu_3P and g-C_3N_4 offers a rectified charge transfer channel, which can lead to a higher H_2 evolution rate for this hybrid that is up to 370 times greater than that achieved from using bare g-C_3N_4. Here, ultrafast time-resolved spectroscopies were employed to illustrate the high charge carrier anti-trapping occurrence in the g-C_3N_4 trap state with a low loading content of Cu_3P. Cu_3P-induced excited electron capturing effectively inhibits photo-charge trapping by the g-C_3N_4 trap band and also increases the charge transfer rate.





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Ion-Exchange Promoted Mutual Synergy between Synthetic Nanomotors

Wu Changjin, Jia Dai, Xiaofeng Li, Jizhuang Wang, Jun Liu, Liang Gao, Jing Zheng, Xiaojun Zhan, Jiawei Chen, Xiang Cheng, Jinyao Tang*

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

Corresponding Email: jinyao@hku.hk

Abstract

Synergistic phenomena are ubiquitous in diverse natural processes, while the intelligent synergy between synthetic active particles remains unexplored. Here we demonstrate the design and manipulation of the artificial synergistic process between the self-propelled ZnO nanorod and sulfonated polystyrene microbeads (SPSBs) promoted by ion-exchange. The ZnO nanorod can slowly dissolve in water through the stabilization of the polar surface and generate cations and anions. The nonsynchronous diffusion of cations and anions form an electric field and propel the ZnO nanorod to move. The SPSBs are capable of absorbing cations along with the accompanying release of protons. When the nanomotor meets the SPSBs, the cations released by the ZnO nanomotor will trigger the ion-exchange of SPSBs and the released protons from SPSBs will enhance the reactivity of the ZnO nanomotor. The chemical communication between ZnO nanorod and SPSBs amplified the motion of both ZnO nanomotor and SPSBs due to the mutually synergetic reaction.

Polarization Taxis of One-Dimensional Sb_2Se_3 Micromotor

Zhan Xiaojun, Jinyao Tang*

Department of Chemistry, The University of Hong Kong, Hong Kong 999077, China;

E-mail: jinyao@hku.hk

Abstract:

Light-driven micro/nanomotors are promising candidates for long envisioned next generation robotics for targeted drug delivery, noninvasive surgery and nano-manipulation. To achieve these fantastic applications, the communication channels between the light and micro/nanomotors are essential for the design and fabrication process of the tiny robotics. Here, a polarization response nanomotor based on one-dimensional crystal Sb_2Se_3 nanowire micromotor is reported firstly to broaden the tool list for light communication. Owing to the asymmetric crystal structure, the linear polarization light shows different absorbtion ability along the axis direction and the orthogonal direction of Sb_2Se_3 nanowire, confirmed by the single nanowire core-shell Sb_2Se_3/ZnO solar cell device. The core-shell Sb_2Se_3/ZnO micromotors without any catalyst exhibit coordinate migration speed with polarization angle between the polarized light. In addition, the migration behavior of crossed nanowire shows the potential to use polarization angle to navigate the micromotor.

Explicit analytical gradients of the orbital-specific-virtual MP2 method for molecular dynamical properties

Ruiyi Zhou, Qiujiang Liang, Jun Yang
Department of Chemistry, The University of Hong Kong, Pukfulam Road, Hong Kong;
juny@hku.hk

Abstract

Previous reports showed that orbital-specific virtual (OSV) approximation can help to build a low-scaling electronic structure with very little loss of accuracy. The successful implementation of this effective electronic structure method in computing molecular static properties provides a possibility that OSV approximation can be applied to the calculations of molecular dynamics properties with high accuracy and efficiency. Herein we integrate the OSV approximation into local second-order Moller-Plesset perturbation theory for geometry optimizations and molecular dynamics. The current poster presents the algorithm and implementation of OSV-MP2 method, the numerical evaluation of OSV-MP2 geometry optimization for baker's test set of molecules and a proof-of-principle demonstration of the low-scaling ab initio molecular dynamics simulation at OSV-MP2 theory.

Fundamentals and analysis of singlet fission materials: A DMRG perspective

Rajat Walia*[1], Jun Yang[1]
[1] Department of Chemistry, The University of Hong Kong, Pok Fu Lam, Hong Kong
*rajat@hku.hk

Singlet Fission (SF) chromophores have emerged as a promising alternative to increase the efficiency of photonic devices[1]. The mechanism of SF process is experimentally poorly understood and the application of modern electronic structure theory methods on these organic molecules (radicals) finds few limitations, for example - the Time-Dependent Density Functional Theory (TD-DFT) underestimates the singlet-triplet gaps[2]. We are working on some multireference (CASCI/CASSCF) calculations to investigate the singlet and triplet energy levels of these molecules and to find the low lying local-exciton (LE) and multi-exciton (ME) quantum states within these molecules.

The use of ab-initio Density Matrix Renormalization Group (ab-DMRG) calculations finds an excellent potential for these molecules by including a relatively large active space in the multireference calculations. High-level multireference calculations have been performed on excited states of pentacene monomers and dimers in DMRG-BLOCK[3] code. We have implemented an extensive wave function analysis[4], based on ab-initio DMRG one- & two-particle state and transition density matrices for providing an adequate notion of the nature of SF charge transfer between fragments and excited states. The projected local spin values are computed for specific fragments in the dimer represents a concise distribution of excited states and pictures the direct evidence for SF processes. Vibronic coupling density analysis[5] has been implemented and carried out to reveal the coupling mechanism between electronic and vibrational degrees of freedom for driving SF charge transfer.

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Highly active electron-affinity for an ultra-low barrier for alkaline ORR in Pd_3Cu

Mingzi Sun, Wu Tong and Bolong Huang*
Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Hum, Kowloon, Hong Kong SAR, China.

*Email: bhuang@polyu.edu.hk

The call for clean and sustainable energy raises tremendous research interests in the fuel cell, which directly converts chemical energy to electricity while the only by-product is water. However, the efficiency of the low-temperature fuel cell is heavily impeded by the sluggish cathode reaction, the oxygen reduction reaction (ORR). Pt, with the highest ORR activity among transition metals, is the state-of-the-art ORR catalyst[1]. However, its expensive cost, scarcity in the earth, and its insufficient catalytic activity altogether hinder the large-scale practical application of low-temperature fuel cells [2]. Extensive effort has been made to improve the catalytic activity of ORR by activating Pt by various methods while finding high activity non-Pt alternatives is more favourable to reduce the expense of Pt. Among the candidates of non-Pt alternatives, Pd stands out due to its similarity to Pt in physical and chemical properties, and its better stability in alkaline condition while being a much more abundant and cheaper choice [2]. Moreover, Pd is predicted to be the second active transition metal catalyst for ORR, and the efficiency will be further improved if the over-binding of adsorbates is resolved.

In this study, the ORR activity of Pd_3Cu in alkaline ORR is theoretically studied, which has been reported to be advantageous to acidic ORR due to the faster kinetics, a more energy favourable pathway and less corrosive condition to the catalytic materials [3]. Our work has supplied a new approach of predicting the predominant ORR mechanism on the surface through the adsorption preference and electron electron-affinity. The DFT calculations have revealed the electronic reactivity as well as adsorption of intermediates on Pd_3Cu surface in alkaline ORR. The unique O_2 adsorption behaviours on the *fcc* site of (111) surface have been observed and lead to the in-depth analysis of the associative reaction mechanism concerning the adsorption strength of intermediates. The overall energetically favourable reaction trend with ultra-low overpotential has been discovered on the electron-affinitive Pd_3Cu as a potential catalyst for alkaline ORR. Our work has strengthened the wider application of d-band-centre theory achieving efficient ORR in an alkaline environment for future applications in fuel cells.

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Time-resolved fluorescence and transient absorption studies on the excited state dynamics of 8-hydroxyquinoline in solution

Bowie Po-Yee Chung, Ruth Chau-Ting Chan, Chris Tsz-Leung Chan, Allen Ka-Wa Wong and Wai-Ming Kwok*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong; *wm.kwok@polyu.edu.hk*.

Abstract

Metal ions play a crucial role in biological process and many neurodegenerative diseases; such as Alzheimer's diseases are reported to be the consequence of metal dyshomeostasis. A small bifunctional molecule, 8-hydroxyquinoline (**8HQ**), features excellent metal-chelating property.[1] This molecule and its derivatives have thus been extensively used for development of effective fluorescent probes for metal detections. However, the underlying mechanism for operation of most of the reported **8HQ**-based fluorescent probes are complex and unclear. Elucidation of the excited state dynamics of **8HQ** is therefore an important issue.

Herein, studies on effect of solvents in controlling excited state proton transfer are presented. Works on the characterization of the photophysical properties (including spectral parameters and kinetic dynamics) of **8HQ** were conducted in varied solvent with different hydrogen bonding capacity. Our combined time-resolved fluorescence and transient absorption studies reveal an interesting solvent-mediated excited state proton transfer process occurring in **8HQ** and how the excited state dynamics of **8HQ** is being modulated by the hydrogen bonding configurations. The result suggests potential of **8HQ** as a "probe" not only for metal ions, but also for property of micro-environment, the network of hydrogen bonding interaction in particular.

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Acknowledgements:

Financial supports from the Research Grants Council of Hong Kong (PolyU/153020/17P) and the Hong Kong Polytechnic University (G-YBAU) are highly acknowledged.

Transient absorption study on the excited state dynamics of N^6-methylated adenine and deoxyadenosine in solution

Allen Ka-Wa Wong, Ruth Chau-Ting Chan, Chris Tsz-Leung Chan,
Bowie Po-Yee Chung and Wai-Ming Kwok*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong (*wm.kwok@polyu.edu.hk*)

Abstract

Recent study shows that N6-methylated adenine (N6MAde) plays an important role in controlling gene expression in eukaryotic cells.[1] The absorption and fluorescence spectra of N6MAde appear similar to its parent molecule adenine (Ade) except for an additional red shifted emission (λ_{max} ~475nm) which is not seen from Ade.[2] The red fluorescence band is likely due to a charge transfer (CT) state formed after the photoexcitation. This is analogous to the case of dimethyl amino-adenine (DMAde), which according to literature exhibits also the dual fluorescence with the red shifted emission resulting from the excited state intramolecular charge transfer.[3-4] In view of the intense current interest in molecular mechanism underlying the photostability and the photo-demaging effect of nucleic bases and its derivatives, and to unveil excited state dynamics including the precise origin of the CT state of N6MAde, we demonstrate herein a femtosecond transient absorption study on DMAde, N6MAde and its derivative N6-methylated deoxyadenosine (N6MdAdo). Our results unveil direct observation and important new insight into the excited state dynamics of these important biological molecules.

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Acknowledgements

Financial supports from the Research Grants Council of Hong Kong (PolyU/153020/17P) and the Hong Kong Polytechnic University (G-YBAU) are highly acknowledged.

Memory Markov State Models for Protein Conformational Dynamics

Siqin Cao[1], Wei Wang[1], Andres Castillo[2], Tom Markland[2], Xuhui Huang[1*]
* xuhuihuang@ust.hk
[1] Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, HK
[2] Department of Chemistry, Stanford University, Stanford, CA, USA

Abstract

We developed a Memory Markov State Model that can model long timescale protein dynamics but built from significantly shorter MD simulations compared to the memoryless MSM. The key insight of our method is to obtain protein dynamics by propagating using the Generalized Master Equation with a memory kernel, which can be obtained by MD simulations with substantially shorter length in comparison with an MSM without memory.

A GPU Acelerated Multi-level DBSCAN Clustering Algorithm for Analyzing Molecular Simulation Trajectories

Song LIU, Wei WANG, Xuhui HUANG*

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

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

xuhuihuang@ust.hk

Abstract: We present a GPU accelerated multi-level DBSCAN clustering method for analysing large-scale molecular dynamics (MD) trajectories. For Boltzmann distributed conformations of a molecular system, regions with high density of MD conformations correspond to the free energy minima. The goal of this algorithm is to find free energy minima from spares to a dense area by increase resolution of DBSCAN clustering in each iteration. By setting a relatively low resolution, ML-DBSCAN could efficiently detect the peaks regions even in a very spares area. By increasing the resolution in the following levels, ML-DBSCAN will focus on the increasing level of the dense area and find the free energy minima belong to this scale of resolution. We anticipate that ML-DBSCAN can be widely applied to split ultra-large MD datasets containing millions of conformations for subsequent construction of core-sets MSMs (Markov State Models).

Report: Newly reparametrized fixed-charge water models compatible with AMOEBA force field

Cong PAN, Chengwen LIU, Pengyu REN and Xuhui HUANG

The Hong Kong University of Science and Technology, Kowloon
pancong@ust.hk

Abstract:

We re-parametrized 2 non-polarizable water models that are compatible with AMOEBA (atomic multipole optimized energetics for biomolecular applications) polarizable force field. With these non-polarizable solvent and polarizable solute applied in simulations, it is possible to highly accelerate the calculation rate without losing too much accuracy. These flexibly bonded and fixed-charge models are fitted to several experimental liquid properties (liquid density, enthalpy of vaporization, dielectric constant, isobaric heat capacity, isother- mal compressibility and thermal expansion coefficient) at 10 different temperatures under 1.0 atm pressure. The structural properties (radial distribution function, self-diffusion constant, and ion solvation free energy) are calculated from MD simulations and compared with reference data to validate the models. Computing efficiency tests of homogeneous bulk water and simple cases of DNA duplex simulations are also performed to further illustrate the feasibility of the new models.

Development of Fast Classification Algorithms to Handle the Heterogeneous Cryo-EM Dataset

Wei Wang, Xuhui Huang*

The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong
Email: xuhuihuang@ust.hk

Cryogenic-electron microscopy (Cryo-EM) has been established as a fundamental structural biology technique in recent decade, benefiting from its potential to resolve the atomic structures of biomolecules at the native condition. The conformational heterogeneity (i.e., multiple conformers co-existing in the sample) can suggest the intrinsic distribution of structures of flexible macromolecules, yet the investigation of such distribution remains a great challenge to both experimentalists and the computer scientist. Currently, people address this heterogeneity issue by building several structures from the experimental images and use the images assigned to each structure as the estimation of population. This approach, however, would be computational intractable for very large dataset as the calculation of the dissimilarity (usually use cross-correlation) of two images is costly. Moreover, the estimation of population is easily affected by the orientations where the structures are indistinguishable.

In our work, we develop a fast two-stage classification algorithm to overcome the above issues. Specifically, we perform classification only on distinguishable viewing angles, where the angles are selected based on the prior knowledge resulting from the principal component analysis results of the structures from the molecular dynamics (MD) simulations. To reduce the computational burden of classification, we adopt some low-dimensional as well as rotationally and translationally invariant features to represent each image. We applied the algorithm to a simulated dataset that mixes five representative structures of bacteria RNA Polymerase, and the population we obtained is consistent with the one we used to generate the dataset. This demonstrates the power of our algorithm in applying to the heterogeneous experimental dataset, through which the population and intrinsic free energy landscape can be better understood.

Optimizing Milestone Locations To Enhance Milestoning Simulations

Yeqing Yu[1], Wei Wang[1], Ron Elber*[4,5], Xuhui Huang*[1,2,3]

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

xuhuihuang@ust.hk

Abstract

Milestoning is a theory and an algorithm that has been widely applied to study the dynamics of complex biological systems. It is based on partitioning the phase space to compartments and running a large number of short molecular dynamics trajectories between milestones or boundaries of the compartments. Given the outputs of the short trajectories and computational matching of the fluxes at the boundaries, Milestoning predicts the kinetics and thermodynamics of the process. Frequently, the milestones are represented by hypersurfaces orthogonal to a one dimensional reaction coordinate (RC). In most applications the milestones are uniformly distributed along the RC.

In the present paper we seek an optimal way to position the milestones along the RC. We propose three cost functions to optimize placement: (a) Reducing the overall computational cost, or minimizing the number of force evaluations, (b) Reducing local computation time at individual milestone (and a processor) and (c) optimizing load balance of the computation to ensure efficient parallelism.

Studies of three systems illustrate the optimization procedures. We use exploratory simulations to optimize the milestone positions on (i) the Mueller potential, (ii) alanine dipeptide in vacuum, and (iii) alanine dipeptide in explicit aqueous solution. We then conducted a straightforward Milestoning calculations using the optimally positioned milestones for comparison with a calculation that employs the non-optimal equally-spaced milestones. We show that milestones obtained from (a) can reduce the computational effort by more than 50% for all three systems, and that a significantly better load balancing is obtained when using methods (b) and (c). We anticipate that these schemes will enhance sampling of Milestoning simulations.

Efficient p-i-n perovskite solar cell via interface modification

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

[1] E-mail: chuaf@connect.ust.hk

[*] E-mail: chsyang@ust.hk

ABSTRACT

As one of the most promising hole transporting material for perovskite solar cell, NiO is widely used in inverted p-i-n perovskite solar cell due to its minor hysteresis, decent hole-conducting properties and easy processability. However, the efficiency of NiO-based perovskite solar cell is still restrained by poor interface between perovskite and nickel oxide layer. Herein, a thin layer of Nickel-Sulphur complex is introduced on NiO by aqueous reaction and greatly improves the photovoltaic performance of subsequent device. It has been revealed that favorable interfacial energetics and Pb-S bonding contribute concurrently to charge transport across perovskite/NiO interface, leading to a champion efficiency at 20.3% on a p-i-n structure device.

Epitaxial Growth of Iron Tungstate Nanosheets on One-dimensional Photoanodes for Efficient Solar Water Oxidation

He Lin,[1] Shihe Yang*

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

[1] Email: hlinag@connect.ust.hk

* Email: chsyang@ust.hk

Abstract:

Type-II heterojunctions have been recognized as an effective structure to significantly improve the charge transport efficiency of photoelectrodes. Herein, a facile method was developed for *in-situ* epitaxial growth of Iron Tungstate (Fe_2WO_6) nanosheets on various one-dimensional nanowire arrays including Fe_2O_3 and WO_3, generating the bespoke photoanodes. Photogenerated electron can be easily transported through the interface between Fe_2WO_6 and Fe_2O_3 (/WO_3) because of lattice match and less Fermi-level pinning. The 2D Fe_2WO_6 nanosheets branching of 1D arrays in epitaxial fashion exhibited significantly enhanced solar water oxidation performance, which is clearly shown in improved light utilizations, enhanced charge separation, as well as decreased electrochemical impedance of the photoelectrode. This work advocates a new paradigm in interface design for optimizing the photoelectrochemical efficiency.

Dynamic Helical Metallopolymers of Platinum(II): Synthesis, Luminescence and Conformational Behavior

Chao Zhao, Shuangshuang Meng and Michael C. W. Chan*

Department of Chemistry, City University of Hong Kong, Tat Chee Avenue, Kowloon.
Email: mcwchan@cityu.edu.hk

The bioinspired development of helical (organic) polymers and their applications have attracted considerable interest. However, the study of metallopolymers with controlled helical sense remains in its infancy, and in such cases the chiral element is directly integrated into the polymer backbone, leading to rigid, "*static*" helicity with high helix inversion barriers. In contrast, "*dynamic*" helical metallopolymers with low helix inversion barriers offer flexibility and potential adaptability, and are more amenable to the development of functionality, but such systems were previously unexplored.

We have developed families of soluble, luminescent glucosyl-substituted poly(M-salphen)-*alt*-(*p*-phenyleneethynylene)s (M = Pt, Zn) that exhibit ordered (helical) coiling of the polymer backbone.[1,2] In this work, new conjugated metallopolymers bearing Pt(II) luminophores have been synthesized, and natural building blocks with different configurations have been incorporated as substituents to introduce helicity into the polymers. Characterization by GPC, NMR, FT-IR, circular dichroism, UV-vis and emission spectroscopy have been undertaken, and interesting photophysical properties and conformational behavior have been observed. These results demonstrate the flexibility, reversibility and dynamic nature of the folded helical conformation in these polymers.

This work was supported by the Research Grants Council of the Hong Kong SAR, China.

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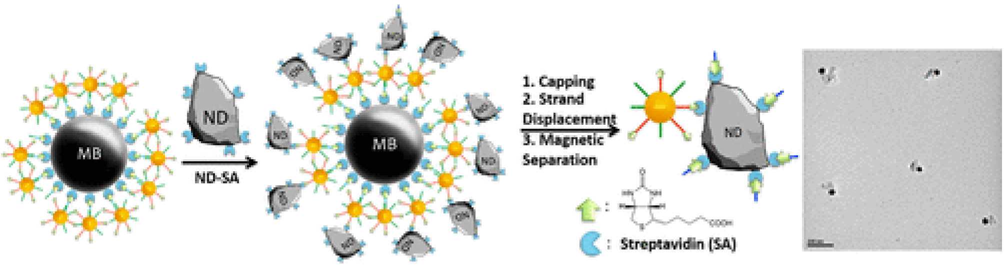
Stepwise Ligand-induced Self-assembly for Facile Fabrication of Nanodiamond–Gold Nanoparticle Dimers via Noncovalent Biotin–Streptavidin Interactions

Miu Shan Chan,[1] Renate Landig,[2,3] Joonhee Choi,[2,4] Hengyun Zhou,[2] Xing Liao,[3] Mikhail D. Lukin,[2] Hongkun Park,[2,3] and Pik Kwan Lo*,[1]

[1] Department of Chemistry, City University of Hong Kong, 83 Tat Chee Avenue, Kowloon Tong, Hong Kong; [2] Department of Physics, [3] Department of Chemistry and Chemical Biology, and [4] School of Engineering and Applied Sciences, Harvard University, Cambridge, Massachusetts 02138, United States; peggylo@cityu.edu.hk

Abstract

Nanodiamond–gold nanoparticle (ND-AuNP) dimers constitute a potent tool for controlled thermal heating of biological systems on the nanoscale, by combining a local light-induced heat source with a sensitive local thermometer. Unfortunately, previous solution-based strategies to build ND-AuNP conjugates resulted in large nanoclusters or a broad population of multimers with limited separation efficiency. Here, we describe a new strategy to synthesize discrete ND-AuNP dimers via the synthesis of biotin-labeled DNA-AuNPs through thiol chemistry and its immobilization onto the magnetic bead (MB) surface, followed by reacting with streptavidin-labeled NDs. The dimers can be easily released from MB via a strand displacement reaction and separated magnetically. Our method is facile, convenient, and scalable, ensuring high-throughput formation of very stable dimer structures. This ligand-induced self-assembly approach enables the preparation of a wide variety of dimers of designated sizes and compositions, thus opening up the possibility that they can be deployed in many biological actuation and sensing applications.



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The Role of Surface Cerium of CeO_2 in Dephosphorylation

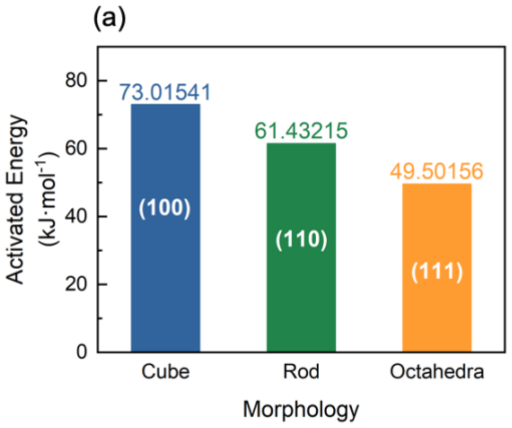
Zicong Tan[a], Yung-Kang Peng[a]*

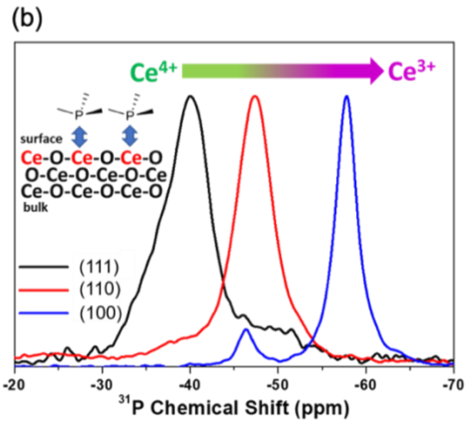
a Department of Chemistry, City University of Hong Kong, Hong Kong SAR, China

* ykpeng@cityu.edu.hk

Abstract

As organophosphorus-based nerve agents can inhibit human neuromuscular enzyme resulting in paralysis and even death, one solution is extracting phosphorus out of phosphorylated molecules as so-called “dephosphorylation”[1]. Recently, as an inorganic catalyst, CeO_2 nanoparticle shows a significant ability in enzyme mimicking for dephosphorylation. It has been demonstrated a promising catalyst due to the effective activation of P-O bond by surface Ce cation for following esters hydrolysis.[2,3] However, very little is known behind the huge difference in activity observed among CeO_2 morphologies in literature[3,4,5] presumably due to the limited information from surface techniques such as Raman and XPS[6]. Herein, dephosphorylation of *p*-nitrophenyl phosphate (*p*-NPP) on CeO_2 morphologies suggests activity in the order of octahedron > rod > cube, which corresponds to the facet activity of (111) > (110) > (100). Our probe-assisted NMR technique, for the first time, shows the dramatic sensitivity towards the facets of CeO_2.It suggests the chemical state of surface Ce on (111)/(100) facet is more Ce^{4+}/Ce^{3+} like while Ce on (110) facet is in between. Accordingly, the difference in Lewis acidity of surface Ce among various host facets is clearly the key factor in facet-dependent dephosphorylation reaction on CeO_2. Compared with conventional surface characterization (e.g. XPS and Raman), probe-assisted NMR is more sensitive to the surface cerium and well explains the active sites in the reaction.





Rational Design of Fluorine-free and Superhydrophobic coating towards Oil-Water Separation

Yuwei Zhu, and To Ngai*

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

E-mail: uvyzhu@gmail.com & tongai@cuhk.edu.hk

Abstract: Superhydrophobic surfaces based on non-fluorinated materials and facile fabrication procedures have always been of great practical value in terms of environmental issues and industrial applications. In this work, by combining bio-based polymer, poly (L-lactic acid) (PLLA) and commercially available hydrophobic silica nanoparticles, a fluorine-free, superhydrophobic coating with hierarchical surface structure and low surface energy was successfully fabricated on different kinds of substrates through our recently developed dip-coating combining with non-solvent induced phase separation (Dip-coating-NIPS) method. The fabricated coating showed super water-repellency, of which the static water contact angle (WCA) and contact angle hysteresis (θ_{Hys}) were determined as $155.7^{\circ} \pm 1.4^{\circ}$ and $5.2^{\circ} \pm 0.4^{\circ}$, respectively. The obtained coating could still exhibit WCA higher than 150°, θ_{Hys} lower than 10° even after water-flushing and tape-peeling. More importantly, the coating could also retain superhydrophobicity under extreme conditions, demonstrating the excellent mechanical durability and chemical stability. Finally, we demonstrated that the fabricated coating could be applied into water-oil separation with excellent separation efficiency.

Facile Synthesis and Fine Morphological Tuning of Branched Hematite (α-Fe_2O_3) Crystals Towards Facet-Directed Photodegradation of Organic Dyes

Joshua Lai, Ken Cham-Fai Leung*

*Department of Chemistry, Hong Kong Baptist University,

Kowloon Tong, Kowloon, Hong Kong

E-mail: cfleung@hkbu.edu.hk

Abstract

Branched hematite (α-Fe_2O_3) inorganic structures, complementary to diffusion-limited aggregation,[1] are commonly formed by the hydrothermal reaction of potassium hexacyanoferrate(III), $K_3[Fe(CN)_6]$, as the iron precursor due to its weak dissociation tendency of the $[Fe(CN)_6]^{3-}$ ions.[2-4] The influence of experimental conditions, such as the concentration, reaction time, pre-nucleation time and heating method, were studied for the morphological tailoring of the crystal habitus. By employing micro-emulsion to inhibit the anisotropic growth direction of $<11\bar{2}0>$,[4] favourable growth was facilitated along $<10\bar{1}0>$ for an unconventional multi-stacked branched structure with an overall conserved hexagonal geometry. Structural characterizations were preliminarily conducted via x-ray diffraction, scanning and transmission electron microscopy. Further studies include the evaluation of the facet-directed photocatalytic activity of the hierarchical structures to degrade different organic dye aqueous solutions.

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Enhanced Photocatalytic Hydrogen Evolution of Carbon Quantum Dot Modified 1D Protonated Nanorods of Graphitic Carbon Nitride

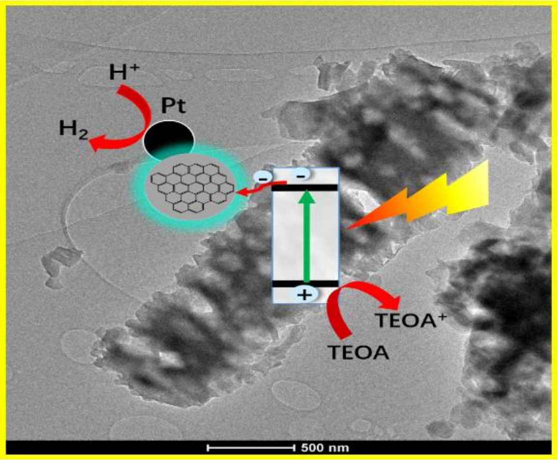
Lingling Li† and Xunjin Zhu*†

†Department of Chemistry, Hong Kong Baptist University, Waterloo Road, Kowloon Tong, Hong Kong P. R. China

Corresponding Author *E-mail: xjzhu@hkbu.edu.hk.

Abstract

1D protonated graphitic carbon nitride (HCN) are prepared through free-template chemical method and further modified with different amount of carbon quantum dots (CQDs) to afford new hybrids denoted as HCNC-x (x represents weight ratio of CQDs) for photocatalytic hydrogen evolution. The immobilization of CQDs onto HCN not only significantly improves the visible-light harvesting, but also prolongs the lifetime of charge carriers upon photoexcitation and suppresses the recombination of electron−hole pairs because of the intimate interface formed between the two components with opposite charges. As a result, the HCNC-0.50 show the highest photocatalytic hydrogen evolution rate of 382 μmol h^{-1} g^{-1} under visible light irritation, which was about 3-fold of pristine HCNC-0.0. Moreover, no decay of activity is observed for the HCNC-x hybrids that is recycled after 12 h photocatalytic reaction.[1]



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Controlling Product Selectivity of Oxygen Reduction Reaction via Rational Design of Electrode Platforms using Affordable Materials

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

Xiaoyong Mo, Edmund C. M. Tse

ABSTRACT

Energy crisis has raised significant attention in recent years. Despite years of research, renewable energy generation, conversion, and storage still suffer from tremendous practical challenges. Notably, fuel cells have yet to fulfil their full potential to convert chemical energy to electricity efficiently. One of the major drawbacks of the state-of-the-art fuel cells is the slow kinetics of the oxygen reduction reaction (ORR) at the cathode.[1] Although Pt-based electrocatalysts achieve high ORR activity, the high price greatly restricts the real-world implementation of fuel cells that utilize Pt and its alloys.[2] Currently, non-precious metals (NPM), such as Co, Fe, and Cu, have been studied as alternative ORR catalysts. However, NPM materials generally reduce O_2 to H_2O while generating O_2^- and H_2O_2 as undesired by-products resulting from incomplete O_2 reduction at the cathode. Also, O_2^- or H_2O_2 causes a degradation of fuel cell components, leading to a decrease in the durability of fuel cells. Herein, our data show that by designing NPM catalysts with precise architecture, the selectivity of ORR to generate H_2O as the only product can be controlled. This strategy can also avoid the activity drop of NPM catalysts.

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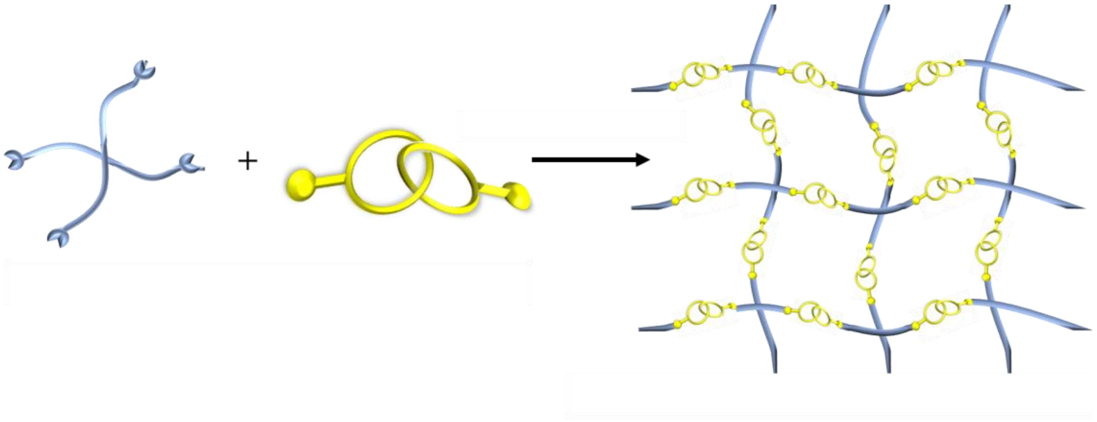
Polymer Network Crosslinked by Catenane

Kong Linghui and Ho Yu Au-Yeung*

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

Email: hoyuay@hku.hk

Catenane is a molecule containing two or more mechanically interlocked macrocycles. Since the linkage is so describe strong as a covalent bond the macrocycles cannot be separated without breaking at least one covalent bond. The interlocked components could move freely within each other[1-2]. Because of the unique topological property, they are promising candidates for exploration of new materials. We here the design of new functional [2]catenane for incorporation into polymer materials as a crosslink. We have designed and studied the incorporation of a [2]catenane as a crosslinker into a four-arm polymer to form a polymer network for studying its mechanical properties.



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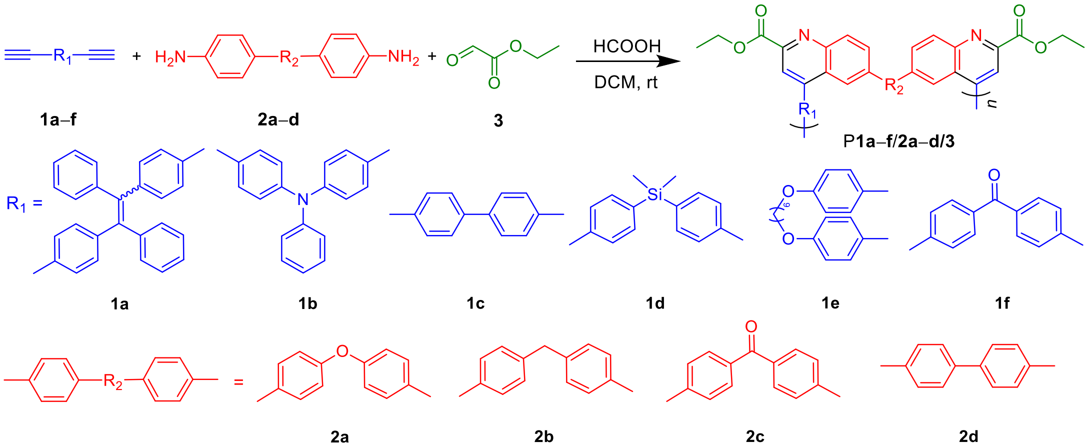
Fluorescence Sensing of Cr(VI) by Functionalized Polyquinolines Synthesized from Metal-Free Multicomponent Polymerization

Yubing Hu, Jacky W. Y. Lam and Ben Zhong Tang*

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

Development of polymerization methodology to afford polymers with unique structures and advanced functionalities is of considerable academic significance and technological implication. Among various multicomponent reactions, the A^3-coupling of aldehyde, alkyne and amine has been established as a convenient and atom-economical method to construct nitrogen-containing heterocycles. Particularly, the development of metal-free polymerizations is highly desirable due to the high cost and biological toxicity of metal catalyst residues. Herein, a facile and highly efficient approach towards functionalized polyquinolines was developed by formic acid-catalyzed multicomponent polymerizations of alkynes, arylamines and glyoxylates (Scheme 1). Conjugated polyquinolines were formed *in situ* with high molecular weights (M_w up to 16 900) in nearly quantitative yields (up to 97.5%). Fluorescence tunable polyquinolines were achieved by altering the electron-donating substituents of the alkyne derivatives. The tetraphenylethene-containing polyquinolines were weakly emissive in solutions but showed intense emission in the solid state, demonstrating an obvious aggregation-induced emission behavior. The *in-situ* generated ethyl quinoline-2-carboxylate endowed the resulting polymers with selective and sensitive fluorescence sensing to Cr(VI) ions. Compared to other metal ions including K^+, Na^+, Mg^{2+}, Ca^{2+}, Al^{3+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Pb^{2+}, Ag^{2+}, Cd^{2+}, Hg^{2+} and Cr^{3+}, the fluorescent sensing of Cr(VI) was more specific with an emission quenching ratio of over 20-fold.



Scheme 1. Polymerization routes to functionalized polyquinolines P**1a–f**/**2a–d**/**3**.

Supramolecular Polymerization with Dynamic Self-Sorting Sequence Control

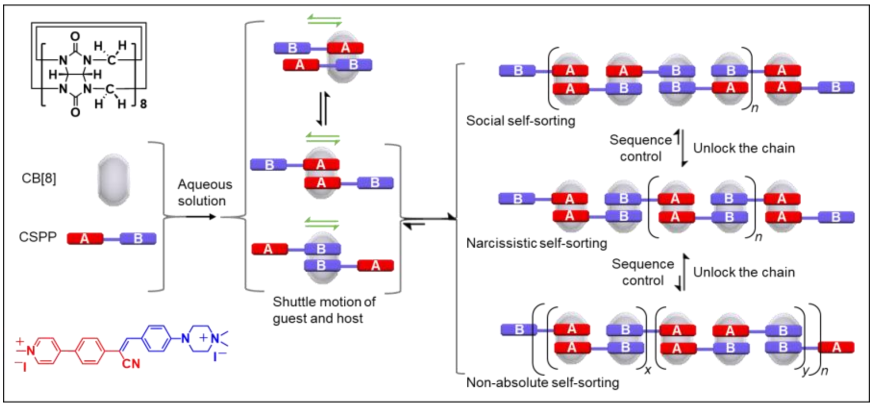
Xiujuan Shi[1], Xinlong Ni[2] and Ben Zhong Tang[1*]

[1]*Department of Chemical and Biological Engineering & Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong. E-mail: tangbenz@ust.hk*

[2]*Guizhou University, Guizhou, China.*

Abstract

Sequence control is very important for both synthetic polymers and biological macromolecules. However, sequence control for both synthetic polymerization and supramolecular polymerization is far from an easy task. Herein, we designed an A-B-type guest molecule, which forms mainly three kinds of ternary complexes with CB[8] as supramolecular monomers to form self-sorting supramolecular polymers with a well-defined sequence of (-AA-BB-)n (Scheme 1). ^{1}H NMR, 2D COSY, 2D NOESY and 2D ROESY spectra demonstrated the process of supramolecular polymerization and their structural changes at each stage of polymerization. Analysis by other techniques including ITC, UV-vis, PL, DLS, DOSY, etc., also proved the successful formation of supramolecular polymers. Our approach provides a new way of thinking for designing sequence-controllable supramolecular polymers. In addition, the water-soluble red-emissive fluorescent supramolecular polymer can detect morphine in artificial urine with considerable sensitivity and accuracy.



Scheme 1. The scheme representation of the dynamic self-sorting sequence control of the supramolecular polymerization of CB[8] and CSPP.

A Simple Approach to Bioconjugation at Diverse Levels: Metal-Free Click Reactions of Activated Alkynes with Native Groups of Biotargets without Prefunctionalization

Xueqian Zhao, Xianglong Hu, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

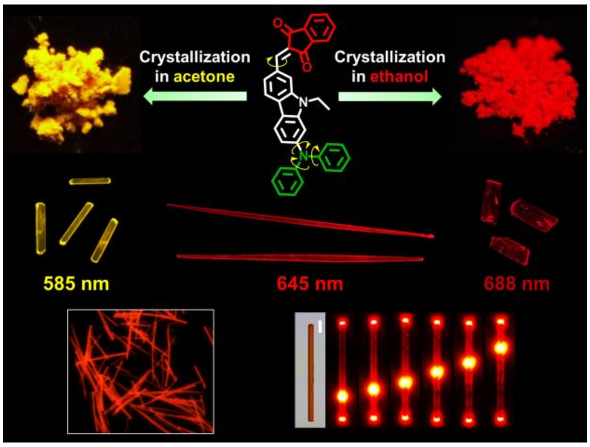
The efficient bioconjugation of functional groups/molecules to the targeted matrix and bio-related species drives the significant development of material science and biomedicine, while the dilemma of metal catalysis, uneasy premodifcation, and limited reaction efficiency in traditional bioconjugation has restricted the booming development to some extent. Here, we provide a strategy for metal-free click bioconjugation at diverse levels based on activated alkynes. As a proof-of-concept, the abundant native groups including amine, thiol, and hydroxyl groups can directly react with activated alkynes without any modification in the absence of metal catalysis. Through this strategy, high-efficient modification and potential functionalization can be achieved for natural polysaccharide, biocompatible polyethylene glycol, synthetic polymers, cell penetrating peptide, protein, fast whole-cell mapping, and even quick differentiation and staining of Gram-positive bacteria, *etc*. Therefore, current metal-free click bioconjugation strategy based on activated alkynes is promising for the development of quick fuorescence labeling and functional modification of many targets and can be widely applied towards the fabrication of complex biomaterials and future in vivo labeling and detection.

Carbazole-Bridged Far Red AIEgen: Crystal Polymorphism, Self-Assembly and Optical Waveguide

Zheng Zheng, Jacky W. Y. Lam and Ben Zhong Tang*

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

Organic materials with aggregation-induced emission (AIE) characteristics have received increasing attentions in recent years because of their potential applications in material science and biological techniques.[1] In this work, a carbazole-bridged far red AIEgen called DC-In with strong fluorescence in both the solid state and in organic solutions was prepared. Interestingly, DC-In displays very strong solvatochromic effect because of push-pull effect of its donor-acceptor structure. The AIE property and self-assembly behavior of DC-In in acetone/water mixture are investigated systematically. Impressively, three single crystals based on DC-In with different luminescence colors (yellow, red and far red) are obtained by controlling the crystallization conditions. The relationship between the emission properties and the crystal structure of DC-In is subsequently investigated. X-ray crystallographic analyses of the three crystals show that there are remarkable differences in the molecular conformation and the molecular packing. Moreover, one of the crystals of DC-In exhibit interesting optical waveguide property.



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Ring-fusion of Non-fullerene Acceptors Based on Perylene Diimides towards Efficient Organic Solar Cells with Small Voltage Losses

Jianquan Zhang, He Yan*

Department of Chemistry, HKUST, Clear Water Bay, Kowloon, Hong Kong, China

Email: hyan@ust.hk

Abstract

Perylene diimide (PDI) is a kind of important non-fullerene electron acceptors in the field of organic solar cells. Previous molecular design of PDI-based acceptors has been directed to those with highly twisted geometries to suppress the excessive aggregation tendency of the PDI units. However, the disrupted molecular packing of these PDI-based acceptors may lead to inferior electron mobilities in the blend films. Here, we studied a series of ring-fused PDI-based acceptors that exhibited more rigidified molecular skeletons, higher absorptivity, upshifted energy levels and enhanced electron mobilities compared with their non-fused counterparts. Importantly, extensive morphological characterizations revealed that after ring-fusion the PDI-based acceptors can obtain better molecular packing and higher domain purities, accounting for the high fill factors of the devices of up to 70%. In combination with donor polymer match and morphology control, high power conversion efficiencies of up to 11% with small voltage losses of c.a. 0.5 V were achieved by the ring-fused PDI-based acceptors. Our work highlights the significance of the ring-fusion strategy in the design of novel PDI-based non-fullerene acceptors.

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Modulating the Activity and Selectivity of Oxygen Reduction Reaction Using a Hybrid Bilayer Membrane System

Tian Zeng; Edmund C. M. Tse

Department of Chemistry, University of Hong Kong, Pokfulam Road, HKSAR, PRC

u3006411@hku.hk; ecmtse@hku.hk

Abstract

Improving the activity and selectivity of the oxygen reduction reaction (ORR), a proton-coupled electron transfer (PCET) cathodic half-cell reaction, is crucial in the widespread utilization of robust fuel cells and alternative energy conversion devices. A catalyst-embedded hybrid bilayer membrane (HBM) is used as an innovative platform to study the mechanism of ORR.[1, 2] A proton transfer agent based on boronic acid is incorporated into the lipid layer of the HBM that contains a covalently-bound Cu catalyst to facilitate proton delivery. Using this HBM construct, we observed the proton transfer rate of this proton carrier was higher than phosphate-based proton carriers. The boronic acid proton transfer agent will lay the foundation for investigating the mechanism of proton carriers through a nanometer-thick HBM.

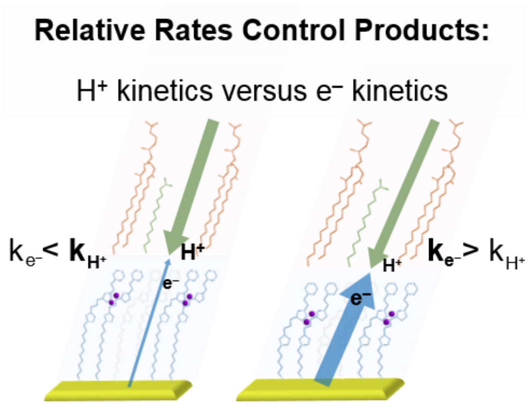

Figure 1. Self-assembled lipid electrodes govern electron and proton transfer rates.

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Synthesis of patchy particles by colloidal extraction

Lyu Dengping, Wang Yufeng[*]
[*]Department of Chemistry, Faculty of Science, The University of Hong Kong,
wanglab@hku.hk

Herein, we present a new strategy for synthesizing anisotropic patchy particles of various kinds. The method, termed “colloidal extraction”, is based on our recent discovery that trimethylamine (TEA) can plasticize and extract linear polymers, e.g., polystyrene, off a non-deformable matrix. The extracted polymer forms the patches, whose number, size, and shapes might be adjusted depending on the kinetics of the extraction process. Specifically, we demonstrate the synthesis of polymer-based dimers, as well as hybrid dimers consisting of a PS patch and a matrix of various materials including titania, hematite, and metal-organic framework particles, etc. In addition, when this method is combined with pre-formed dimer particles, two-patch, three-component particles can be fabricated with pre-defined patch location and size ratio. When further functionalized, such particles show precisely controlled locomotive behavior such as steering with tunable curvature. Our synthetic method offers a new strategy for manipulating the anisotropic particle shapes and will further widen the functionality and applications for self-assembly and active colloids.

Dynamic assembly of a binary dye-sensitized active colloids

Yijiang Mu and Yufeng Wang*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong
Email: u3005475@hku.hk

Abstract:

Driven by constant energy input such as light irradiation, active colloids may form dynamic assemblies such as “swarms” or “living crystals”. [1, 2]However, the complexity of these assemblies is still limited as the particles normally receive energy from single controlling signal, such as UV light. Here, we construct a dye-sensitized titania active colloidal system, where titania particles can be coded with a distinct spectral response, and therefore be controlled by independent light signals. The interactions between each type of particles, which originate from light-induced phoretic effect, can be tuned individually by the intensity of its corresponding light. This eventually leads to particle phase separation and form layer-by-layer crystal structures. This dually controlled active colloidal system is able to introduce the binary assembly principles into nonequilibrium system, increasing structural complexity.

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Unimolecular micelles via block co-polymer functionalized metal organic cages

Lang Wang, Yufeng Wang, The University of Hong Kong

wanglab@hku.hk

Abstract

Micellar nanoparticles are widely used as colloidal carriers in biomedical engineering due to their distinctive hydrophobic core and hydrophilic shell structure. However, conventional amphiphilic micelles are subject to high size dispersity and low stability which limit their applications. The study of unimolecular micelles attracts great attention thanks to their covalently bound core and therefore showing high stability, core of which, however, requires multiple synthetic and purification steps, in addition, the number of arms cannot be precisely controlled. Herein we utilized a kind of materials as the core of unimolecular micelles called metal organic cages, in which the arm of micelles can be precisely controlled and form uniform unimolecular micelles which we named BCPMM via simple two step assembly, the BCPMM exhibits low critical micelle concentration and low toxicity, and is thus promising to be used as next generation of nanoparticle drug carriers.

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Patchy metal-organic framework colloids

Wei Xu, Yufeng Wang*

Department of Chemistry, The University of Hong Kong, Pofulam, Hong Kong

Email: u3005713@connect.hku.hk

Abstract:

Patchy particles hold much promise for creating complex and open structures. Here we introduce a new type of patchy particles, pMOF, synthesized by exposing or modifying selected facets of the crystalline polyhedral metal-organic framework colloids (CMOFs) via a seeded-growth mechanism. In one case, we use polymers to partially embed CMOFs, producing Janus particles with low-symmetry, triangular or pyramidal patches. In another case, two-patch particles are made by growing a new MOF layers on specific surfaces. By adjusting the reagents and modulator, the morphology of those pMOFs can be well controlled. Currently, we are assembling those particles into higher order structures. They may also have potential applications as colloidal carrier and micro-motors.

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Ni/Ni_3S_2 Nanoparticles Encapsulated by S-doped Carbon Nanosheet Arrays as a Highly Efficient Electrocatalyst for Hydrogen Evolution

Yong Li, Chui-Shan Tsang, Mengjie Liu, Liangsheng Hu, Kyeong S. Hwang, and Lawrence Yoon Suk Lee*

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

E-mail address: lawrence.ys.lee@polyu.edu.hk

Abstract

Three-dimensional (3D) carbon-based catalysts grown on a substrate exhibit superior electrocatalytic activities towards hydrogen evolution reaction (HER).[1,2] Herein, a novel method is described to in-situ form S-doped carbon nanosheet arrays-encapsulated Hybrid Ni/Ni_3S_2 nanoparticles on carbon cloth. This Ni/Ni_3S_2/SC NSAs provides a large surface area and high conductivity to work as an efficient HER catalyst with excellent activity and stability. The overpotential can reach 90 mV at a current density of 10 mA cm^{-2} along with a small Tafel slope of 81 mV dec^{-1}. Our work clearly discussed the strong electronic interactions between hybrid Ni/Ni_3S_2 nanoparticles and S doped carbon nanosheets and confirmed the real active sites of this composite. Theoretical calculations were employed to analyze the influence of S-O bond in the S doped C nanosheets towards HER. This study offers not only an effective way to synthesize 3D carbon-based structure on substrate, but also some valuable insights for the future design of these catalysts containing transition metal compounds and heteroatoms doped carbon materials.

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Morphologic, structural, and catalytic correlation of MOFs under electrochemical environment: A case study using ZIF-67

Weiran Zheng[1], Mengjie Liu[1], Lawrence Yoon Suk Lee*
Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR, China
E-mail address: lawrence.ys.lee@polyu.edu.hk

Abstract

Metal-Organic Frameworks (MOFs) serve as promising candidates in many electrochemical applications, due to the robust open structure and the directly exposed metal nodes to aqueous environments. Numerous researchers have utilized MOFs as catalysts with excellent catalytic activities or templates for further fabrication. However, the structural evolution of MOFs during electrochemical processes are yet to be clarified, such as stability and real catalytic species. In this work, the material ZIF-67 was symmetrically investigated by correlating the morphology, structure and catalytic activity towards water oxidation in alkaline electrolyte. Three anodic oxidation peaks in CV plots indicated the Co^{2+} nodes inside ZIF-67 underwent serval electrochemical processes: the exposure to the surface (I), the deposition of $Co(OH)_2$ (II) and the generation of high valance Co species coupled with OER (III). The morphologic evolution from cubes to aggregated spheres are observed along the CV studies.

Based on current results, we propose that ZIF-67 is not stable and will go through both morphologic and structural evolution during routing CV studies, which is an indication that current research works employing MOFs as electrocatalysts needs closer study to identify the real active species.

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Development of Defect-rich Tungsten Oxide Nanoplate as Photocatalyst for Hydrogen Evolution

Xiandi Zhang, Chui-Shan Tsang, Lawrence Yoon Suk Lee*
Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon
E-mail address: lawrence.ys.lee@polyu.edu.hk

Abstract

Tungsten trioxide (WO_3) as an n-type semiconductor has a band gap between 2.6 eV to 2.8 eV.[1] It is a functional material with widespread applications in various fields, such as electrocatalysts, photoelectrochemical water splitting, lithium ion battery and so on.[2] Moreover, various crystal structures of WO_3 such as triclinic, orthorhombic, tetragonal, cubic, monoclinic and hexagonal structure have attracted a lot of attention.[3] Therefore, we prepared three different phases (monoclinic, orthorhombic and cubic) of WO_3 with introduction of oxygen vacancies currently by a novel and relatively mild method. We demonstrate that the amount of oxygen vacancy can be well adjusted by changing the concentration of reducing agents. Also, a relationship between polymorphic transition and oxygen vacancy amount was built up. Importantly, as a well-known photocatalyst for oxygen evolution reaction, the activity can be enhanced with increasing vacancies in WO_{3-x}.

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Hydrotalcite-Templated Ultrathin Two-Dimensional Carbon Nanosheets with *In Situ* Sulfur Doping for High-Performance Sodium Ion Battery Anode

Kang Ding, Lawrence Yoon Suk Lee* and Kwok Yin Wong*

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

Email: kwok-yin.wong@polyu.edu.hk; lawrence.ys.lee@polyu.edu.hk

Abstract

Sulfur-doped carbon is a promising anode material for room-temperature sodium ion batteries (SIBs) owing to its extra active sites and expanded interlayer distance to accommodate rich sodium ions.[1] However, high-rate performance of many sulfur-doped carbons is far from satisfactory due to the inferior structures. Here, Mg-Al hydrotalcites are used as two-dimensional (2D) templates and containers to confine sulfur-containing organic species, finally giving ultrathin 2D carbon nanosheets doped with high-content sulfur after carbonization. When applied as anode in SIBs, the optimal carbon nanosheets can deliver a specific capacity of 336.3 mAh g^{-1} at 100 mA g^{-1} and superior rate capability with a capacity of 125 mAh g^{-1} even at 10 A g^{-1}. Moreover, the electrode remains stable even after 1000 cycles. The high capacity and excellent high-rate performance of the 2D sulfur doped carbon nanosheets are ascribed to sulfur doping, 2D sheet-like structure as well as large surface area. Further, electrochemical analysis of the battery reveals that the capacitive effect increases with accelerated charging-discharging rate. The study provides a promising strategy to prepare high-performance 2D carbon material in SIBs, which can be applied to the fabrication of 2D carbon nanosheets doped beyond sulfur as well.

Reference

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Balancing Cavity Space and Core Size in a Yolk-Shell Nano-photocatalyst for Hydrogen Evolution from Water

Wei Liu, Guangchao Zheng, Enna Ha, Lok-yan So, Lawrence Yoon Suk Lee, Kwok-Yin Wong*

Dept. of Applied Biology and Chemical Technology, The State Key Laboratory of Chemical Biology and Drug Discovery, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR, China.

kwok-yin.wong@polyu.edu.hk

Yolk-shell plasmonic metal-semiconductor photo-catalysts have shown significant enhancement from individual semiconductor nano-materials. It is widely accepted that the photo-catalytic activity is closely related to the amount of photo-generated electron-hole pairs, which is strongly dependent on the capability of the light absorption of the photo-catalyst. Knowing that in the hollow structure, light can be reflected and scattered then redirected to nearly all directions, facilitating the use of incident light by an increased light path length. Since the multiple light reflection and scattering in-between the yolk and shell are responsible for an enhanced local-field of plasmonic metal, a boosted photocatalytic performance can be expected by optimizing the space in-between and size of plasmonic core in this hetero-nanostructure. Aside from precious plasmonic metals (Au, Ag), and semiconductors of weak photo-response from wide bandgap (above 3 eV) (TiO_2) and toxic nature (CdS), respectively. A plasmonic metal of earth-abundant element and green semiconductors with a suitable bandgap for greater light harvesting are therefore needed. Herein, Cu-Cu_xS ($1\leq x \leq 2$) with yolk-shell structure has been constructed to introduce multiple light reflections and scattering, enabling light collision with the Cu yolk and the Cu_xS shell. This structure not only increases the light path length but allows for surface plasmon resonance (SPR) coupling between the plasmonic Cu and plasmonic Cu_xS, provides a platform to study their photocatalytic activities. By varying the space in-between using different size of plasmonic core, optimization of the photo-catalytic performance is studied. The plasmonic coupling of Cu with Cu_xS suggests an avenue for SPR-promoted photocatalysis not only due to an enhanced light harvesting but a basic understanding of SPR couplings of two plasmonic components.

A Trifunctional Bipolar Compound for Aqueous Organic Redox Flow Batteries

Chun Wai Tang, Bin Liu, Tianshou Zhao *, and Guochen Jia *

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

Redox flow battery is a rechargeable battery used for sustainable, large-scale energy storage (Fig 1). Aqueous organic redox flow batteries (AORFBs) have recently drawn substantial attention as the environmentally friendly alternatives to tradition non-aqueous redox flow batteries due to their potential to achieve high energy density and low cost. However, one of the obstacles hindering the development of AORFBs is the crossover of electroactive species between two half-cells, resulting in rapid and irreversible capacity decay. Herein, we report a novel aqueous organic bipolar material **[(NPr)(BPy)]I₂** acting as both catholyte, anolyte. In addition, the material can also function as charge carrier so that no additive supporting electrolytes are needed, representing the first example of trifunctional bipolar species in redox flow battery (Fig 2).

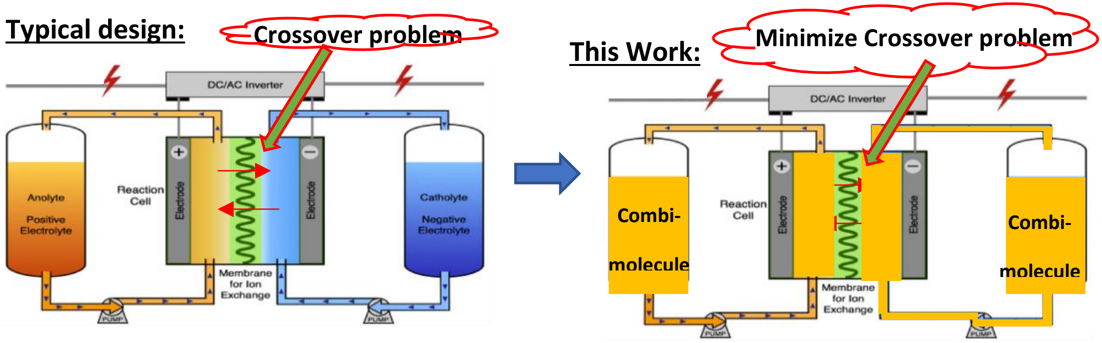
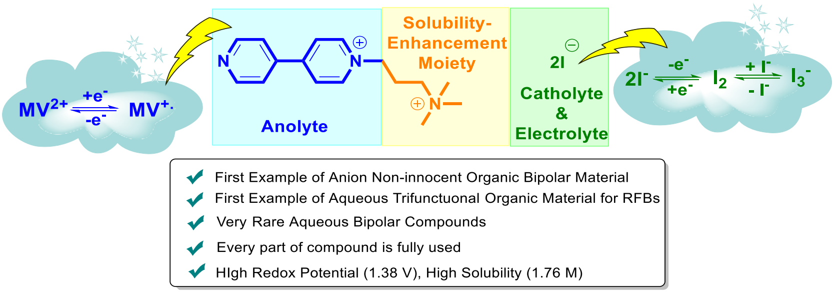


Figure 1. Schematic diagram of redox flow battery.



- ✓ First Example of Anion Non-innocent Organic Bipolar Material
- ✓ First Example of Aqueous Trifunctuonal Organic Material for RFBs
- ✓ Very Rare Aqueous Bipolar Compounds
- ✓ Every part of compound is fully used
- ✓ HIgh Redox Potential (1.38 V), High Solubility (1.76 M)

Figure 2. Design of trifunctional bipolar compound.

Boosting the efficiency of organic persistent room-temperature phosphorescence by intramolecular triplet-triplet energy transfer

Tsz Shing Cheung, Weijun Zhao, Ben Zhong Tang

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

Abstract

Persistent luminescence is an extraordinary phenomenon where the emission sustains even after the cease of excitation. However, the development of organic persistent luminescent materials, such as organic persistent room-temperature phosphorescence (OPRTP), lags because of their low efficiency. Moreover, the traditional strategies of efficiency enhancement conflicts with the lifetime prolongation for OPRTP, setting an irreconcilable obstacle. Here, we report a new strategy to boost the efficiency of OPRTP by intramolecular triplet-triplet energy transfer (TTET). TTET is a well-known photophysical process to exchange both the spin and energy between molecules or intramolecular fragments. Incorporation of (bromo)-dibenzofuran to carbazole results in high phosphorescence quantum yield of up to 41% and lifetime of 0.54 s under ambient conditions. The (Bromo)-dibenzofuran provides an intramolecular triplet-state bridge and boosts the intersystem crossing, to lead to a near quantitative exothermic triplet–triplet energy transfer to repopulate the lowest triplet-state of carbazole. All these factors work together to contribute the efficient OPRTP. The present results shows that such an approach can resolve the conflicts between efficiency and lifetime and provides a novel and useful strategy to design efficient OPRTP materials. This rational design strategy should be applicable for exploring novel OPRTPs with high-tech applications.

Non-Stoichiometry Promoted Polymerization of Internal Alkynes and Pyrazoles to Functional Poly(indazole)s

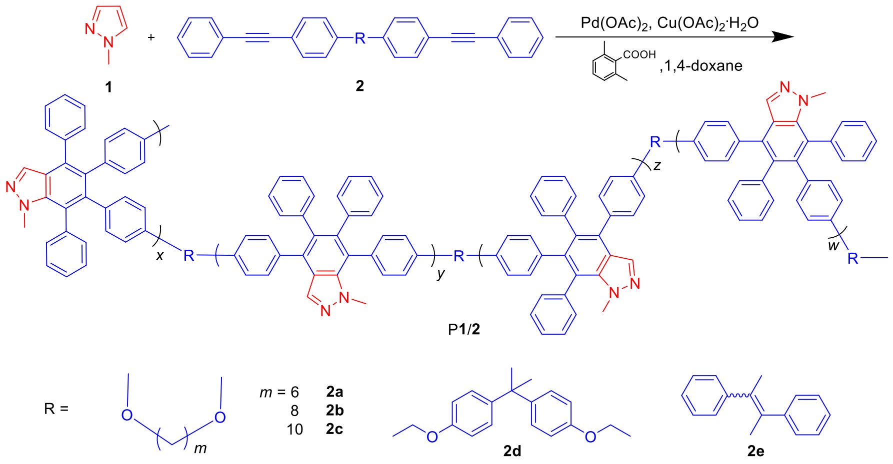
Qingqing Gao, Ruoyao Zhang, Zijie Qiu, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

A new monomer stoichiometry imbalance-promoted strategy for synthesizing poly(indazole)s (PIs) with novel functionality was described in this work. This oxidative polyannulation of internal diynes and 1-methylpyrazole was catalyzed by palladium species in 1,4-dixane at 120 °C with copper acetate monohydrate as oxidants, affording a series of PIs with high molecular weights (M_w up 35 800) in satisfactory yields (up to 84.0 %). Their thin solid films on silica wafers showed high and tunable and refractive indices (n = 1.7858–1.6042) in a wide wavelength region from 400 nm to 900 nm. Moreover, PIs exhibit high thermal stability, losing little of their weights at high temperature of 321–353 °C. Due to its high photosensitivity and strong solid-state emission, P**1/2e** thin film was successfully fabricated into a two-dimensional photopattern with high resolution and sharp edges. This novel polyannulation is an example of non-traditional non-stoichiometry-promoted polymerization and its mechanism was systematically studied. Furthermore, PIs can be used as effective dye to distinguish live or dead cells.

Scheme 1. Polymerization of Pyrazole and Internal Diynes to Poly(indazole)s



Novel AIE Platform Based on Phenothiazine

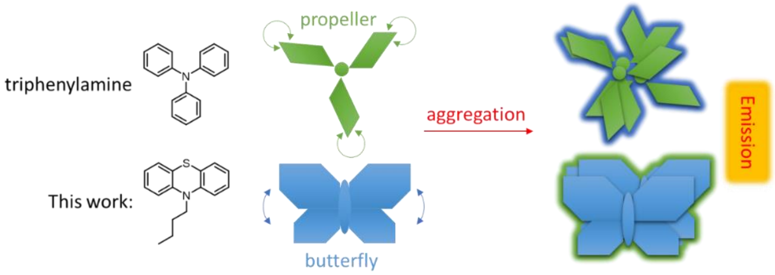
Junyi Gong[ab], Xiangzhi Song*[b], Ben Zhong Tang*[a]

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

[b] College of Chemistry and Chemical Engineering, Central South University, Changsha
410083, Hunan, China. E-mail: xzsong@csu.edu.cn.

Abstract

Nowadays, most of aggregation-induced emission luminogens (AIEgens) with donor (D)–acceptor (A) structures are based on propeller-shaped triphenylamine (TPA) as electron donor. After years of development, TPA-related AIEgens are comprehensive and highly developed. In this contribution, we used phenothiazine (PTZ) instead of TPA as electron donor for designing new AIEgens. 11 PTZ derivatives were facilely synthesized through Knoevenagal condensation. Almost all the PTZ dyes are emissive at the red spectral region of above 600 nm. In addition, PTZ10 and PTZ11 were found emissive at the NIR region with high solid-state fluorescence quantum yield (~5 %). Since PTZ contains no any rotatable elements like normal AIEgens, we investigated the exact driving force for the AIE behaviour of the PTZ dyes through single crystal analysis and comprehensive density function theory calculation, from which the restriction of intramolecular vibration was proved to be the AIE mechanism. Moreover, we used PTZ6 with a fairly high fluorescence quantum yield (~20 %), to selectively track the lipid droplets of HeLa cells with very high contrast, demonstrating a high potential of the PTZ dyes for practical applications.



Scheme 1. Schematic view of the AIE mechanism of triphenylamine and phenothiazine.

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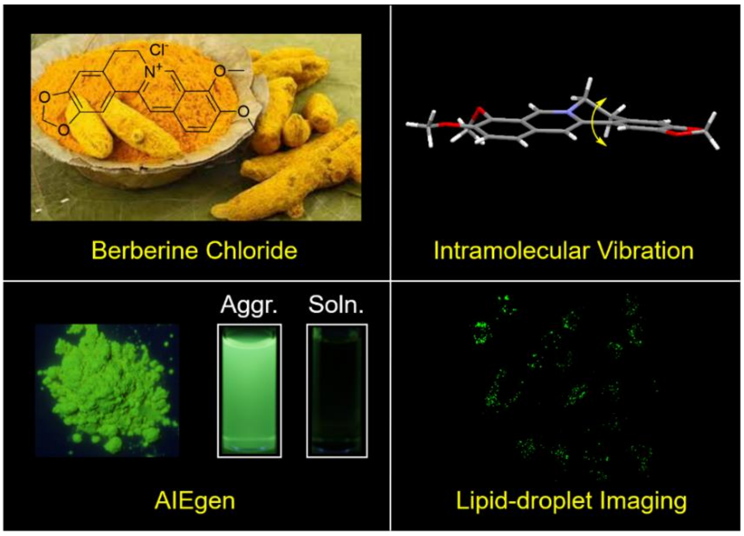
Exploration of biocompatible AIEgens from natural resources

Yuan Gu, Ryan T. K. Kwok, Jacky W. Y. Lam and Ben Zhong Tang*

Department of Chemical and Biological Engineering & Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China. E-mail: tangbenz@ust.hk

Abstract

Luminogens with aggregation-induced emission (AIEgens) characteristics have been well developed and applied in various areas such as bio-imaging, theranostics, organic photoelectronics and chemo/bio sensors. However, most of the reported AIEgens suffer from the disadvantages of complex organic synthesis and high cost, as well as environmental unfriendly and hard degradation, which have largely limited their real applications. In this work, we discovered that berberine chloride, a natural isoquinoline alkaloid isolated from Chinese herbal plants, served as an unconventional rotor-free AIEgen with bright solid-state emission and water-soluble characteristic. Single crystal structure analysis and optical property, viscosity, and host–guest interaction studies suggested that intramolecular vibration and twisted intramolecular charge transfer were responsible for the AIE phenomenon of berberine chloride. Moreover, berberine chloride was biocompatible and could specifically target lipid droplets in a fluorescence turn-on and wash-free manner, demonstrating the great potential of natural products as promising AIE probes.



Photomodulatable Polymers Synthesized by a Monomer Nonstoichiometric Strategy

Ting Han, Jacky W. Y. Lam and Ben Zhong Tang*

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

E-mail: tangbenz@ust.hk

Abstract

Photomodulatable polymers with light-responsive optical properties have attracted great interest over recent decades due to the increasing demands on smart optical materials. The synthesis of main-chain photomodulatable polymers are generally achieved by step-growth polymerizations of A_2 + B_2 monomers. However, these polymerizations often use limited and synthetically difficult difunctional monomers with photoresponsive moieties. Meanwhile, a strict control on the monomer stoichiometry must be met to produce high molecular weight polymers despite of the difficulty of realizing such stoichiometric conditions in practice.

In this work, we developed a straightforward monomer nonstoichiometric stepwise polymerization strategy to in-situ generate photomodulatable spirocyclic polymers from commercially available monofunctional monomers. The palladium-catalyzed spiroannulation polymerizations of naphthols and internal diynes proceed efficiently under monomer nonstoichiometric conditions and the presence of excess naphthol monomers significantly improves the polymerization efficiency possibly due to the "reactive intermediate" mechanism. This unique monomer-nonstoichiometry-promoted polymerization effect allows the preparation of telechelic spirocyclic polymers with reactive triple-bond end groups for further functionalization. The obtained spirocyclic polymers show excellent film-forming ability, high thermal and morphological stability, and interesting photomodulatable optical properties. Well-resolved two-dimensional fluorescent photopatterns with both "turn-off" and "turn-on" modes can be readily fabricated based on the photobleaching and photoactivation process of different polymer films under strong UV irradiation. Furthermore, we innovatively utilized the photomodulatable refractive index of these polymer thin films to permanently modify the resonance wavelengths of microring resonators in integrated silicon photonics by UV irradiation.

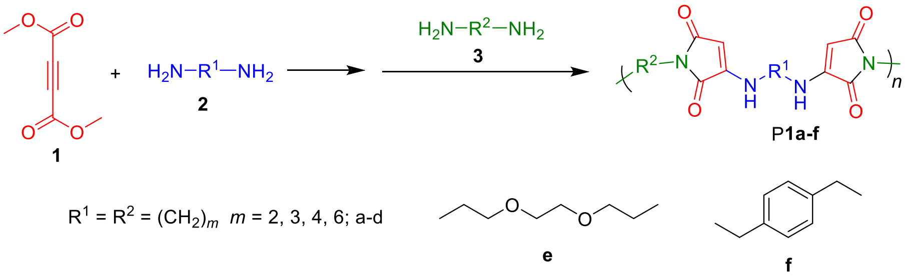
Catalyst-Free Multicomponent Tandem Polymerizations of Alkyne and Amines Toward Nonconventional Luminescent Poly(aminomaleimide)s

Benzhao He, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

Nonconventional luminophores are featured with weak or no conjugation and possess no large fused cyclic rings. They have attracted much interest from researchers as they provide a new insight into the photophysical process of light emission.[1-3] Their excellent biocompatibility and good biodegradability also enable them to find potential applications in a variety of biomedical areas, such as fluorescent bioprobe, drug delivery and gene carrier.



In this work, a multicomponent tandem polymerization of alkyne and amines for the efficient preparation of nonconventional luminescent poly(aminomaleimide)s was established. Through systematic optimization of the reaction conditions, several soluble and thermally stable poly(aminomaleimide)s with moderate molecular weights (M_w up to 6 760) and well-defined structures were obtained in excellent yields (up to 95%). The resulting polymers show high fluorescence efficiency in both dilute solutions and aggregate state. Cell viability assay by MTT show that the polymers have a low cytotoxicity. This make them suitable for use as fluorescent bioprobe and gene carrier. This new multicomponent tandem polymerization opens great opportunities for preparing functional nonconventional luminescent polymeric materials.

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A functioning macroscopic "Rubik's Cube®" assembled *via* controllable dynamic covalent interactions

Xiaofan Ji,[1] Zhao Li,[1] Jacky W. Y. Lam,[1] Jonathan L. Sessler[2,]* and Ben Zhong Tang[1,]*
[1]*Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China.*
E-mail: tangbenz@ust.hk
[2]*Department of Chemistry, The University of Texas at Austin, Austin, Texas 78712-1224, United States. E-mail: sessler@cm.utexas.edu*

Abstract

The organization of functional molecules to form dynamic macroscopic assemblies is a hallmark of living systems. Here, we report the dynamic behavior of macroscopic assembly via controllable dynamic covalent interactions. Seven dynamic acylhydrazone bond-containing hydrogels, showing different fluorescent colors, were assembled by hand into a Rubik's Cube®-like structure (RC, Figure 1). In analogy to traditional Rubik's Cubes®, the layers making up the hydrogel RC can be rotated either horizontally or vertically to change its pattern. However, in contrast to Rubik's Cubes®, the hydrogel RC may be modified either ex situ or via direct application of a chemical stimulus to produce new color arrangements. The present system thus allows dynamic control over macroscopic structure and patterning through both physical and chemical means.

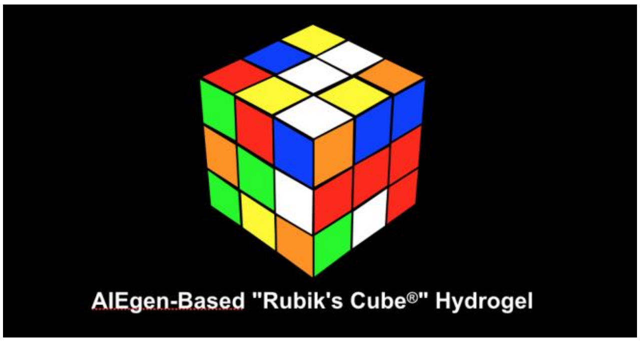

Figure 1. Cartoon representation of the AIE-based “Rubik’s Cube®” hydrogel.

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Strategies to Enhance the Photosensitization: Polymerization and the Donor-Acceptor Even-Odd Effect

Yuanyuan Li, Ryan T. K. Kwok, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

A particular challenge in the design of organic photosensitizers (PSs) with donor–acceptor (D-A) structures is that it is based on trial and error rather than specific rules. Now these challenges are addressed by proposing two efficient strategies to enhance the photosensitization efficiency: polymerization-facilitated photosensitization and the D-A even–odd effect. Conjugated polymers have been found to exhibit a higher $^1O_2$ generation efficiency than their small molecular counterparts. Furthermore, PSs with A-D-A structures show enhanced photosensitization efficiency over those with D-A-D structures. Theoretical calculations suggest an enhanced intersystem crossing efficiency by these strategies. Both in vitro and in vivo experiments demonstrate that the resulting materials can be used as photosensitizers in image-guided photodynamic anticancer therapy. These guidelines are applicable to other polymers and small molecules to lead to the development of new PSs.

In-situ Generation of Azonia-containing Polyelectrolytes for Luminescent Photopatterning and Superbug Killing

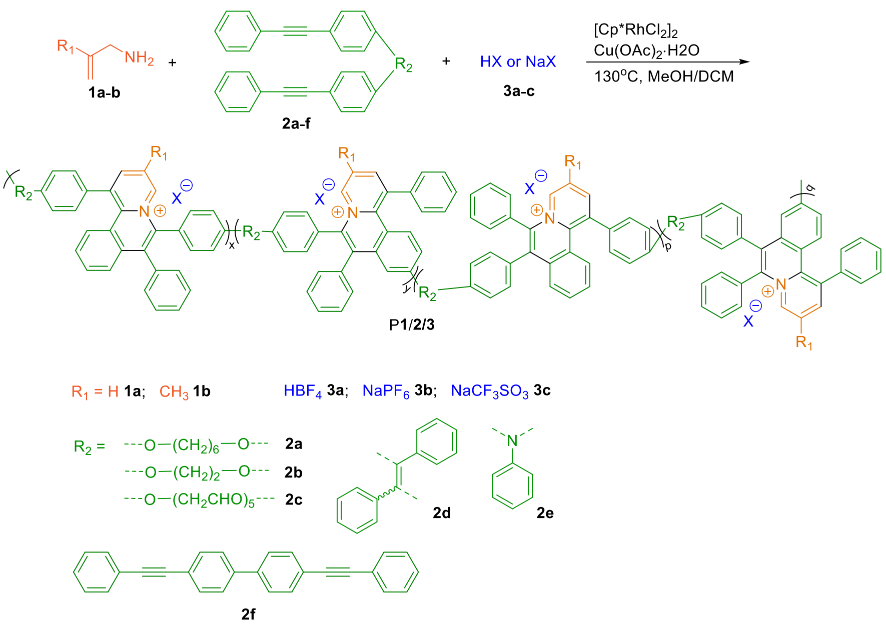
Xiaolin Liu, Jacky W. Y. Lam, Ben Zhong Tang*

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

Abstract

Polyelectrolytes play an important role in both natural biological systems and human society. Thus, their synthesis, especially speciality polyelectrolytes, and study are essential for biomimicry and creating new materials. In this study, we developed an efficient synthetic methodology by using readily accessible nonionic reactant in the presence of commercially available cheap ionic species to in-situ generate azonia polyelectrolyte in a one pot manner (Scheme 1). The resulting polyelectrolytes are emission in the solid state and form readily luminescent photopatterns with different colors. The extraordinary strong ability of reactive oxygen species (ROS) generation of the polymers enables them to impressively kill methicillin-resistant *Staphylococcus aureus* (MRSA), a drug resistant superbug, both in vitro and in vivo without acquired resistance.

Scheme 1. Syntheses of azonia-containing polyelectrolyte

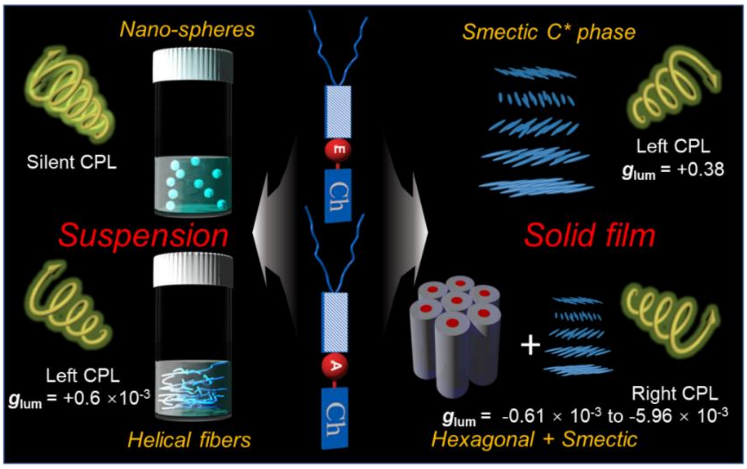


Tunable Circularly Polarized Luminescence from Molecular Assemblies of Chiral AIEgens

Fengyan SONG, Jacky W. Y. Lam and Ben Zhong Tang*
Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China.
E-mail: tangbenz@ust.hk

Abstract

Circularly polarized light (CPL) is important to chiral photonic technologies.[1] In molecular systems, besides their intrinsic chemical structures, the architectures of molecular assemblies at the mesoscopic scale also account for the final macroscopic CPL properties. Herein, a liquid crystalline assembled system called DPCE-ECh exhibiting smectic C* phase with a high dissymmetry factor (g_{CD} = -0.20 and g_{lum} = +0.38) is reported. The DPCE-ECh film exhibits intense CPL due to the intrinsic helical structure of the molecular assembles with weak contribution of Bragg reflection and helical axis parallel to the direction of the glass substrate. To the best of our knowledge, this large g_{lum} factor is very rare for organic compounds even in the assembled state formed by annealing at smectic liquid crystalline phase.



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A Robust Serum-Albumin-Responsive AIEgen Enables Latent Bloodstain Visualization in High Resolution and Reliability for Crime Scene Investigation

Zhaoyu Wang, Pengfei Zhang, Haixiang Liu, and Ben Zhong Tang*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Hong Kong; tangbenz@ust.hk

Abstract

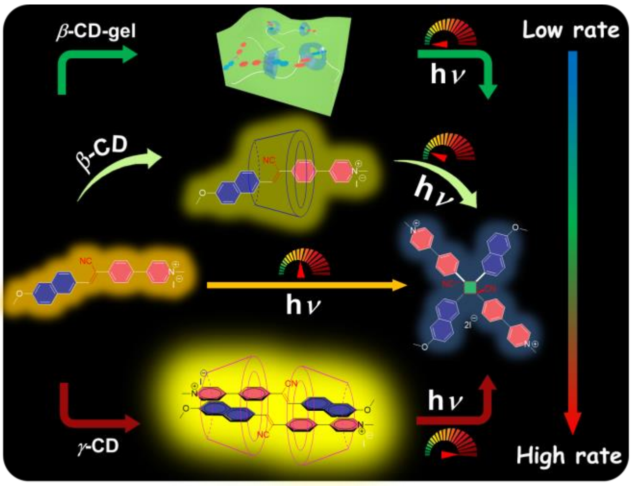
Bloodstains provide admissible information for crime scene investigators. The ability to resolve latent bloodstains that are commonly found in real scenarios is therefore pivotal to public security. Here we report a facile approach for invisible bloodstain visualization based on the Click reaction between serum albumin and TPE-MI, an aggregation-induced emission luminogen (AIEgen). Compared to the widely adopted methods based on the harsh catalytic oxidation activity of hemoglobin, this working principle benefits from the specificity of the mild catalyst-free thiol-ene Click reaction that improves the reliability and resolution. In addition, the mild conditions preserve DNA information and bloodstain patterns, and the excellent photophysical properties of the AIEgen afford high sensitivity and stability (> 1 yr). Such excellent performance cannot be achieved by conventional AIEgens and aggregation-caused quenching luminogens with similar structures. The TPE-MI outperforms the benchmark luminol-based technique in visualizing latent bloodstains as showcased in two mock crime scenes: spattered blood track and transfer blood fingerprint. The disclosed method is an advancement in forensic science that could inspire future development of technology for bloodstain visualization.

Molecular Transmission: Visible and Rate-Controllable Photoreactivity and Synergy of Aggregation-Induced Emission and Host−Guest Assembly

Peifa Wei, Zhao Li, Jacky W. Y. Lam and Ben Zhong Tang*

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

The ability to precisely modulate reaction rates like controlling speeds by the transmission of engines is highly desirable and challenging. Herein, a regio- and stereo-selective photodimerization with four tunable rates was realized at the molecular level: (i) normal rate without adding macrocycles (ν_1), (ii) greatly accelerated rate with the formation of a 2:2 complex between γ-cyclodextrin (γ-CD) and AIE luminogen (AIEgen) (ν_2), (iii) deactivated reaction by 1:1 binding of β-cyclodextrin (β-CD) with an AIEgen (ν_3), (iv) completely inhibited reaction in the β-CD-based hydrogel (ν_4).[1] The restriction of intramolecular motions of AIEgen activates the fluorescence of the transmission with the rate of $\nu_2 > \nu_1 > \nu_3 > \nu_4 \approx 0$, which not only endows intuitive mechanistic insights and in situ trackability to the microscopic process, but also amplifies and visualizes "subtle" reversible reaction. Microscopic mechanism was also applied to construct a porous hydrogel-based microreactor with microscopic visualization and greatly accelerated performance. The present approach demonstrated a powerful platform for the understanding, monitoring and controlling reaction kinetics.



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In-situ Generation of Red Emissive AIEgens from Commercial Sources for Non-doped OLEDs

Ying Yu[1], Zeng Xu[2], Zheng Zhao[1], Jacky W. Y. Lam[1], Anjun Qin[2], Ben Zhong Tang[1]*

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

[2]State Key Laboratory of Luminescent Materials and Devices, South China University
of Technology, Guangzhou, China

Abstract

Luminescent materials with red emission are promising materials for optoelectronic devices and biological science[1]. However, their synthesis is often complicated. In this work, we developed a facile approach to red-emissive luminogens with aggregation-induced emission (AIE) characteristics from commercially available reactants. The new compounds, abbreviated as PN-BTZ-Cz and DP-BTZ-Cz, were prepared by coupling of 4,7-dibromo benzo[c][1,2,5]thiadiazole with (1-naphehyl)phenylamine or diphenylamine followed by reaction of the monobromo-substituted compounds with carbazole. Although all the reactants were AIE-inactive, PN-BTZ-Cz and DP-BTZ-Cz showed AIE characteristics. This suggested that the AIE chromophores were generated in-situ through the reactions. PN-BTZ-Cz and DP-BTZ-Cz showed red emission with high fluorescence quantum yields of 42.2% and 38.3% in the film state, respectively. Non-doped OLEDs with a configuration of ITO/HATCN/TAPC/PN-BTZ-Cz or DP-BTZ-Cz/Bphen/Liq/Al, were fabricated, which emitted red electroluminescence at a low turn-on voltage (down to 2.8 V) with maximum external quantum yield of up to 2.7%.

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Drawing a Clear Mechanistic Picture for the Aggregation-Induced Emission Process

Haoke Zhang, Ryan T. K. Kwok, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

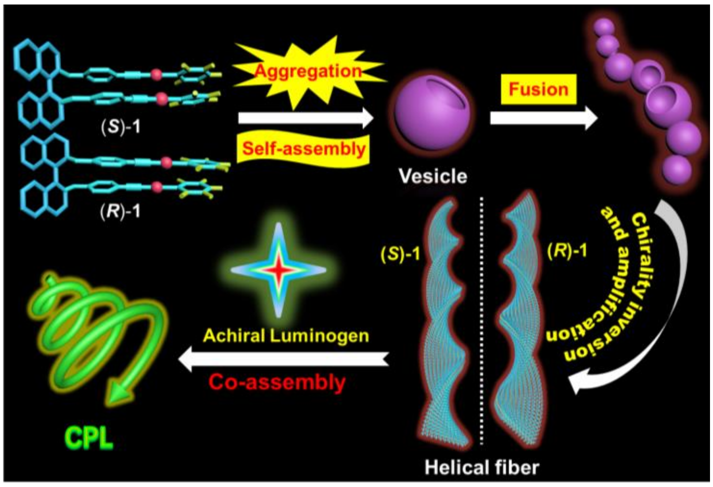
Aggregation-induced emission (AIE) luminogens together with quantum dots, P-dots and upconversion particles are unique luminescent materials that can revolutionize high-technology applications. Since its discovery in 2001, many AIE luminogens (AIEgens) such as tetraphenylethylene (TPE), siloles and their derivatives were developed and explored for various applications such as biological probes, chemical sensing and optoelectronic devices. Although tremendous efforts had been put to understand the mechanism of the AIE process, only an ambiguous and unpersuasive picture was drawn. In this work, a series of simple but archetypical AIEgens, namely (*E*)-1,2-bis(2,4,6-trimethylphenyl)ethene, (*E*)-1,2-bis(2,6-dimethylphenyl)ethene and 1,4-bis(2,4,6-trimethylphenyl)benzene were developed. Interestingly, changing the position of the methyl group from 6- to 5-position generated their structural counterparts with no AIE characteristics. Experimental and computational studies on these two systems revealed that the excited-state phenyl ring twisting, bond stretching and double-bond torsion contributed mainly to the nonradiative decay of the AIEgens in solution, through which a clear mechanistic picture for the AIE process was drawn. Intramolecular planarity and intermolecular through-space interaction were considered and proved to be the reason for bathochromic shift of absorption and emission in some non-AIE molecules. The new design strategy for the construction of AIEgens and the clear mechanistic picture of the AIE process presented in this work were expected to promote the development of new photophysical theories.

Real-Time Monitoring of Hierarchical Self-assembly and Induction of Circularly Polarized Luminescence of Achiral Luminogens

Jing Zhang, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract



Constructing artificial helical structures through hierarchical self-assembly and exploring the underlying mechanism are important, as they help get insight into structures, processes and functions of the biological helices and facilitate the development of material science and nanotechnology. Herein, two enantiomers of chiral Au(I) complexes named (***S***)-**1** and (***R***)-**1** were synthesized with impressive spontaneous hierarchical self-assembly transitions from vesicles to helical fibers. Impressive chirality inversion and amplification were accompanied with the assembly transition, as elucidated by the results of *in situ* and time-dependent circular dichroism spectroscopy and scanning electron microscopy. The two enantiomers could serve as ideal chiral templates to co-assemble with other achiral luminogens to efficiently induce the resulting co-assembly systems to show circularly polarized luminescence (CPL). Our work thus provides a simple but efficient way to explore the sophisticated self-assembly process and presents a facile and effective strategy to fabricate architectures with CPL.

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Surface engineered Silk-based substrate as an alternative for repair of articular cartilage superficial zone

Dorsa Dehghan-Baniani[a,b], Babak Mehrjou[c], Dong Wang[d], Paul Chu[c], Reza Bagheri[b], Atefeh Solouk[e], Hongkai Wu[a,d*]

[a] Department of Chemical and Biological Engineering, Division of Biomedical Engineering, The Hong Kong University of Science and Technology, Hong Kong, China

[b] Polymeric Materials Research Group, Department of Materials Science and Engineering, Sharif University of Technology, Tehran, P.O. Box 11155-9466, Iran

[c] Department of Physics, Department of Materials Science and Engineering, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, China

[d] Department of Chemistry, The Hong Kong University of Science and Technology, Hong Kong, China. chhkwu@ust.hk

[e] Department of Biomedical Engineering, Amirkabir University of Technology, Tehran, Iran

Articular cartilage suffers from limited self-repair capacity; accordingly, it is needed to develop treatment strategies which are able to restore its function appropriately. Recently, tissue engineering approaches have provided promising solutions for repairing the articular cartilage defects. However, it is still needed to address many challenges for cartilage tissue engineering. One of these key challenges is reformation of the zones observed in the native articular cartilage to obtain suitable cartilage functionality. In this research, we prepare a scaffold mimicking the superficial zone of native articular cartilage based on silk with high mechanical properties. Silk fibroin derived from Bombyx mori cocoons is a suitable biomaterial for various biomedical applications. However, the lack of innate cell-interactive domains limits its practical usage. Here, we address this need by functionalization of silk using plasma immersion ion implantation (PIII). Besides, we control the morphology of human adipose mesenchymal stem cells (hAMSCs) by creating nanopatterns on the silk substrates using colloidal lithography which leads to smaller water contact angles compared to non-treated and PIII-treated silk substrates. Then, we load kartogenin (KGN), a small molecule which promotes chondrogenesis, onto the nanopatterned PIII-treated silk films to enhance the attachment, proliferation and chondrogenesis of hAMSCs. Results suggest that this system can be considered as an alternative for articular cartilage superficial zone repair.

Investigating the effect of RNA Binding Protein Lin28B on RNA structure and function

Xin DING, Jieyu ZHAO, Chun Kit KWOK

Department of Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong SAR, China.
Email: ckkwok42@cityu.edu.hk

Abstract

Lin28B is a conserved RNA binding protein that plays an important role in gene regulation, cell metabolism and tumorigenesis. Current data about the RNA structure of Lin28B-interacting transcripts are not well-defined, and the associated molecular mechanisms are missing, which limit our understanding of the interaction modes between Lin28B protein with target RNAs. In this study, we designed small hairpin RNAs (shRNAs) to target Lin28B RNA at coding region and 3'- untranslated region. Using lentivirus transfection and shRNA-mediated gene knockdown approach, we found a decrease in Lin28B protein level by western blot assay, which supported that our shRNA constructs can suppress the targeted protein expression. To further decipher the underlying relationship between Lin28B protein and RNA structure, we aim to develop a refined, high-throughput, transcriptome-wide platform called RNA structure sequencing (RNA structure-seq) that allows the mapping of RNA structure with and without Lin28B knockdown. This method is able to identify the functionally important RNA secondary structural elements such as hairpins and G-quadruplexes, and report their regulatory roles in translation and other biological processes. Our findings might also provide new insights for future study of the mechanistic role of RNA-protein interactions in gene function and cancer.

Heavy Metal Contamination of Sedimentary Microplastics in Hong Kong

Wenjie Li[1], Hoi-Shing Lo[1], Nora Fung-Yee Tam[1], Siu-Gin Cheung[1,2,*]

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

[2]State Key Laboratory of Marine Pollution, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong SAR; bhsgche@cityu.edu.hk

Abstract

This is the first study of heavy metal (As, Cd, Ni, Mn, Cu) contamination of microplastics on sandy beaches in Hong Kong. Three study sites are located in the eastern waters (Pak Lap Wan, Stanley Bay, Tung Lung Chau Island) and the remaining sites in the western waters (Tai Pai Tsui, Ha Pak Nai and Shui Hau Wan). The mean concentration of Mn (52.88 mg kg^{-1}) was the highest and followed by Cu (4.09 mg kg^{-1}), Ni (0.36 mg kg^{-1}), As (0.07 mg kg^{-1}), and Cd (0.06 mg kg^{-1}). Western sites have significantly higher average concentrations of Ni but eastern sites have higher concentrations of Cd. No regional difference was found for As, Mn and Cu. The results indicate that the source was different for different metals. As a large number of marine biological species are known to ingest microplastics, the study of heavy metal contamination of microplastics will help assess the potential risk of bioaccumulation and biomagnification of heavy metals through trophic transfer.

Spectroscopic analysis reveals the effect of a single nucleotide bulge on G-quadruplex structures

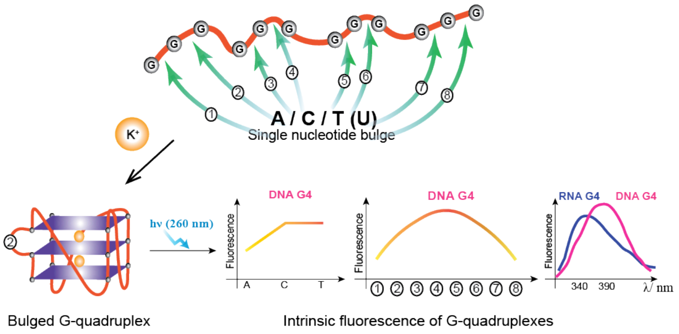
Chun-Yin Chan[a], Mubarak I. Umar[a] and Chun Kit Kwok*

Department of Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong SAR, China. Email: ckkwok42@cityu.edu.hk

[a] These authors contributed equally to this work

Abstract

Over the years, formation of G-quadruplexes (G4s) have been reported with different G-stretch lengths, G-stretch repeats, loop lengths, loop sequences, dangling nucleotides and co-solutes. Nonetheless, little is known about the bulge effect on the intrinsic fluorescence of non-canonical G4s, and until now no data have been reported, which compare the spectroscopic features of bulged G4s of the same sequence in DNA and RNA. Hence, we investigated and revealed the effects of bulge position and identity on G-quadruplexes using three simple and label-free spectroscopic techniques. Interestingly, we uncovered significant differences in the spectroscopic features of bulged DNA and RNA G-quadruplexes, and demonstrate that intrinsic fluorescence can be generally used to detect the formation of canonical and non-canonical G-quadruplexes[1].



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Investigating the role of 3’ untranslated region RNA G-quadruplex structures on mammalian post-transcriptional gene regulation

Kaixin LYU[1], Eugene Yui Ching CHOW[2], Minh T.N. Le[3], Ting Fung CHAN[2] and Chun Kit KWOK[1,*]

[1]Department of Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong SAR, China. [*]Email: ckkwok42@cityu.edu.hk

[2]School of Life Sciences, Centre of Soybean Research, State Key Laboratory of Agrobiotechnology, The Chinese University of Hong Kong, Shatin, Hong Kong.

[3]Department of Biomedical Sciences, College of Veterinary Medicine and Life Sciences, City University of Hong Kong, Kowloon, Hong Kong.

Abstract

RNA G-quadruplex (rG4) structures have been proposed to play crucial roles in a myriad of fundamental biological processes, such as transcription and translation. Bioinformatic analysis predicts conserved rG4 clusters in both human and mouse untranslated region(3’UTR), with miRNA targeting regions nearby. However, the structural and functional role of 3'UTR G-quadruplex on translation and microRNA target site accessibility remain unknown. Our specific candidate of interest is located at the 3'UTR of amyloid precursor protein(APP), which is linked to Alzheimer disease. We performed spectroscopic and SHALiPE assay to demonstrate the formation of it *in vitro*. Besides, cell imaging using rG4 fluorescent turn-on probe fused with antisense oligonucleotide revealed its formation in human cells. We conducted dual luciferase reporter gene assay in HEK293T cells to interrogate the effect of rG4 structure on translation. We also utilized quantitative RT-PCR to ensure the effect observed is not due to the change in luciferase mRNA expression level. The formation of rG4 structure and its mechanistic role in post-transcriptional regulation are important aspects for further exploring rG4 biology and its significance in both basic and applied biosciences.

Investigation of The Protein Interactome of MALAT1 G-quadruplex Structure

Xi MOU[1], Eugene Yui Ching CHOW[2], Akira ISHIGURO[3], Ting Fung CHAN[2], Chun Kit KWOK[1,*]

[1]Department of Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong SAR, China. Email: ckkwok42@cityu.edu.hk

[2]School of Life Sciences, Center of Soybean Research, State Key Laboratory of Agrobiotechnology, The Chinese University of Hong Kong, Shatin, Hong Kong

[3]Research Center for Micro-Nano Technology, University of Hosei, Midori-cho 3-11-15, Koganei, Tokyo 184-0003, Japan

Abstract

Metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) is a highly conserved cancer-promoting long non-coding RNA (lncRNA) that interacts with RNA-binding proteins to participate in transcription and post-transcriptional regulations in cells. Studies have reported that the change in MALAT1 expression level controls cell proliferation, metastasis, and invasion *in vitro* and *in vivo*, suggesting its critical role in the regulation of cancer progression and metastasis. In this study, we identified several RNA G-quadruplex (rG4) motifs in MALAT1 by RNA G-quadruplex structure sequencing (rG4-seq). Using RNA pull-down and surface plasmon resonance (SPR) assay, we showed that some RNA-binding proteins interact with rG4 motifs in MALAT1 with high specificity and affinity. Motivated by these initial results, we aim at exploring the rG4-protein interactions and functional role of the rG4 structure in MALAT1 in more details. We hope this work could establish lncRNA structure-function relationship and reveal new and important molecular mechanism of MALAT1 in gene function and in cancer.

Systematic Evaluation and Optimization on the Experimental Steps in RNA G-quadruplex Structure Sequencing

Pui Yan YEUNG[1], Jieyu ZHAO[1], HuiQi HONG[2,3], Leilei CHEN[3,4], Chun Kit KWOK[1]

[1]*Department of Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong SAR, China.*

[2]*Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117549, Singapore.*

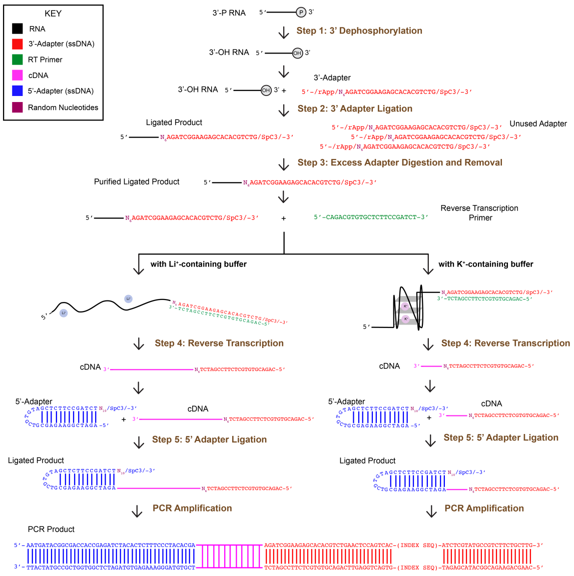
[3]*Cancer Science Institute of Singapore, National University of Singapore, Singapore 117599, Singapore.*

[4]*Department of Anatomy, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117594, Singapore.*

Email: ckkwok42@cityu.edu.hk

Abstract

Guanine (G)-rich sequences in RNA can fold into stacks of G-quartets, and assembly into secondary structure called RNA G-quadruplex (rG4). To map the rG4s in a high-throughput and transcriptome-wide manner, we have previously developed RNA G-quadruplex Structure Sequencing (rG4-seq). Yet, its current limitations to further utilities are i) high RNA input needed, ii) long preparation time required, and iii) lack of a robust experimental pipeline. Here, we evaluate and optimize the 5 key steps involved (See scheme). Overall, we have lowered the RNA input and shortened the preparation time. This improved method can be applied to the structurome studies and other biological applications that require cDNA library preparation in a more efficient manner.



Dual-Functional, Cationic Peptide-Coated Nanodiamond Systems: Facilitating Gene Delivery to the Nucleus for Enhanced Disease Therapy

Hoi Man Leung,[1] Miu Shan Chan, [1] Ling Sum Liu, [1] Sze Wing Wong, [1] Tsz Wan Lo, [1] Cia-Hin Lau,[2] Chung Tin,[2] and Pik Kwan Lo*,[1]

[1] Department of Chemistry, City University of Hong Kong, 83 Tat Chee Avenue, Kowloon Tong, Hong Kong; [2] Department of Biomedical Engineering, City University of Hong Kong, 83 Tat Chee Avenue, Kowloon Tong, Hong Kong**;** peggylo@cityu.edu.hk

Abstract

Nanodiamond becomes a promising candidate among the carbon-based nanomaterials in the recent decades. With the superior thermal stability and chemical inertness, excellent cellular uptake, innate biocompatibility, low cytotoxicity and non-photobleaching fluorescent property, they can be functionalized as a therapeutic agent or diagnostic tool through the chemical modifications. We demonstrate the use of nanodiamonds as a platform for effective delivery of biomolecule with nucleus targeting property. With the peptide modified surface, it enables nanodiamonds to bind with the negative nucleic acid via electrostatic force. Antisense oligonucleotide 4625 is applied as an example to be transported, the suppression of Bcl-2 and Bcl-xL anti-apoptotic genes and triggering of apoptosis in breast carcinoma MCF-7 indicate the enhanced drug delivery efficiency. Therefore, nanodiamonds is a promising nano-carrier to enhance the cellular delivery of certain biomolecules.

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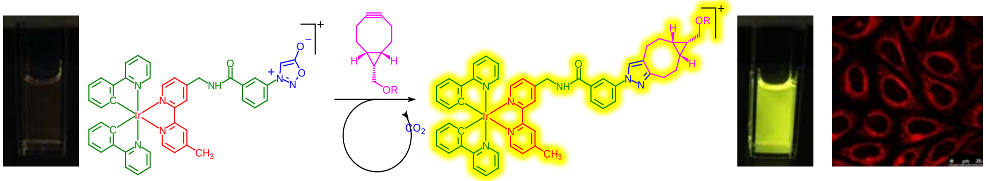
Exploitation of Environment-sensitive Luminophores in the Design of Sydnone-based Bioorthogonal Imaging Reagents

Lawrence Cho-Cheung Lee, Hugo Man-Hin Cheung, Hua-Wei Liu, 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

Bioorthogonal probes have been developed as versatile tools for the specific labeling and imaging of biomolecules in their native environments. Recently, sydnone derivatives have been identified as new bioorthogonal reaction partners of alkynes in [3+2] cycloaddition reactions. They undergo strain-promoted sydnone–alkyne cycloaddition (SPSAC) reaction with strained alkynes, resulting in the formation of substituted pyrazoles as the products with the extrusion of carbon dioxide. With our ongoing interest in the development of luminescent transition metal complexes as cellular probes and bioimaging reagents, we modified sydnone with cyclometalated iridium(III) polypyridine complexes to afford novel bioorthogonal imaging reagents with highly environment-sensitive emission properties. These complexes displayed significant emission enhancement upon SPSAC reaction in aqueous solution, and were utilized to label alkyne-modified proteins and image ceramide molecules in live cells.



We thank City University of Hong Kong (Project No. 9610351) and Hong Kong Research Grants Council (Project No. CityU 11300017 and CityU 11302116) for financial support.

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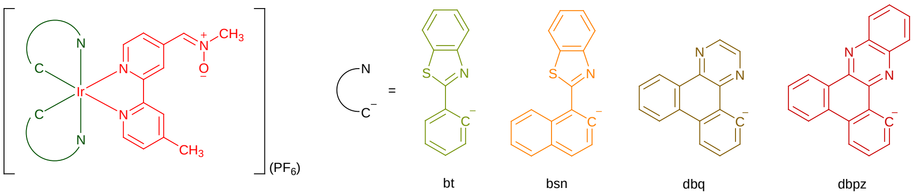
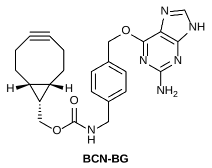
Utilization of Phosphorogenic Iridium(III) Nitrone Complexes as Synthetic Probes for the SNAP-tag Protein

Kam-Keung Leung, Hua-Wei Liu, 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

The SNAP-tag is a self-labeling protein that is used to study the expression and functions of proteins of interest (POI) in live cells. This protein relies on the specific reaction with synthetic probes containing a benzylguanine (BG) moiety. Despite the large number of organic probes developed, luminogenic probes with high signal-to-noise ratio are limited. In this study, a new class of phosphorogenic iridium(III) nitrone complexes are designed for two-step labeling of SNAP-tag to confer luminogenic properties and controllable singlet oxygen ($^1O_2$) generation on the system. In this strategy, a strained alkyne-modified substrate BCN-BG was used to label SNAP-tag, which was then reacted with the iridium(III) nitrone complexes. These complexes were weakly emissive with minimized $^1O_2$ generation due to quenching of the nitrone moiety. However, they displayed a significant increase in emission intensity upon reactions with the strained alkyne BCN-OH (*ca.* 7.2 – 47.1) and BCN-modified BSA (*ca.* 82.9 – 327.1). The emission enhancement was associated with significant $^1O_2$ generation (Φ_Δ up to 0.91) of the complexes. Confocal images revealed that CHO-K1 cells expressing organelle-specific SNAP-tag exhibited intense and long-lived emission only in presence of both BCN-BG and the complexes.





We thank the Hong Kong Research Grants Council (Project No. CityU 11302116 and T42-103/16-N) and the Hong Kong Research Grants Council, National Natural Science Foundation of China (Project N_CityU113/15), for financial support.

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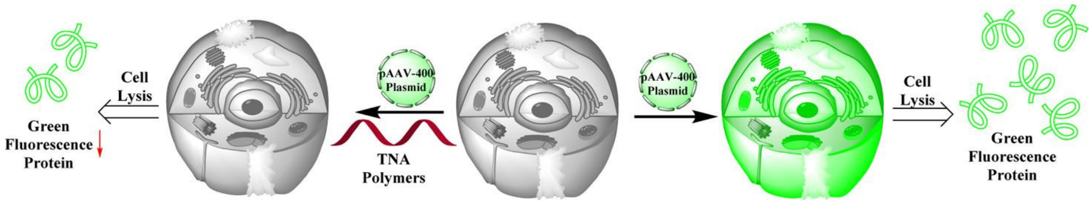
α-L-Threose Nucleic Acids as Biocompatible Antisense Oligonucleotides for Suppressing Gene Expression in Living Cells

Ling Sum Liu, Hoi Man Leung, Dick Yan Tam, Tsz Wan Lo, Sze Wing Wong, and Pik Kwan Lo*

Department of Chemistry, City University of Hong Kong, 83 Tat Chee Avenue,
Kowloon Tong, Hong Kong; peggylo@cityu.edu.hk

Abstract

We herein explore the biological properties and evaluate the potency of sequence-designed α-L-Threose nucleic acid (TNA) polymers to suppress gene expression in living environments. We found that sequence-specific TNA macromolecules exhibit strong affinity and specificity towards the complementary RNA targets, are highly biocompatible and non-toxic in living cell system, and readily enter a number of cell lines without using transfecting agents. Particularly, TNA exhibited much stronger enzymatic resistance toward fetal bovine serum or human serum as compared to traditional antisense oligonucleotide which mean that the intrinsic structure of TNA is thoroughly resistant to biological degradation. Importantly, the efficacy of TNA molecule with GFP target sequence (anti-GFP TNAs) as antisense agents was firstly demonstrated in living cells in which these polymers revealed high antisense activity in terms of the degree of inhibition of GFP gene expression. The GFP gene inhibition studies in HeLa and HEK293 cells characterize sequence-controlled TNA as a functional biomaterial and a valuable alternative to traditional antisense oligonucleotide such as PNAs, MOs and LNAs for a wide range of applications in drug discovery and life science research.



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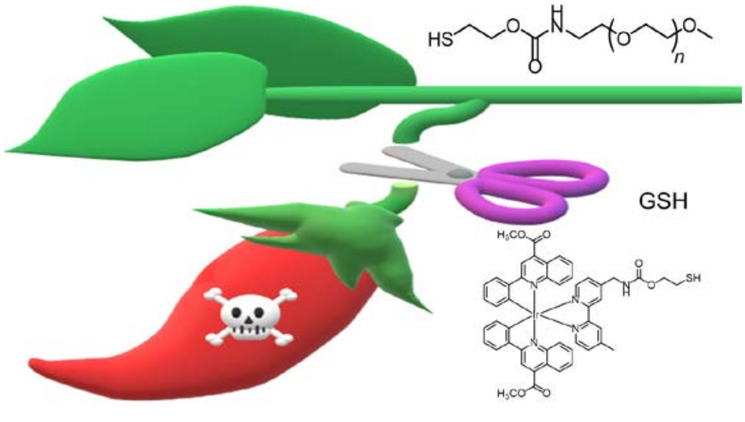
Luminescent Iridium(III) Polypyridine Complexes with a Disulfide Linker as Biological Sensors and Cytotoxic Agents

Justin Shum, Steve Po-Yam Li 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

The combination of therapeutic effects and imaging capability within one molecular system has been of great interest. An approach to this strategy involves the development of multicomponent constructs that can selectively target cancer cells and deliver cytotoxic agents while being monitored by both *in vitro* and *in vivo* means. The construct generally, requires the synthesis of a relatively complex system comprising an imaging reporter, a caged chemotherapeutic drug, a cleavable linker, and a cancer-targeting ligand. Among the cleavable linkers currently being used, disulfide linkage is particularly attractive. Cancer cells have a comparatively high level of intracellular thiols such as glutathione and it is envisaged that the attachment of a PEG pendant to luminescent iridium(III) polypyridine complexes via a disulfide linker can also result in stimuli-responsive cleavage and the subsequent release of the cytotoxic complex. Herein, we report the synthesis and characterization of two novel cyclometalated iridium(III) PEG complexes with a disulfide bond linkage and a bimetallic iridium(III)-rhenium(I) complex.



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DNA Nanotubes Conjugated with Antibodies for Diagnosis of Hepatocellular Carcinoma (HCC)

Fei Wang and Pik Kwan Lo *

Department of Chemistry, City University of Hong Kong, 83 Tat Chee Avenue, Kowloon Tong, Hong Kong; peggylo@cityu.edu.hk

Abstract

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and is one of the leading cause of cancer deaths worldwide. It is of particular significance to develop a diagnosis system with sensitivity and specificity for the early detection of HCC. Recent work indicates that simultaneous determination of multiple HCC biomarkers, such as alpha-fetoprotein (AFP), *lens culinaris* agglutinin-reactive fraction of alpha-fetoprotein (AFP-L3) and des-gamma-carboxy prothrombin (DCP), may have a greater accuracy in HCC detection than determination of each of them alone. In this work, we will develop a versatile HCC detection system based on antibodies-decorated 3D triangular-shaped DNA nanotubes, with recognition of AFP, AFP-L3 and DCP. The system could be potentially employed for clinical diagnosis of HCC.

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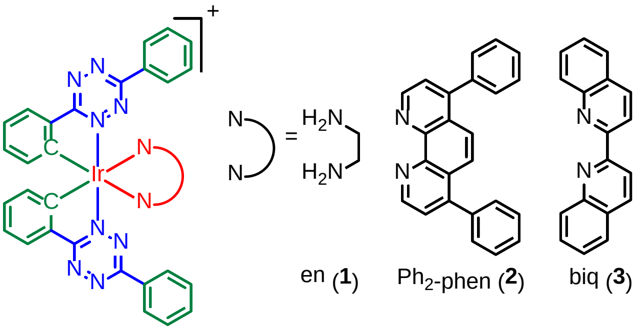
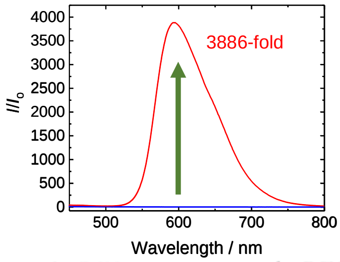
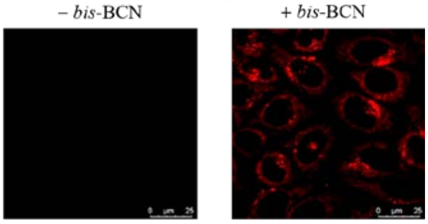
Luminogenic Iridium(III) Bis-tetrazine Complexes as Double-clicking Two-point Binders and Bioorthogonal Probes for Bioimaging and Photocytotoxic Applications

Alex Man-Hei Yip 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

Luminogenic bioorthogonal probes have emerged as very useful tools to visualize biomolecules in complex cellular environments through “turn-on” emission and high selectivity toward unique functional groups that minimize the background luminescence of unreacted reagents. Recently, there has been a strong focus on the design of luminogenic bioorthogonal probes that rely on the emission quenching effect of the tetrazine moiety. Herein, we report the synthesis, characterization, and photophysical studies of three novel luminogenic cyclometalated iridium(III) bis-tetrazine complexes. The applications of these complexes as luminogenic double-clicking two-point binders for the derivatives of a strained alkyne, bicyclo[6.1.0]non-4-yne (BCN) were examined. The cellular uptake efficiency and (photo)cytotoxicity of the complexes were also studied by ICP-MS and MTT assays, respectively.







We thank the Hong Kong Research Grants Council (Project No. CityU 11300017) for financial support.

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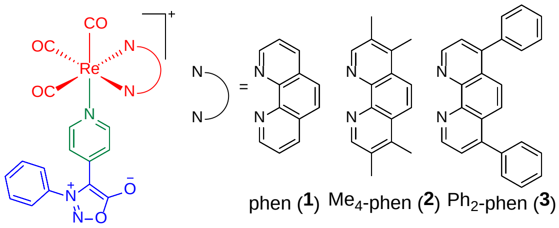
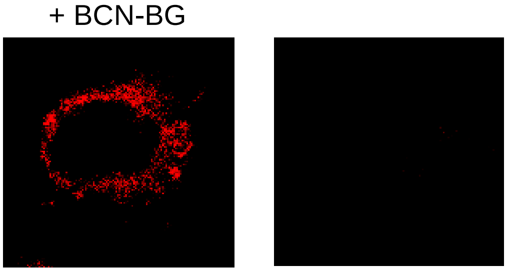
Novel Rhenium(I) Tricarbonyl Polypyridine Sydnone Complexes for Phosphorogenic Bioorthogonal Labeling of Live Cells

Peizhi Zhang, Justin Shum, 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

Bioorthogonal chemistry has allowed for selective labeling in living systems, through the introduction of a biomolecule modified with a chemical reporter and the subsequent specific reaction with a bioorthogonal probe. Notably, the development of bioorthogonal smart probes (turn-on probes) has received great attention. Past works on luminogenic bioorthogonal probes have mainly utilized phosphine, azide, and tetrazine ligation. Due to the youth of the field, there is an increasing demand for new bioorthogonal reactions to expand the chemical biology toolbox. Hence, we report the synthesis, characterization, and photophysical studies of three novel phosphorogenic rhenium(I) tricarbonyl polypyridine sydnone complexes as bioorthogonal probes for live cells. These complexes were weakly or non-emissive and exhibited significant emission enhancement upon strain-promoted sydnone-alkyne cycloaddition. These complexes were used to study the intracellular distribution of bicyclo[6.1.0]non-4-yne (BCN) derivatives in live cells by laser-scanning confocal microscopy.





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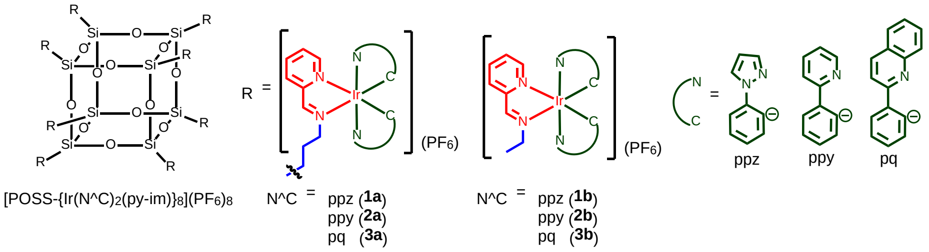
Luminescent Molecular Octopuses with a Polyhedral Oligomeric Silsesquioxane (POSS) Core and Iridium(III) Polypyridine Arms: Synthesis, Aggregation Induced Emission, Cellular Uptake and Bioimaging Studies

Jing-Hui Zhu, [a] Ben Zhong Tang,*[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. Fax: +852 3442 0522. E-mail address: bhkenlo@cityu.edu.hk*

[b] *Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, P. R. China.*

A new class of luminescent molecular hybrids with eight cyclometalated iridium(III) polypyridine complexes grafted on a polyhedral oligomeric silsesquioxane (POSS) unit were synthesized and characterized. The photophysical properties including aggregation induced emission (AIE), and biological characteristics of these complexes were examined and compared with those of their POSS-free counterparts. The dark cytotoxicity and photocytotoxicity of all these complexes were studied using the MTT assay. Additionally, the cellular uptake efficiency and intracellular localization of these complexes were investigated by inductively coupled plasma-mass spectrometry (ICP-MS) and laser-scanning confocal microscopy (LSCM).



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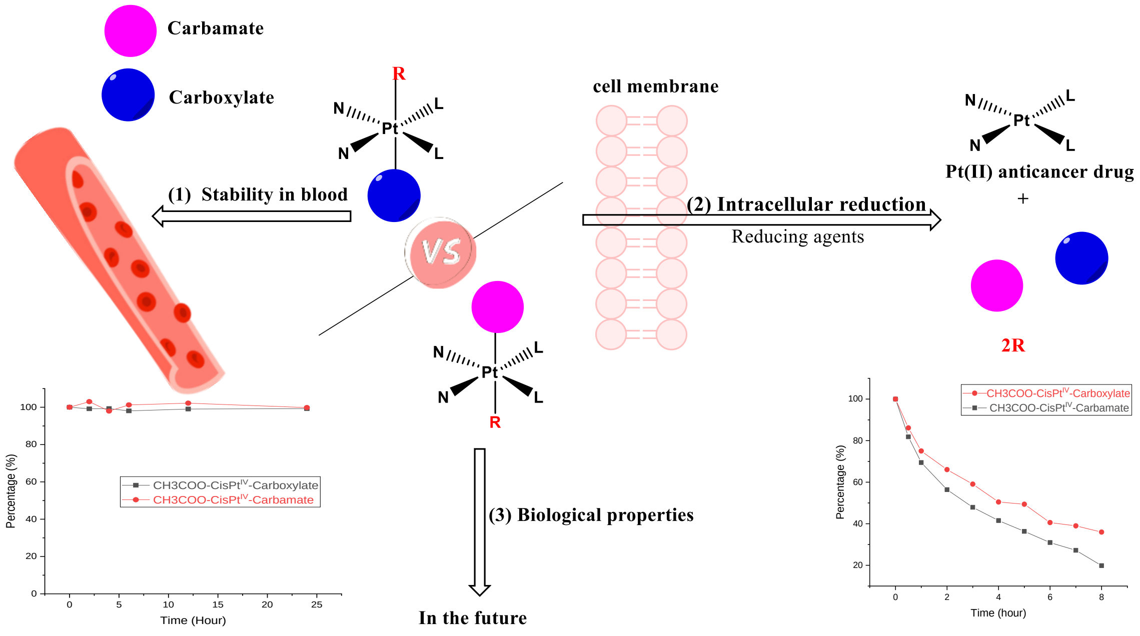
Synthesis and characterization of Pt(IV)-based anticancer prodrugs bearing carbamate or carboxylate axial ligands for enhanced anticancer efficiency

Shu Chen and Gunagyu Zhu*

Department of Chemistry, City University of Hong Kong

E-mail: guangzhu@cityu.edu.hk

Abstract: Pt(IV) complexes represent a class of promising next-generation of anticancer prodrugs. Given that the introduction of two extra axial ligands has dramatic effects on the physicochemical properties of Pt(IV) prodrugs, choosing appropriate ligands is the key for the development of effective Pt(IV) complexes. In this study, ten pairs of asymmetric Pt(IV) complexes bearing one axial carboxylate or carbamate axial ligand were synthesized. The stability of the complexes was tested and the rates of substitution and reduction in physiological conditions of each pair were investigated and compared. Biological properties of the compounds are also evaluated. This research will not only pave the way for the rational design of desired Pt-based anticancer prodrugs but also provide possible interpretation for further elucidating structure-activity relationships.



A nucleus-targeted and photocaged Pt(IV) anticancer prodrug with enhanced anticancer activity and distinct mechanism of action

Zhiqin Deng,[1, 2] Zoufeng Xu,[1, 2] Na Wang,[1, 2] and Guangyu Zhu*[1, 2]
[1]Department of Chemistry, City University of Hong Kong, Hong Kong SAR, P. R. China.
[2]City University of Hong Kong Shenzhen Research Institute, Shenzhen, P. R. China
Email: guangzhu@cityu.edu.hk

Abstract

Targeted anticancer prodrugs that can be controllably activated conveniently are highly desired for personalized precision medicine of cancer therapy. Development of such prodrugs is still challenging. In this study, we reported the design and synthesis of a photoactivatable Pt(IV) prodrug that can specifically accumulate in the nucleus. The inactivated Pt(IV) prodrug is very stable and non-fluorescent in the physiological environment. Once upon visible light irradiation, it can be effectively reduced into oxaliplatin and release coumarin, and the process can be used to monitor the activation and cellular localization of the complex. Compared with oxaliplatin, the Pt(IV) prodrug not only has up to 96-fold increased photocytotoxicity but also presents much higher tumor penetration ability. Importantly, the Pt(IV) prodrug was found to conquer Pt-resistance through a distinct mechanism of action to result in cell cycle arrest, apoptosis and senescence. Furthermore, the activated Pt(IV) prodrug also showed much higher efficiency to induce immunogenic cell death (ICD) which may contribute to the treatment outcome in the tumor environment. Overall, we provide a novel strategy to rational design the photocaged and nucleus-targeted anticancer prodrugs; our result may help researchers better understand the mechanism of action of platinum-based anticancer drugs.

An Upconversion Nanoplatform Loaded with Controllably-Activated Platinum(IV) Prodrug for Enhanced Cancer Therapy

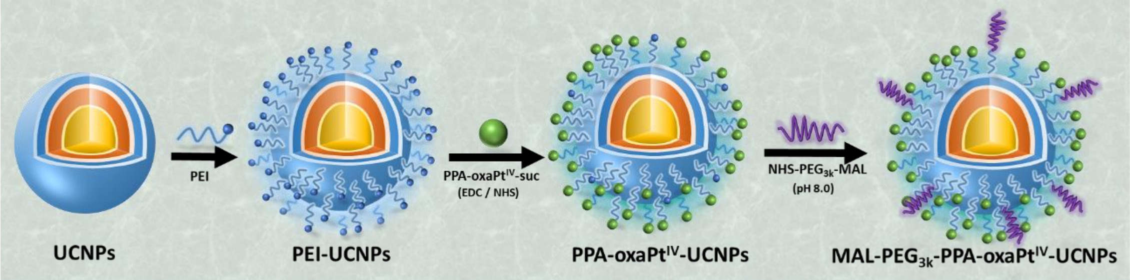
Na Wang[1], Zhiqin Deng[1], Qi Zhu[2], Jianxiong Zhao[2], Wei Kong[2], Feng Wang[2], and Guangyu ZHU[*1]

[1]Department of Chemistry, City University of Hong Kong; [2]Department of Materials Science, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong;

(Email: guangzhu@cityu.edu.hk)

Abstract

The strategy of targeted anticancer therapy for chemotherapeutically resistant cancer is extremely desired. Although Pt-based anticancer drugs are used as the first-line treatment in the clinic, their therapeutic outcome is limited by the side effects. To address the challenge, we combined chemotherapy together with photodynamic therapy (PDT) to realize cancer precision therapy. We report a set of PEG-modified upconversion nanoplatform bearing photoactivatable oxaliplatin-based platinum(IV) complexes. This modified nanoparticles not only show improvement in biocompatibility, but also efficient cancer cell accumulation. The Pt(IV) prodrug on the nanoplatform is quite stable in the dark, and can only be activated with the energy transfer from the upconversion nanoparticles (UCNPs) upon irradiation at 808 nm. By releasing oxaliplatin and reactive oxygen species (ROS) after near-infrared (NIR) irradiation, this nanoplatform can effectively kill cancer cells and conquer drug resistance in the deeper site of the tumor tissue, which increases the biomedical utilization of UCNPs as both nanoprobes and nanocarriers of platinum-based complexes towards resistant cancer cells for combinational therapy.



Synthesis, Cytotoxicity, and Mechanistic Investigation of Platinum(IV) Anticancer Prodrugs Containing PARP Inhibitors

Zoufeng Xu, Cai Li, Zixuan Tong, Qiyuan Zhou, Man-kit Tse and Guangyu Zhu*
Department of Chemistry, City University of Hong Kong, 83 Tat Chee Avenue, Hong Kong SAR; Email: *guangzhu@cityu.edu.hk*

Abstract

The development of Pt(IV) anticancer prodrugs in recent decades provides one of the most promising opportunities to overcome the challenges faced by the traditional Pt(II) anticancer drugs. Choosing appropriate bioactive molecules as the axial ligands of Pt(IV) complexes could dramatically alter the properties of the Pt(IV) prodrugs. Currently, many clinical trials using combinations of Pt drugs and PARP-1 inhibitors (PARPi) have been carried out, with the hope that such combinations will lead to enhanced therapeutic outcomes against the tumor. Herein, we report the design, synthesis, and evaluation of Pt(IV) anticancer prodrugs containing PARPi at the axial position. We first obtained 7 potential PARPi and then conjugated them with cisplatin-based Pt(IV) prodrugs. Both the synthesized PARPi ligands and the PARPi-Pt conjugates [PARPi-Pt(IV)] show inhibitory effects against PARP-1's catalytic activity with IC_{50} values as low as 6.2 nM. The PARPi-Pt(IV) conjugates are active in several human cancer cell lines and the leading ones display the ability to overcome cisplatin resistance. We demonstrated that the representative PARPi-Pt(IV) conjugates efficiently entered cells, bound to genomic DNA, disturbed cell cycle distribution, and induced apoptotic cell death in both cisplatin-sensitive and -resistant cells. Our study provides a strategy to improve the cytotoxicity of Pt(IV)-based anticancer drugs and overcome cisplatin-resistance by using a small-molecule anticancer prodrug that simultaneously damages DNA and inhibits PARP.

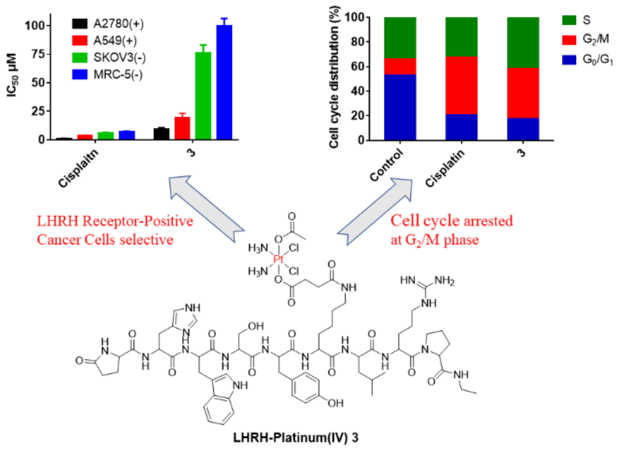
Synthesis and Cytotoxic Study of a Platinum(IV) Anticancer Prodrug with Selectivity for LHRH Receptor-Positive Cancer Cells

Houzong Yao, Zoufeng Xu, Cai Li, and Guangyu Zhu *

Department of Chemistry, City University of Hong Kong, 83 Tat Chee Ave, Hong Kong SAR, People's Republic of China; * E-mail: guangzhu@cityu.edu.hk.

Abstract

Platinum drugs including cisplatin are wildly used in clinics to treat various types of cancer. The lack of cancer-cell selectivity, however, is one of the major problems that lead to side effects in normal tissues. Luteinizing hormone-releasing hormone (LHRH) receptors are overexpressed in many types of cancer cells but rarely presented in normal cells, making LHRH a good candidate for cancer-targeting. In this study, we report the synthesis and cytotoxic study of a novel LHRH-platinum(IV) anticancer prodrug. Cytotoxic study reveals that this prodrug selectively targets LHRH receptor-positive cancer cells with the IC_{50} values 5 - 8 times lower than those in LHRH receptor-negative cells. In addition, the introduction of LHRH peptide enhances the cellular accumulation in a receptor-mediated endocytosis manner. Moreover, the LHRH-platinum(IV) prodrug was proved to kill cancer cells by binding to the genomic DNA, inducing apoptosis, and arresting the cell cycle at the G_2/M phase. In summary, we report the first example of LHRH-platinum(IV) anticancer prodrug having largely improved selectivity towards LHRH receptor-positive cancer cells than cisplatin.



Genetic Instability of TGGAA Repeats in Spinocerebellar Ataxia Type 31

Tongxin Yang and Sik Lok Lam*

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

Abstract

Pentanucleotide TGGAA repeat expansions in introns between *BEAN* and *TK2* genes on human chromosome 16q22.1 have been found to associate with spinocerebellar ataxia type 31 (SCA 31), which is an autosomal-dominant neurodegenerative disorder showing progressive cerebellar ataxia.[1] As the formation of non-B DNA secondary structures during DNA replication, repair or recombination processes has been proposed to cause repeat expansions,[2] we speculated that TGGAA repeats may also be able to form some non-B secondary structures. As a result, we used high-resolution nuclear magnetic resonance (NMR) spectroscopy to investigate the solution structural behaviors of sequences containing two to five TGGAA repeats. Our NMR results show that the sequence containing two repeats adopted a minidumbbell structure which comprises two TGGAA pentaloops, while the sequence containing three or five repeats formed a hairpin conformer. The sequence containing four repeats were found to adopt two larger dumbbell structures, one folded by the first and third repeats and the other folded by the second and fourth repeats. The results of this study reveal that TGGAA repeats are capable of forming various non-B secondary structures, which may be the origin of genetic instability in SCA31. This work is supported by Direct Grant (4053323) from The Chinese University of Hong Kong.

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Facile Synthesis of Cyclic Peptide Conjugated Photosensitizers for Targeted Photodynamic Therapy

Jacky C. H. Chu,[a] Caixia Yang,[a] Clarence T. T. Wong,[a] Wing-Ping Fong,[b]
and Dennis K. P. Ng*,[a]
[a] Department of Chemistry, The Chinese University of Hong Kong, Shatin, N. T., Hong Kong, China
[b] School of Life Sciences, The Chinese University of Hong Kong, Shatin, N. T., Hong Kong, China
(E-mail: dkpn@cuhk.edu.hk)

Abstract

The tumor-targeting capability of photosensitizers plays a crucial role in determining the therapeutic efficacy of photodynamic therapy. Conjugation with various tumor-specific peptides has been shown to be an effective strategy for targeted delivery of theranostic agents through receptor-mediated endocytosis.[1] However, the proteolytic instability of peptides limits the application in this aspect. As an improved approach, cyclic peptides are more resistance to both exo- and endo-proteases and show enhanced targeting specificity.[2] With the increasing prevalence of cyclic peptides, the incorporation of cyclic peptides with functional probes for biomedical applications has become important. However, the commonly used methods of peptide cyclization and conjugation, such as amide formation, copper-catalyzed azide-alkyne cycloaddition, and Sonogashira cross-coupling are relatively tedious and have limitations.[3] Herein, we report a novel one-pot cyclization/conjugation approach using a bifunctional linker, where one side is used for the peptide cyclization and the other for the conjugation with a photosensitizer. With this method, a series of cyclic peptide-conjugated boron dipyrromethene (BODIPY)-based photosensitizers have been synthesized readily without using any non-canonical amino acids, metal catalysts, and coupling reagents. The distyryl BODIPY analogue conjugated with a cyclic RGD (Arg-Gly-Asp) peptide, which has been widely used for specifically binding to the tumor cells overexpressed with $\alpha_v\beta_3$ integrin,[4] exhibits excellent in vitro photodynamic activity and in vivo tumor localization property.

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Selective Photodynamic Eradication of Senescent Cells with β-Galactosidase-Activated Photosensitizers

Junlong Xiong,[a] Ka-Wing Yeung,[b] Clarence T. T. Wong,[a] Wing-Ping Fong,[b] and Dennis K. P. Ng*,[a]

[a] *Department of Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China.*
E-mail: dkpn@cuhk.edu.hk

[b] *School of Life Sciences, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China.*

Abstract

Cell senescence is a process in which cells cease dividing and enter a permanent state of cell cycle arrest. The main purpose of cellular senescence is to prevent the proliferation of damaged or stressed cells and to trigger tissue repair.[1] However, upon persistent damage or during aging, the dynamic process of tissue repair becomes inefficient and senescent cells tend to accumulate. Accumulation of senescent cells is thought to impair tissue function in which they reside and accelerate biological aging.[2] It has been demonstrated that genetic clearance of senescent cells ameliorates various aging-associated diseases, prevents or delays age-related deterioration, and extends the longevity.[3] β-Galactosidase (β-gal) is a glycoside hydrolase enzyme that catalyzes the hydrolysis of β-galactosides into galactose moieties through the breaking of the glycosidic bonds. Interestingly, the increased β-gal activity has long been reported in senescent cells, allowing this senescence-associated β-gal to be an important biomarker for senescence.[4] As part of our continued interest in the development of activatable photosensitizers for photodynamic therapy, we report herein a series of boron dipyrromethene (BODIPY) derivatives conjugated with galactose moieties as β-gal-activated photosensitizers for photodynamic eradication of senescent cells. Our in vitro results demonstrate that these photosensitizers can be selectively activated in senescent A549 lung carcinoma cells.

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Peptide SAL ester synthesis and application

Wenjie Ma, Xuechen Li*

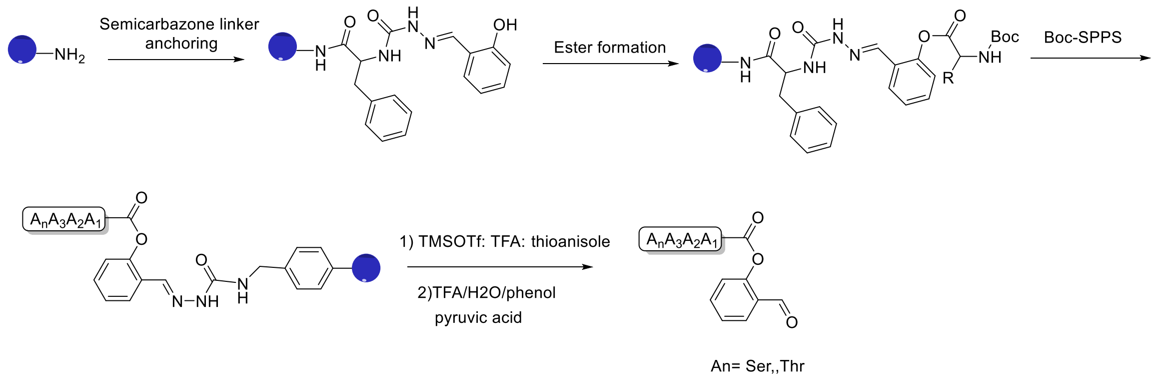
lvaima@naver.com

Abstract

Chemical synthesis makes it possible to modify proteins at specific amino acid residues. Peptide ligations enable construct complex proteins through shorter peptide segments. Serine/Threonine ligation (STL) plays an important role in complex protein total synthesis. STL can ligate an unprotected C-terminal salicylaldehyde ester and an unprotected N-terminal Ser/Thr together, giving an *N,O*-benzylidene acetal intermediate, which can be converted to native amide bond with acid treatment.

Therefore, salicylaldehyde ester preparation is significant to STL reaction. And here, a facile and fast SAL ester synthesis strategy was introduced. SAL ester was prepared on solid phase. First, a semicarbazone linker was anchored on AM resin, then the sequence was elongated with Boc-SPPS strategy, finally SAL ester was generated after TFA cocktail and pyruvic acid treatment. The SAL esters generated with this synthesis strategy are of high purity.

This facile, fast and pure SAL ester preparation strategy paves another path for STL reaction.



Small Molecule Ligand for Targeting Toxic RNA in Huntington's Disease

Matthew Ho Yan Lau, Shaohong Peng, Chun-Ho Wong, Ho Yin Edwin Chan, Ho Yu Au-Yeung*

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

Email: hoyuay@hku.hk

Abstract

Huntington's Disease is an inherited and fatal neurodegenerative disorder caused by an expansion mutation in the CAG-repeat region of the huntingtin gene (*HTT*), which causes the production of toxic CAG-repeat RNA transcript as one of the disease-causing species.[1,2] We report here the development of a family of small molecule inhibitors based on a bisamidinium RNA grove binder as potential ligands for the toxic CAG-repeat RNA. Binding strengths of the ligands were determined by isothermal titration calorimetry (ITC), and binding modes were established using molecular dynamics and nuclear Overhauser effect spectroscopy (NOESY). Changes in nitrogenous base content of genomic DNA in cells, which indicate disease progression and correction, was studied by ultra performance liquid chromatography - mass spectrometry (UPLC-MS)

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Highly Selective Fluorescent Probes for Ascorbate Detection in Living Cells

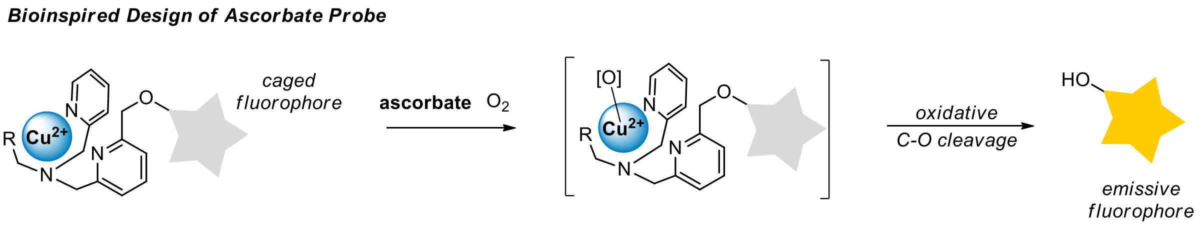
Zuo Hang Yu , Ho Yu Au-Yeung *

Email: hoyuay@hku.hk

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

Abstract

We report here the development of a new reaction-based ascorbate probes inspired by the LMPOs copper monooxyganese.[1]. With the new ascorbate-triggered copper-mediated oxidative cleavage, ascorbate detection can be achieved with a fluorescence siganl. The probes are very senstivie and selective towards ascorbate against a broad range of reducing agents and biological antioxodants. We successfully apply the probes in sensing ascorbate in commerical drink samples, human plasma, serum and live cells for imaing and flow cytometry.



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Luminescent ruffled iridium(III) porphyrin complexes containing N-heterocyclic carbene ligands: structures, spectroscopies and potent antitumor activities under dark and light irradiation conditions

Tsz-Lung Lam,[a] *Ka-Chung Tong,*[a] *Yang Chen,*[a] *Wai-Lun Kwong,*[a] *Xiangguo Guan,*[a] *Ming-De Li,*[a] *Vanessa Kar-Yan Lo,*[a] *Sharon Lai-Fung Chan,*[b] *David Lee Phillips,*[a] *Chun-Nam Lok,*[a] *and Chi-Ming Che**[a]

[a] State Key Laboratory of Synthetic Chemistry, Institute of Molecular Functional Materials, HKU-CAS Joint Laboratory on New Materials and Department of Chemistry, The University of Hong Kong; kctong12@hku.hk.

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

A panel of iridium(III) porphyrin complexes containing axial N-heterocyclic carbene (NHC) ligand(s) were synthesized and characterized. X-ray crystal structures of different bis-NHC complexes display ruffled porphyrin rings with long Ir–C_{NHC} bonds of 2.100–2.152 °A. $[Ir^{III}(por)(IMe)_2]^+$ complexes (por = ttp and oep) are efficient photosensitizers for $^1O_2$ generation (Φ_{so} = 0.64 and 0.88). The near-infrared phosphorescence of Ir^{III}(por)–NHC complexes from the porphyrin-based $^3(\pi, \pi^*)$ state features broad emission bands at 701–754 nm. The bis-NHC complexes exhibit potent dark cytotoxicity towards a panel of cancer cells with IC_{50} values at submicromolar levels. The cytotoxicity of these complexes could be further enhanced upon light irradiation with IC_{50} values at nanomolar levels in association with the light induced generation of reactive oxygen species (ROS). Bioimaging of $[Ir^{III}(oep)(IMe)_2]^+$ (**2c**) treated cells indicates that this Ir complex mainly targets the endoplasmic reticulum. It catalyzes the photoinduced generation of singlet oxygen and triggers protein oxidation, cell cycle arrest, apoptosis and the inhibition of angiogenesis. It also causes pronounced photoinduced inhibition of tumor growth in a mouse model of human cancer.

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Study on the protein-protein interactions with Shc1 central region at different sites phosphorylated

Peizhong Chen[1,2], Ruijun Tian[2] and Xuechen Li[1]

[1] Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong

[2] Department of Chemistry, SUSTech, Xueyuan Road, Nanshan District, Shenzhen, China

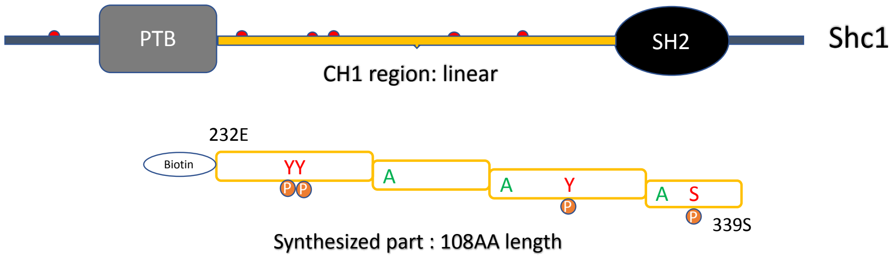
xuechenl@hku.hk

tianrj@sustech.edu.cn

Abstract

Cell surface receptors play important roles in cell signal transduction. As an important scaffold protein, Shc1 is concerned with many important cytoplasmic processes, especially downstream signaling of EGFR pathway[1]. The phosphorylation of protein Shc1 at different sites will drive it to bind different proteins, triggering different cellular events to regulate cell behaviors.

The central region (CH1) between the phosphotyrosine (pTyr)-binding (PTB) domain and SH2 domain contains many reversible phosphorylation sites (like a switch) to regulate Shc1 binding proteins. The phosphorylation of 239Y and 313Y in CH1 region creates a binding motif (pYXN) to recruit Grb2 receptor through the binding to SH2 domain in Grb2, which will activate certain kinase pathway1. However, the proteins recruited by pY240 and pS335 remains unclear. To fully understand the protein recruitment by Shc1 and the effects on the downstream signal pathways triggered by the binding event, we synthesized the CH1 region with these sites phosphorylated. By affinity purification and mass spectrometry (AP–MS) experiment, proteins recruited to certain phosphorylated site could be revealed. Through Fmoc-based solid phase peptide synthesis (SPPS) and native chemical ligation (NCL)2, we succeeded in synthesizing the 108-residue peptide probe of the CH1 region with four sites phosphorylated (239Y, 240Y, 313Y and 335S). Volcano plots showed some newly detected proteins and western blot will be carried out to validate these proteins.



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Peptide Stapling via Ser/Thr Ligation

Carina Hey Pui Cheung, Jianchao Xu, Xuechen Li*

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

Email: xuechenl@hku.hk

Stapled peptide is a class of promising protein-protein interaction (PPI) inhibitors that can increase binding potency and cell permeability[1]. Recently, our group has designed a novel peptide stapling strategy with our in-house Ser/Thr ligation which we previously developed for protein chemical synthesis[2] and head-to-tail peptide cyclization[3]. Ser/Thr ligation involves the chemoselective reaction between unprotected peptide C-terminal salicylaldehyde ester with N-terminal serine or threonine of another or the same peptide sequence to afford an *N,O*-benzylidene acetal intermediate and the subsequent acidolysis generates the peptidic Xaa-Ser/Thr linkage at the ligation site.

In this study, we successfully employed Ser/Thr ligation-mediated cyclization to synthesis side chain-to-side chain cyclic peptides. We identified the benzofuran moiety as the peptide salicylaldehyde ester surrogate and hydroxyl lysine building block or Dap-Ser dipeptide as the hydroxyl amino functionality. By incorporating these key reacting counterparts for Ser/Thr ligation into the peptide side chains, stapled peptides with a hydrophilic hydroxyl-lactam stapling linker could be readily synthesized. These stapled peptide inhibitors could be a useful tool to study the action mechanisms of PPI *in vivo*.

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Design, synthesis and selection of single display DNA encoded dynamic library (sd-DEDL)

Yuqing Deng, Xiaoyu Li

Abstract

Dynamic combinatorial library (DCL) has emerged as an efficient tool for ligand discovery and biomedical research. However, the applications of DCLs have been significantly hampered by low library diversity. As unique DNA tags can encode millions and billions compound structures in DNA encoded chemical library (DEL), we developed a single display DNA encoded dynamic library (sd-DEDL) method to circumvent the advantages of DCL and DEL. A set of DNA-encoded building blocks (BBs) will compete for a non-DNA-conjugated "anchor", a known binder for the target, through reversible imine reactions, thereby forming a dynamic library and locking the equilibrium by reductive amination. We demonstrated the feasibility of sd-DEDL and applied it to find novel hits with high activity in target BRD4 which provide a broadly appropriate method for drug discovery against biological targets.

De Novo Synthesis of Bacterial Pseudaminic Acid Analogues

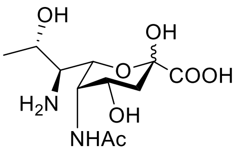
Xing Guo, Ruohan Wei, Han Liu, Xuechen Li*
Department of Chemistry, The State Key Laboratory of Synthetic Chemistry,
The University of Hong Kong, Hong Kong, China

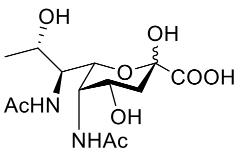
E-mail: xuechenl@hku.hk

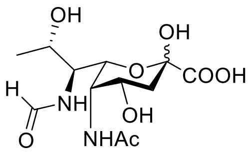
Abstract

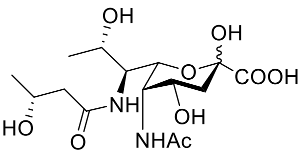
Pseudaminic acid is similar to eukaryotic sialic acid. Since the first discovery of Pseudaminic acid in 1984, more and more pseudaminic acid analogues have been identified and isolated from different bacteria. Previous research has shown that pseudaminic acid analogues were widely distributed in multiple Gram-negative bacteria as important parts of cell external glycans and play a potential role in host-bacterial interactions and in the virulence of many clinically relevant.

In 2017, we reported a novel idea for de novo synthesis of pseudaminic acid and its functionalized derivatives from easily commercially available L-allo-threonine after 17 steps in 9% yield. An aldol-type based reaction via the glycine thioester isonitrile to create the 1,3-anti-diamino skeleton in the synthetic route. Different reaction conditions were screened to create best stereochemistry condition to synthesize the 1,3-anti-diamino precursor with desired: undesired=5: 1. Fukuyama reduction and the Barbier-type reaction based on indium-mediated were applied to establish the pseudaminic acid skeleton. Moreover, we have studied the stereocontrolled selective glycosylation of the pseudaminic acid glycosyl donors via azide protecting groups.









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A bifunctional photo-reactive amino acid enables identification of host-pathogen protein interactions

Siyue Huang, Xiaomeng Li, Xiang David Li
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong
Email: Xiangli@hku.hk

Abstract

Bacterial pathogens are bacteria that have the ability to infect a host and cause diseases. Comparative genomics and mutagenesis studies have revealed that the pathogen virulence factors are important for infection, but their precise biochemical mechanisms and their dynamic expression patterns need further investigation (1). Recently, the residue-specific incorporation of non-canonical or modified amino acid reporters into proteins has made it possible to accurately analyze the newly synthesized pathogen proteins during the infection of mammalian cells (2). However, global identification of the interactions between bacterial pathogens and host target proteins still remains a challenge.

Here we designed a novel bifunctional photo-reactive amino acid reporter which contains 1) a diazirine group allowing UV-mediated photo-cross-linking to fix the protein-protein interactions; 2) an alkyne group enabling the bio-orthogonal ligation for purification and visualization. We screened out a mutant methionyl-tRNA synthetase (L13G) which could readily and residue-specifically incorporate this non-canonical amino acid reporter into salmonella proteomes. In addition, we demonstrated that dzANA could be cell-selectively incorporated in salmonella expressing mutant methionyl-tRNA synthetase, while not mammalian cells during infection. More importantly, dzANA, after being incorporated, enables the photo-cross-linking of host-pathogen protein-protein interactions upon UV irradiation. We expect that dzANA, coupled with state-of-the-art mass spectrometry, would allow the proteome-widely photo-cross-linking of host-pathogen protein-protein interactions.

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DNA-Programmed Affinity Labeling of Membrane Proteins on Live Cells Enables Multiple Applications

Yiran Huang,[†] Ling Meng,[†] Langdong Chen,[‡] Qigui Nie,[§] Yu Zhou,[†] Shilian Yang,[§] Xiaomeng Li,[†]
Haipeng Zhou,[‖] Yizhou Li,[§]* Yan Cao,[‡]* and Xiaoyu Li[†]*

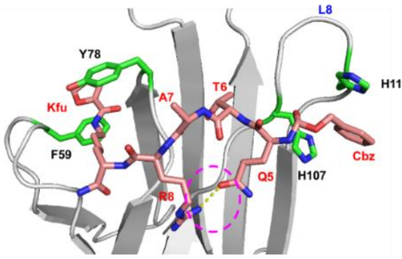
Modification of cell surface with DNA enables cell tagging and introduces programmability to cells for various applications in biochemical research. Hence numerous methods have been developed for cell labeling with DNA strands. However, most of the covalent labeling methods are not target-specific, while non-covalent methods lack labeling stability. Herein we describe a novel method where DNA tags can be covalently linked to the target protein selectively on cell membrane using DNA-Programmed Affinity Labeling (DPAL), a method previously developed by our group. With DPAL, after labeling, the binding site of the target protein is restored with a toehold replacement procedure, making it available for subsequent applications. We have validated the feasibility and specificity of this method, and we have also demonstrated that the DNA tagged cells can subsequently serve as multipurpose platform for diverse applications utilizing the programmability of the DNA tag including cell imaging, targeted drug delivery, cell sorting and programmed cell assembly. Notably, we show that this method can be used for the screening of small molecule ligands against membrane proteins directly on the surface of live cells.

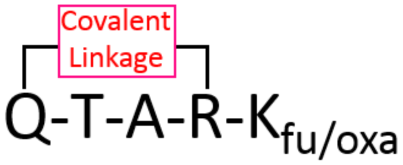
Design, Synthesis and Evaluation of AF9 YEATS Domain Inhibitor

Yixiang Jiang, Xin Li and Xiang David Li*
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong
E-mail: xiangli@hku.hk

Abstract

Histone post-translational modifications (PTMs), by serving as the docking platforms for effector proteins (or readers) that specifically bind to them, signal the diverse downstream cellular processes. The development of chemical modulators for the readers of histone PTMs has provided powerful tools to interrogate the readers' biological functions. The YEATS domain has been newly characterized as a reader of histone lysine acetylation (Kac) and crotonylation (Kcr), whose functional outcomes remained largely exclusive. To fill this knowledge gap, our previous study has developed a series of peptide-based YEATS domain inhibitors by targeting a unique π-π-π stacking interaction at the Kcr binding site. Co-crystal structure analysis revealed that the Gln(Q5) and Arg(R8) residues in the inhibitor form an intramolecular hydrogen bond when bind to the AF9 YEATS domain. We reasoned that cyclic peptides, in which the Gln and Arg are connected via a covalent linkage, may possess favorable properties. Herein, several cyclic peptide inhibitors with submicromolar affinities and high selectivity have been designed and evaluated. This work also introduces a novel strategy for designing selective cyclic peptide inhibitors.





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Chemical Biology Study on High Mobility Group A Protein (HMGA) Post-translational Modifications

Heng Liu, Han Liu and Xuechen Li*

Department of Chemistry, The University of Hong Kong; Email: xuechenl@hku.hk

Abstract

High mobility group (HMG) proteins are a class of abundant non-histone nuclear proteins, among which HMGA1a is well-known for its regulation of transcription as well as relationship to tumour formation and disease development.[1] In the last decades, various post-translational modifications (PTMs) on HMGA1a have been identified,[2-4] which are further proved to be very important to the physiological activities of mammal cells. However, functions of some PTMs and the cross-talk among them are yet to be defined, which is due to difficulties in obtaining homogeneous HMGA1a protein with site-specific modifications. Over the past few years, we have developed Ser/Thr ligation (STL), which have been effectively used to synthesis homogeneously modified proteins.[5] Here, we applied Ser/Thr ligation to chemically synthesize homogeneous HMGA1a protein with site-specific lysine acetylations (64/66/70/73), which are located in the protein-binding domain of this protein. Further *in vitro* study suggests that these acetylations do not significantly affect the CK2-catalyzed phosphorylation on the HMGA1a acidic tail.

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Chemical protein synthesis via Serine/threonine ligation

Jiamei Liu and Xuechen Li*;
Department of Chemistry, The University of Hong Kong,
Pokfulam Road, Hong Kong SAR, China

Email: xuechenl@hku.hk

Chemical protein synthesis provides us an important method to investigate the relationship between structure and biological activity of different proteins, as well as to modify proteins, such as glycosylation and phosphorylation, thus we can further investigate the acting mechanism of proteins in organism. In addition, we can synthesize modified proteins with good biological activity via chemical protein synthesis and finally put them into clinical treatment.

Protein SLAMF4 (also known as 2B4) is a heterophilic receptor of the signaling lymphocytic activation molecule (SLAM) family. It is involved in many biological processes, such as signal transduction, the activation of NK cell mediated cytotoxicity, the induction of secretion of IFN-Υ and so on [1]. Our group has developed a chemoselective peptide ligation strategy which is through salicylaldehyde (SAL) ester at the C-terminus of peptide and an N-terminal threonine or serine, named Ser/Thr ligation (STL) [2]. Herein we designed a synthesis for SLAMF4 by combining the solid phase peptide synthesis (SPPS) and serine/threonine ligation (STL). In addition, we will investigate the biological function of SLAMF4 with phosphorylation.

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Chemical proteomic approach to identify histone lysine succinylation “Eraser” in yeast

Gaofei Tian, Xiang David Li
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, China; xiangli@hku.hk

Abstract

Posttranslational modifications (PTMs) of histones represent a crucial mechanism in regulating nucleosome and chromatin dynamics during a variety of DNA-based cellular processes such as replication, transcription and DNA damage repair. Lysine succinylation (Ksucc) is a newly identified histone PTM, which is evolutionarily conserved from yeast to human[1]. Known of its regulating enzyme (e.g. writer which catalyze the addition of Ksucc and eraser which remove Ksucc) is critical for our understanding the biological function of Ksucc. CobB protein in E.coli as well as Sirt5 and Sirt7 in mammalian cell has been reported as ‘eraser’ for Ksucc[2]. However the eraser for Ksucc in yeast is still unknown.

Here we used a quantitative chemical proteomics approach (cross-linking-assisted and SILAC-based protein identification (CLASPI)[3]) to comprehensively profile 'eraser' enzymes that recognize a lysine-27 succinylated histone H3 (H3K27succ) mark in yeast. CDC1 protein, which previous known as a metallophosphoesterase, was identified as a potential ‘eraser’ for H3K27succ. Then we tried different strategies to overexpress and purify CDC1 protein in yeast.

Later, we will perform binding assay with purified CDC1 protein to test its binding toward H3K27succ peptide. Enzymatic assay will also be performed to test its desuccinylation activity.

Nucleosome-based photoaffinity probes to interrogate histone modifiers

(WU YIPING, HKU Supervisor: Prof. Xiang David Li)

Abstract:

In eukaryotic cells, genomic DNA is wrapped around histone octamers, assembling into nucleosomes, which are the basic unit of chromatins. In nucleosomes, the histones are not only a DNA wrapping scaffold, but also engaged in various protein-protein interactions, such as the recruitment of histone modifiers. Post-translational modifications (PTMs) of histones is a fundamental and crucial mechanism underlying the regulation of DNA-associated cellular processes. The dysregulation of histone PTMs can result in aberrant gene-transcription and deficient DNA damage repair, which are the causes of various diseases such as cancer. The regulation and function of histone PTMs rely on the chromatin-associated proteins that modify (e.g. 'writers' and 'erasers') histones and interpret (e.g. 'readers') the modifications. Since interactions between histones and associated proteins can be weak and transient, photoaffinity probes have been generated to form covalent linkages. However, the existing peptide-based photoaffinity probes can hardly mimic the nucleosome globular environment, which can be a key for protein recognition and binding. In this regard, we developed nucleosome-based photoaffinity probes to both identify the histone interacting proteins and investigate the molecular mechanisms of specific binding and recognition. Here, we focus on Dot1L-mediated H3K79 methylation, developing Dot1L-specific photo-nucleosome probes and deciphering the interaction surface information.

Bi-functional OPA-Alkyne linkers for protein modification

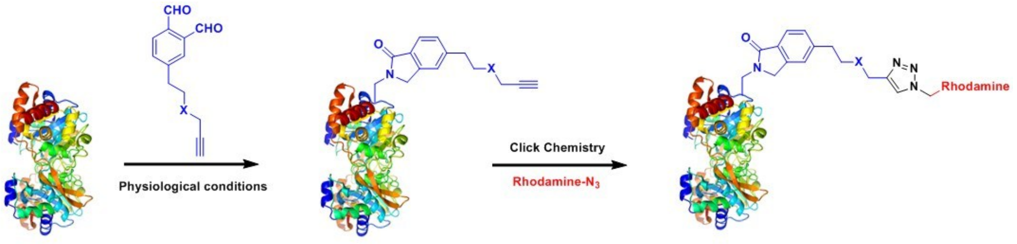
Yue Zhang, Xuechen Li*
Department of Chemistry, The State Key Laboratory of Synthetic Chemistry,
The University of Hong Kong, Hong Kong, China

E-mail: xuechenl@hku.hk

Abstract

Bioconjugation is an important way to prepare hybrid constructs from small molecules (drugs, dyes, etc.) and biomolecules (peptides, proteins, polysaccharides, nucleic acids, etc.). Development of novel bioconjugation reaction with high selectivity and efficiency is highly desired for the discovery of hybrid functional molecules, including biological probes, therapeutics, and functional materials. Recently, our group developed a lysine-selective bioconjugation reaction based on *ortho*-phthalaldehyde (OPA) via phthalimidine formation (PT ligation).[1] This PT ligation shows high selectivity for accessible lysine residues on the proteins and provides better protein bioconjugation (e.g. wider PH, faster conversion, non-hydrolysable agent) than the traditionally used NHS ester chemistry.

Recently, we prepared a series of OPA-based bifunctional linkers for protein modification. The introduction of protonizable structural unit significantly improves the solubility of the linker molecules and minimized the aggregation of the modified proteins. The alkyne group would facilitate further conjugation of functional species (fluorophores, biotin tag, etc.) via click chemistry.



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Title of Poster

Probing Histone Deacetylase Protein Complexes by DNA-Programmed Photo-Affinity Labeling

Jianfu Zhang, and **Xiaoyu Li***

xiaoyuli@hku.hk

Abstract

Recently, our group developed a method named DNA programmed affinity labeling (DPAL). In DPAL, functions of protein binding, cross-linking, and tagging that usually exist in a single probe are decoupled to two complementary DNA probes (binding probe and capture probe, abbreviated as BP and CP). After SM binds to the target, the DNA tag in BP guides CP hybridization, which places the photo-crosslinking group in proximity to the protein for cross-linking under light irradiation[1,2,3]. Through incorporating enzyme inhibitor into DNA-based probes, we can utilize the unique multi-probe feature of DNA-programmed photo-affinity labeling to label and capture proteins associated with the targeted enzyme in these complexes. By changing the sequence of the complimentary DNA strand, we change the location of the photo-crosslinking group, which allows capturing of different proteins in these complexes. DPAL is a recently developed methodology, which is newly applied to the area of proteomics. Compared to traditional methodologies, which usually uses tri-functional small molecule to capture protein complexes, DPAL can capture proteins in various locations of the protein complexes by changing the sequence of the complimentary CPs without revising the structure of the inhibitor conjugated to BP.

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A bioinformatics approach to quantify bacterial biosynthetic gene clusters in whole-metagenome samples

Mohamad Koohi-Moghadam[1,2,3], Junwen Wang[2,3,*], Hongzhe Sun[1,*]

[1]Department of Chemistry, The University of Hong Kong, Hong Kong SAR, P.R. China;
[2]Center for Genomic Sciences, The University of Hong Kong, Hong Kong SAR, P.R. China;
[3]Department of Health Sciences Research and Center for Individualized Medicine, Mayo Clinic, Scottsdale, AZ 85259, USA; E-mail: m.koohi.m@gmail.com

Research into host-pathogen interactions have been expanded during recent years by recruiting advanced technology such as next generation sequencing (NGS) (1-3). Bacteria as the most important human pathogen can play important roles on human health using their secondary metabolites. These secondary metabolites are small molecules which are produced by bacterial biosynthetic gene clusters (BGCs). We develop a bioinformatics approach to compare the abundance of bacterial BGCs which produce different types of secondary metabolites in whole-metagenome samples. Using this pipeline, we quantified the BGCs of samples who are suffered from colorectal cancer. The results show BGCs which produce siderophores are more abundant in case samples. Siderophores are small compounds with ability to chelate Fe^{3+}. Bacteria use these compounds to acquire and solubilize ferric iron from the host during infection.

*We thank the Research Grants Council of Hong Kong (*17333616 and 17307017*) and the University of Hong Kong (for a studentship to KM) for financial support.*

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Structures Of Urease Accessory Proteins And Their Insights Into Urease Maturation In *Helicobacter Pylori*

Man Hon YUEN, Yu Hang FONG, Yap Shing NIM, Kam Bo WONG
School Of Life Science, The Chinese University Of Hong Kong, Shatin, Hong Kong
yuenmanhonnicholas@gmail.com

Urease is a nickel-containing metalloenzyme that catalyzes the hydrolysis of urea, which produces the acid neutralizing ammonia that is essential for the survival of *Helicobacter pylori* (a peptic ulcer causing pathogen) in the human stomach. Maturation of urease involves carbamylation of an active lysine residue and insertion of two nickel ions at its active site. This process is facilitated by four urease accessory proteins, UreE, UreF, UreG, and UreH.

To understand how urease accessory proteins interact with each other to facilitate urease maturation, we have determined the crystal structures of UreF$_2$H$_2$ and UreG$_2$F$_2$H$_2$ complexes. UreF$_2$ contains a flexible C-terminal tail that forms an extra helix and a F-tail loop stabilized by Arg-250. These newly formed structures facilitate the recruitment of UreG to form a UreG$_2$F$_2$H$_2$ complex. From the structure of the UreG$_2$F$_2$H$_2$ complex, it illustrates that the dimerization of UreG assemble its nickel binding site by bringing the two conserved CPH motifs at the dimerization interface. Addition of nickel and GTP to the UreG$_2$F$_2$H$_2$ complex releases a GTP/nickel-bound UreG dimer that can activate urease *in-vitro* in the presence of the UreF$_2$H$_2$ complex.

Recently, we have determined the crystal structure of the GTP/nickel-bound UreG dimer, which shows the conformational difference of UreG under different nucleotide-bound states. This reveals how GTP hydrolysis induces conformational changes that dissociate the UreG dimer and release its bound nickel. Using mutagenesis study along with activity assay and interaction study by static light scattering, it provides insights into the role of UreG in the delivery of nickel during urease maturation.

Mode of Action of Designed Bactericidal Short Cationic Peptides Derived from the Phenol-soluble Modulins by Functional Fragments Combination Approach

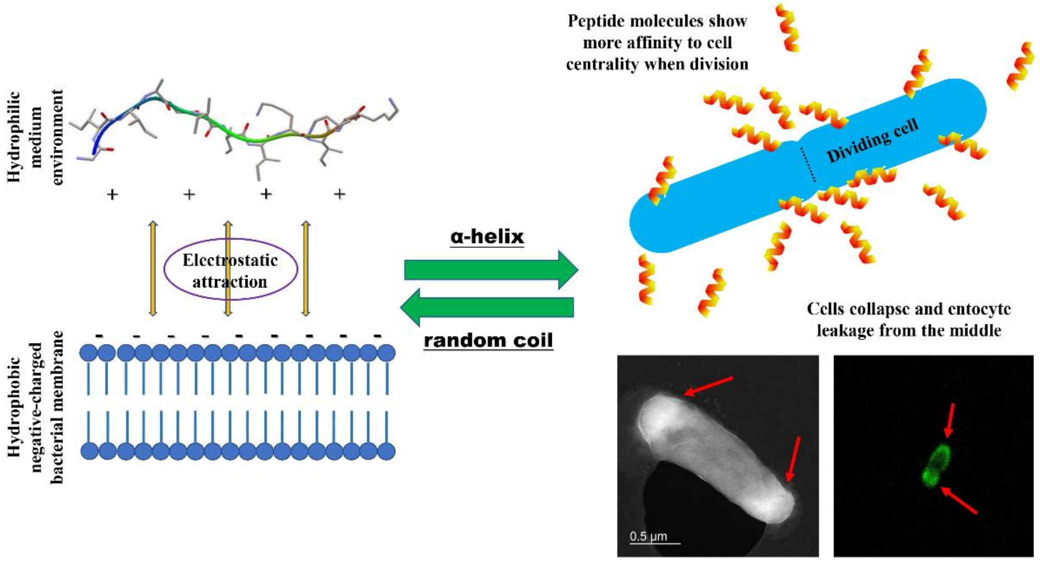
Ping Zeng, Chen Xu, Qipeng Cheng, Jun Liu, Wei Gao, Kwok-Yin Wong, Sheng Chen[*] and Kin-Fai Chan[*]

State Key Laboratory of Chemical Biology and Drug Discovery and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University.

Email: Sheng.chen@polyu.edu.hk; kf.chan@polyu.edu.hk

Abstract

Phenol-soluble modulins (PSMs) are a large series of peptide toxins produced by Staphylococcus aureus.[1] Based on the amino acid sequences of PSMs α1, α2 and α4, we have designed and synthesized a small library of short cationic peptides. These novel compounds can transform their secondary structure from random coil to α-helix in hydrophobic surroundings. Electrostatic attraction between positive-charged peptides and negative-charged bacterial membrane endows them greater selectivity compared to PSMs.[2] The most promising one GIIAGIIIKIKK-NH_2 (zp3) exhibits MIC to *E.coli 25922* (8μM) and clinically isolated β-lactam resistant bacterial strains (8μM to *Citrobacter freundii* 35) while keeping low hemolysis (<5% at 256μM). We proposed that zp3 molecules show more affinity to cell centrality when division and lead to cell collapse and entocyte leakage from the middle of *E.coli* by STEM and fluorescence imaging.



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A metabolomics study of the acupoint sticking therapy effect on guinea pigs with allergic asthma using UPLC-ESI-QTOF-MS

Mengheng LI, Shi-jian Xiang, Chi-On Chan, Qiang Liu and Daniel Kam-Wah Mok*
Department of Applied Biology and Chemical Technology,
The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China
Correspondence should be addressed to Dr. Daniel Kam-Wah Mok, bcdaniel@polyu.edu.hk.

Abstract

Accumulated clinical evidence in Chinese communities suggested that acupoint sticking therapy (AST) could be a promising treatment for asthma-related diseases. However, the underlying mechanism is still poorly understood. In this study, we aimed to investigate the mechanism of the anti-inflammatory effect of AST with 'Treatment of Winter Disease in Summer' (TWDS) prescription by using metabolomics. Allergic asthma in guinea pig was sensitized and challenged by ovalbumin (OVA). The serum metabolomics profiles were acquired by using ultraperformance liquid chromatography combined with electrospray ionization quadrupole time-of-flight mass spectrometry (UPLC-ESI-QTOF-MS). The overall results confirmed that AST with TWDS prescription had a significant protective effect against OVA-induced allergic asthma in guinea pig. From biological aspect, this treatment not only attenuated airway inflammation and collagen deposition in the airway, but also decreased the levels of IL-4, IL-5, IL-13 and IgE in serum. From metabolomics aspect, the abnormal metabolisms of phospholipid, sphingolipid, purine, amino acid and level of epinephrine were restored back to the normal. In conclusion, this study demonstrated that metabolomics provides a better understanding of the mechanism of AST with TWDS on OVA-induced allergic asthma.

HBx-K130M/V131I promotes liver tumorigenesis in transgenic mice via AKT/FOXO1 signaling pathway and arachidonic acid metabolism

Tung-Ting Sham, Amy P Chiu, Barbara R Tschida, Lilian H Lo, Branden S Moriarity, Xiao-Xiao Li, Regina C Lo, David E Hinton, Dewi K Rowlands, Chi-On Chan, Daniel Kam-wah Mok*, David A Largaespada, Nadia Warner, Vincent W Keng*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China (daniel.mok@polyu.edu.hk / vincent.keng@polyu.edu.hk).

Chronic hepatitis B viral (HBV) infection remains a high underlying cause for hepatocellular carcinoma worldwide, especially in Asia, while the genetic mechanisms behind this remain unclear. This study elucidated the mechanisms contributing to tumor development induced by the HBV X (HBx) gene of predominantly Asian genotype B HBV and its common HBx variants *in vivo*.

Since HBx mutant (Mut, K130M/V131I) type had a stronger tumorigenic effect than its wild type (WT) variant, un-targeted metabolomics analysis using serum from HBx-B Mut/*shp53*, WT/*shp53* and Empty/*shp53* injected mice was performed using Ultra Performance Liquid Chromatography-Orbitrap-Mass spectroscopy to determine metabolic changes.

A significantly higher abundance of xanthine, its downstream metabolites urate and 5-hydroxyisourate were detected in mutant cohort compared to its wild-type cohort. 9,10-DiHOME and 12,13-DiHOME involved in linoleic acid metabolism were significantly reduced in mutant serum than that in wild-type serum. The levels of taurine-conjugated bile acids were significantly reduced in the mutant cohort compared to its wild-type cohort. This finding was consistent with the RNA-seq result that the expression level of *Cyp7a1*, which encodes the key enzyme that converts cholesterol to bile acids, was significantly down-regulated.

HBx mutant induced inflammation via arachidonic acid metabolism by accumulation of pro-inflammatory factors such as the different types of prostaglandins, leukotriene-B4 and 12-HETE to the infected tissues. Taken together, these results provide a potential mechanism whereby HBV encoding X_K130M/V131I may contribute to the high rate of hepatocellular carcinoma observed clinically in patient cohorts containing these mutations.

This project was supported by The Shenzhen Science and Technology Innovation Commission (JCYJ20170413154748190 , JCYJ20160229173844278 and JCYJ20160330171116798), Health Medical Research Fund (11122171), Food and Health Bureau (Hong Kong), NSFC/RGC Joint Research Scheme (3-RAA3) and the NIH IMVTP grant No. T32 AI083196-04, GRF (15302718) and FDS (UGC/FDS25/M06/16 and UGC/FDS25/M02/17) of the Research Grants Council of Hong Kong, HKCMMS Project, and the Large Equipment Funds and University Research Facility in UCEA and in ULS of the Hong Kong Polytechnic University.

Discovery of Inhibitors of FtsZ and FtsA

Ruo-Lan DU, Ning SUN, Kwok-Yin WONG*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong; kwok-yin.wong@polyu.edu.hk

Abstract

Antibiotic resistance has increased dramatically in recent years, posing great pressure on public health[1]. Discovery of alternative antibiotics with novel targets will be significant in this fight with resistant strains, like MRSA[2]. In bacterial cytokinesis, FtsZ acts as the platform for the landing of other division proteins involved in divisome[3]. FtsA anchors the platform to the membrane, which is also crucial in the function of divisome. If we can find inhibitors of FtsZ and FtsA, cell division in resistant strains can be blocked or disturbed, leading to cell lysis.

In this study, at first, a computer-aided drug screening method was exploited to identify FtsZ and FtsA inhibitors. After finding some potent inhibitors, they were subjected to bacterial growth inhibitory tests. Then we tried to confirm the targets of those with comparatively higher antibacterial activity are FtsZ or FtsA through many *in vivo* and in *vitro* studies. Additionally, the FIC value of the inhibitors of FtsZ and FtsA was also calculated to show their synergistic effects.

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Expression and Structure of the Bacterial Cell Division Protein Complex FtsQBL

Fu Rong GONG, Kwok-Yin WONG*
Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong; kwok-yin.wong@polyu.edu.hk

Abstract

Cell division in gram-negative bacteria is a process of cell membranes and peptidoglycan cell wall constrictions to divide a mother cell into two daughter cells. The bacterial cell division is controlled by a piece of complicated enzymatic machinery named divisome. Over thirty different proteins have been determined to participate in divisome assembly, and ten proteins, including FtsQBL trimeric protein complex, are essential for the proper functioning of divisome. FtsQBL is important in the way to control the peptidoglycan synthesis. Even though the X-ray crystal of FtsQB has already been studied, the structure and conformation of the trimeric FtsQBL protein complex, however, still remain unclear. In this project, amino acids that are involved in the binding interface between FtsQBL trimeric complex are investigated by applying amide hydrogen/deuterium exchange mass spectroscopy (HDX-MS), to localize FtsQ/B/L peptides with varied protection pattern against deuterium exchange reaction upon complex formation.

Interaction Study of Full-Length Bacterial Cell Division Protein Complex FtsQBL

Wai-Po KONG, Kwok-Yin WONG*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong; kwok-yin.wong@polyu.edu.hk

Abstract

The bacterial division is a process of mother cell progress into two daughters. One of the important procedures is separating cell membranes and peptidoglycan cell wall. This series of action is controlled by a piece of complicated enzymatic machinery, divisome. To fulfill this dramatic action, more than fifteen different proteins are involved. Within that determined protein, participant of ten proteins is crucial. Including protein complex FtsQBL, a largely linear hierarchy order interaction is essential for divisome function[1]. The formation of trimeric protein complex FtsQBL is key of controlling downstream proteins; FtsQBL is critical for regulating cell division by initiate septal peptidoglycan synthesis. FtsQ, B and L are membrane proteins. Crystal structure of the individual protein, some complex or with peptide are studied, however, mainly focused on the periplasmic domain[2, 3]. The interaction of the full-length trimeric complex remains unclear. In this project, an alternative method is used to study the amino acids involved in the binding interface. Amide hydrogen/deuterium exchange mass spectroscopy (HDX-MS) is applied to localize peptides in different protection pattern against deuterium exchange reaction; Studying the buried interface in different complex formation.

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pH-Responsive Targeted Gold Nanoparticles For In Vivo Photoacoustic Imaging of Tumor Microenvironment

Li SY, Lui DKH, Li X, Gu YJ, Wong WT*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University

w.t.wong@polyu.edu.hk

Highly-efficient targeting probes are desirable for disease diagnosis and functional imaging.[1] The acidic microenvironment of tumor tissues has proven to be one of the major differences from other normal tissues. We herein introduce a way to endow gold nanoparticles with tunable pH-aggregation behavior by modifying the nanoparticle surface with mixed self-assembly monolayers, which can be stable at the pH of blood and normal tissues but aggregate instantly in response to the acidic extracellular pH in tumors.[2] By adjusting the surface ligand composition was used to study the general principle of tailing of the pH-induced aggregation behaviors of nanoparticles. With proper surface ligand composition, the pH-responsive active tumor-targeting c(RGDyk)-MHDA/LSC@AuNPs nanoprobe was obtained to evaluate the effect of nanoparticles' aggregation for in vivo photoacoustic imaging. Intravenous administration of nanoprobe to U87MG tumor-bearing nude mice showed PA imaging contrasts in tumors almost 3-fold higher than for the blocking group. Quantitative biodistribution data revealed that 2.72 ug/g of nanoprobe had accumulated in the U87 MG tumor after 24 h post-injection. This result highlights the pH-responsive targeted AuNPs as platform to developed smart photoacoustic probe with significant diagnosis capabilities.

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Discovery of Natural Products as Potential Peptidoglycan Glycosyltransferase Inhibitors

Zhiguang LIANG, Yong Wang, Wing-Lam Cheong, and Kwok-Yin Wong*

Department of Applied Biology and Chemical Technology, The Hong Kong
Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR, China
E-mail: bckywong@polyu.edu.hk

Abstract

With the emergence of varieties of drug-resistant strains, it is urgent to identify novel antibacterial agents. Biosynthesis of peptidoglycan as drug target has been proven to have clinical applications. Bacterial peptidoglycan glycosyltransferase (GT), catalyzing the formation of peptidoglycan, is a potential antibacterial drug target. This enzyme possesses several advantages such as easily accessible from the periplasm, absent in mammalian cells and highly conserved encoding genes in both wild-type and drug-resistant strains. Currently, there is still no GT inhibitor in clinical use. Many natural product-based compounds exhibit potent antimicrobial activities with low cytotoxicity. With development of genomics and techniques, once discarded natural compounds with low bioactivities and narrow spectrum could be reinvestigated and modified to generate new structures which possess potent antibacterial activities.[1] In our group, we are going to screen natural products as lead compounds of potential GT inhibitors. We have tested many natural compounds and found compound 10-27b with isatin core exhibited a moderate antibacterial activity with MIC values of 24, 48 and 96 μg/mL against *B. subtilis, S. aureus and E. coli*, respectively.[2] We will further validate its binding target by lipid II(substrate of GT)-based fluorescent bioassays.

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Corneal Neovascularisation: Disease Monitor with Ultrasound Power DopplerEG-

Lui DKH, Li SY, Gu YJ and Wong WT*

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

w.t.wong@polyu.edu.hk

Corneal neovascularisation (CoNV) is a pathological condition that could severely affect individual's visual acuity and it is also one of the major causes of blindness worldwide. New blood vessels grow from pre-existing vessels and completely obstructs light from penetrating the cornea. Numerous factors may contribute to CoNV such as chemical burns, infection/inflammation and ischemia. Clinical treatment for CoNV includes but not limited to topical use of corticosteroid, and laser photocoagulation.[1] Current clinical visualisation method employs slit lamp to monitor CoNV progression. However, analysing the image obtained from slit lamp could be subjective. Thus, limiting its utility in reflecting the true pathological progression.

With the aim of providing objective evaluation of CoNV, we would like to utilise a three-dimensional Power Doppler Ultrasound unit (Vevo 2100; FUJIFILM VisualSonics) for label-free quantification of CoNV. We employed alkali-burn injury rodent model of CoNV as our animal model to confirm our hypothesis. Coupling with slit lamp, the ultrasound data might offer more in-depth information regarding disease progression and treatment outcome.

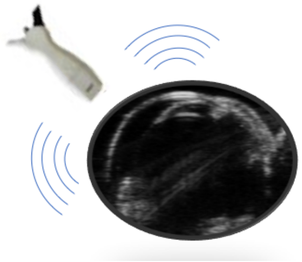

Figure 1. Ultrasound image of rat eye

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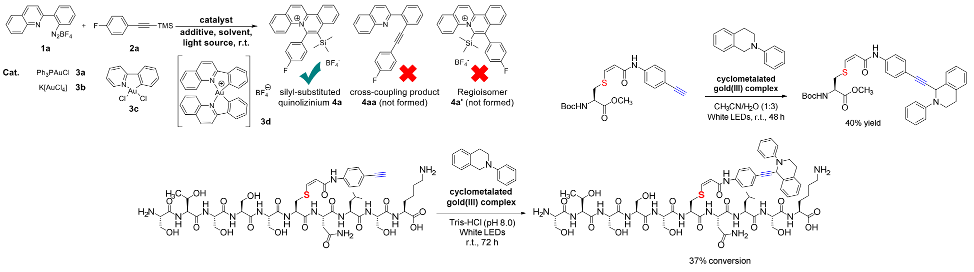
Visible Light-Induced Gold-Catalyzed Photooxidative Alkynylation of Tetrahydroisoquinolines

Wa-Yi O, Jie-Ren Deng, Rui Tang, and Man-Kin Wong*

State Key Laboratory of Chemical Biology and Drug Discovery, and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, China

(Email: wa-yi-kitty.o@connect.polyu.hk)

A new series of fluorescent quinolizinium compounds have been developed.[1] The quinoliziniums possessed tunable emission properties in visible light region and large Stokes shifts (up to 6,797 cm^{-1}). Based on this work, we set out to combine gold and visible light photoredox catalysis for alkynylation of tetrahydroisoquinolines. We found that treatment of tetrahydroisoquinolines with terminal alkynes and a catalytic amount of cyclometalated gold(III) complexes gave alkynylated products with up to 73% isolated yields under irradiation (White, LEDs 5W) in 48 h under air at room temperature. Interestingly, the product distribution varied with the electronic properties of substituents on the terminal alkynes, in which electron-withdrawing 4-ethynylanisole led to more favorable alkynylation. This newly developed methodology could be employed in multifunctional modification of peptides and proteins in aqueous medium.



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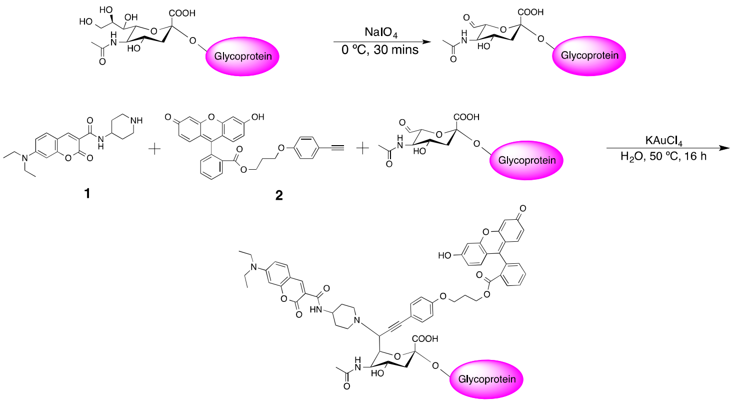
Fluorescent Labelling of Glycoproteins by FRET-based Probes via a Gold(III)-mediated Three-component Coupling Reaction

Hoi-Yi Sit, Bin Yang, Karen Ka-Yan Kung, John Siu-Lun Tam,* and Man-Kin Wong*

State Key Laboratory of Chemical Biology and Drug Discovery, and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, China

(Presenting author email: hoi-yi-jess.sit@connect.polyu.hk)

A novel approach for site-specific fluorescent labelling of glycoproteins based on FRET-based probes via a gold(III)-mediated three-component coupling reaction in aqueous medium was developed. It involves the periodate oxidation of terminal sialic acid groups on the glycoproteins into aldehydes, followed by a one-pot gold(III)-mediated three-component coupling reaction between the aldehydes, an amine-linked fluorescent dye and an alkyne-linked fluorescent dye. The resulting single-site formation of fluorescent propargylamine products exhibit FRET from the donor fluorophore to the acceptor fluorophore. This glycoprotein labelling approach achieves multi-functionalization of glycoproteins with high selectivity. Good linear correlation was exhibited between the concentration of the labelled glycoproteins and the fluorescent signals by ratiometric analysis of FRET signals.



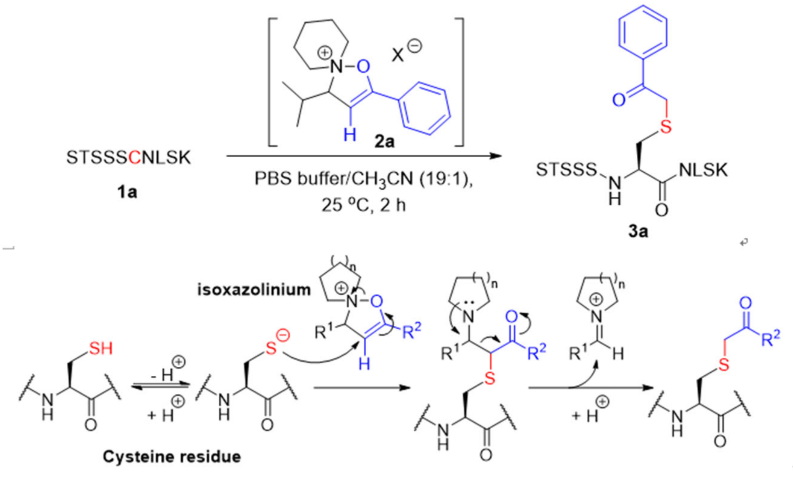
Sit, H. Y.; Yang, B.; Kung, K. K. Y.; Tam, J. S. L.; Wong. M. K. (manuscript submitted)

Chemoselective and Photocleavable Cysteine Modification of Peptides and Proteins Using Isoxazoliniums Generated *in situ* via Silver Catalysis

Wai-Ming Yip,[†] Jie-Ren Deng,[†] Sai-Fung Chung,[†,§] Alan Siu-Lun Leung,[†,§] Bin Yang,[†]
Man-Chung Choi,[†,§] Jian-Fang Cui,[†] Karen Ka-Yan Kung,[†] Zhen Zhang,[†] Kar-Wai Lo,[†]
Yun-Chung Leung*,[†,§] and Man-Kin Wong*,[†]

[†]State Key Laboratory of Chemical Biology and Drug Discovery, and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, China
[§]Henry Cheng Research Laboratory for Drug Development and Lo Ka Chung Centre for Natural Anti-Cancer Drug Development, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, China

A comprehensive study on a newly developed isoxazolinium-mediated cysteine modification of peptides and proteins is presented. Versatile isoxazolinium reagents could be modularly prepared *via* gold and silver catalysis. Using a stoichiometric amount of isoxazolinium reagents generated *in situ* from a catalytic amount of silver salts, cysteine-containing peptides could be efficiently modified to afford products in nearly complete conversions. The modification was highly chemoselective towards free cysteine residue and the resulting phenylacyl thioether linkage was stable towards excess thiol-containing reagents and reducing reagents. For protein bioconjugation, free cysteine containing proteins **HSA** and **BSA**, as well as a site-directed mutated therapeutic protein (**BCArg**) could be efficiently and selectively labelled using small amounts of the isoxazolinium reagents. Labelling peptides and proteins with functional moieties such as fluorescent tags have also been performed and analyzed by LC-MS and SDS-PAGE analyses. Besides, it has been found that the phenylacyl thioether linkage bearing an alkyne moiety could be rapidly cleaved under irradiation of UV-A light, giving the formation of a thioaldehyde moiety, which could be converted back to cysteine by reduction



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Corresponding author email: mankin.wong@polyu.edu.hk

Lasso-based Prediction of Collision Cross Section Values for Analysis of Lipids by Ion Mobility Mass Spectrometry

Jianying Wang[1,2], Yinghao Yin[2], Guizhong Xin[2,]*, Zhongping Yao[1,]*

1. Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University

2. Department of Chinese Medicines Analysis, China Pharmaceutical University

Email of corresponding author: zhongping.yao@polyu.edu.hk

Abstract

Collision cross section (CCS) values generated from ion mobility mass spectrometry (IM-MS) has been commonly employed to facilitate lipid identification.[1,2] However, this is hindered by the limited available lipid standards.[3] Though recently CCS values were predicted using computational calculation, the prediction accuracy was not generally good and the predicted CCS values of lipid isomers were almost identical. To address this challenge, here the least absolute shrinkage and selection operator (LASSO)-based prediction method was developed for prediction of CCS values of lipids. In this method, molecular descriptors were screened and optimized to reflect the structural difference among lipid isomers. The use of molecular descriptors together with a wealth of standard CCS values for lipids significantly improved the accuracy of the model. Its accuracy was externally validated with median relative errors (MRE) of <1.1%. This approach also allowed differentiation of geometric and positional isomers, even for those isomers that cannot be separated using their experimental CCS values. Applications of this approach indicated that it could practically reduce false-positive identification in the IM-MS-based lipidomics.

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Study of Dynamics and Kinetics of β-Lactamases towards Antibiotics by Hydrogen/Deuterium Exchange Mass Spectrometry

Tsz-Fung Wong, Pui-Kin So, Liwen Huang, Zhong-Ping Yao*

Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University. Email: zhongping.yao@polyu.edu.hk

Production of β-lactamases renders bacteria invulnerable towards β-lactam antibiotics and is the major cause of antibiotics resistance. In recent years, extended spectrum β-lactamases (ESBLs), which are mutated from wild-type β-lactamases and are insusceptible to even later generation antibiotics, have been discovered, leading to more severe health threat worldwide. In this study, structural and dynamic properties of a series of mutants of TEM-1, a class A β-lactamase, were investigated by hydrogen/deuterium exchange mass spectrometry (HDX-MS), in order to obtain insights into their interactions with the antibiotics. Global HDX-MS revealed that the flexibility of TEM-ESBLs was higher than that of TEM-1. Local HDX-MS study further revealed that the expansion of binding pocket of TEM-ESBLs enabled better accommodation of bulky side chains of third generation cephalosporins and thus the enhancement of the hydrolytic power of TEM-ESBLs.

This work was supported by the Hong Kong Research Grants Council (grant Nos. PolyU 153348/16P and C5031-14E).

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Biochemical and structural characterization of CGI-58

Thi Thuy Hoa Ha, Jie Shi, and Zhihong Guo*

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

Comparative Gene Identification-58 (CGI-58) is an α/β hydrolase protein without catalytic ability which plays an important role in lipid metabolism in mammals and plants. In humans, mutations of CGI-58 cause the Chanarin-Dorfman syndrome, a rare neutral lipid storage disease characterized by accumulation of lipid droplets in liver, skin, skeletal muscle, and blood cells that normally store no neutral lipids[1]. In adipocytes, CGI-58 is associated with lipid droplets through interacting with perilipin 1 in a basal lipolytic state, but it activates triacylglycerol hydrolase adipose triglyceride lipase (ATGL) on the lipid droplet surface and is also released into the cytosol upon catecholamine stimulation[2]. However, how CGI-58 activates ATGL is still unclear. Here we attempt to shed light on the biological roles of CGI-58 using both biochemical and structural approached. We have successfully solubilized CGI-58 in the presence of Tween 20 in an *E. coli* expression system and obtained enough amount of the pure protein for crystallization. Since Tween 20 is structurally similar to triacylglycerol, we hypothesize that CGI-58 is a triacylglycerol carrier and a co-substrate of ATGL. Toward this end, we explored different approaches to directly use triacylglycerol to stabilize the protein and attempted to determine its interaction with the neutral lipid. In the meantime, we carried out crystallization screen and optimization for the purified protein. Progress will be reported on these studies.

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Acknowledgement: This work was financially supported by GRF601413 and N_HKUST621/13 from the Research Grants Council of the HKSAR Government.

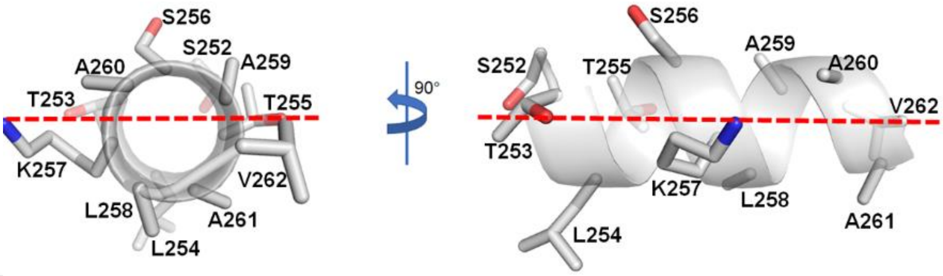
Identification of an amphipathic peptide sensor of the fluid membrane microdomains in *Bacillus subtilis*

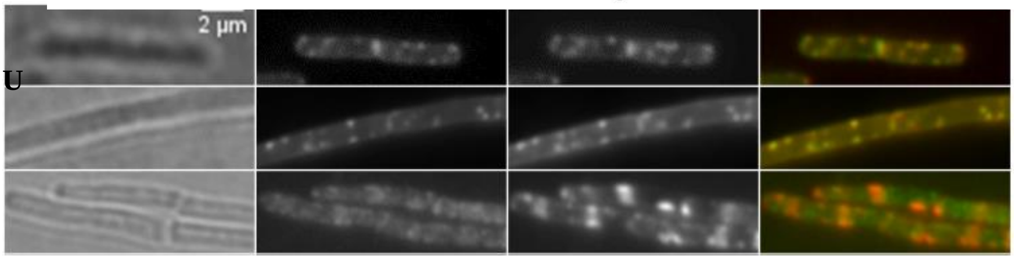
Yiping Jiang, Xin Dai, Mingming Qin, Zhihong Guo*

Department of Chemistry and State Key Laboratory for Molecular Neuroscience, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China

Email: *chguo@ust.hk*

Phosphate acyltransferase PlsX is a monotopic membrane protein catalyzing the first chemical step in the phospholipid biosynthesis of many bacteria. Recently, its biological function has been linked to its localization to the newly found membrane microdomains called regions of increased fluidity (RIFs) in *Bacillus subtilis*. However, little is known about the mechanism of its specific association with the microdomains and how the PlsX-RIFs association affects cell growth. Here, we show that two symmetric nine-residue amphipathic α-peptides at the exposed end of the four-helix bundle stem in its dimeric structure are responsible for the subcellular localization. This is based on its delocalization to cytosol or other positions of cell membrane when the amphipathic interaction is disrupted. Our results show that the short amphipathic α-peptides recognize RIFs by limiting the hydrophobic interaction in a narrow range close to a minimum level. They suggest that controlling the hydrophobic interaction with the acyl groups of membrane lipids is likely a critical factor in protein recruitment to the fluid membrane microdomains. Furthermore, we determined the putative effect of the RIFs localization on the growth rate of the bacteria.





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Acknowledgment: This work was supported by National Natural Science Foundation of China (Grant 21877094).

Mechanism-based inhibition of the essential thiamine-dependent enzyme of the vitamin K_2 biosynthesis

Tin-Lok Li, Zhihong Guo*

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

**Email address:* chguo@ust.hk

Abstract

MenD is a thiamine diphosphate and metal-ion-dependent enzyme catalyzing a conjugate addition reaction of 2-ketoglutarate to isochorismate in vitamin K_2 biosynthesis. From its crystal structure, the conserved amino acid residues Arg413 and Arg395 in *Escherichia coli* (*E. coli*) MenD are found to be crucial for the binding and orientation of substrates during the catalysis. Mutations of these conserved residues have been found to form an inactive tetrahedral post-decarboxylation intermediate in an alternate binding site to disable the catalysis.[1] Based on this unique mechanism, we designed analogs of the 2-ketoglutarate substrate as the suicide inhibitors of the enzyme. These inhibitors are synthesized and characterized for their inhibition of MenD orthologues from *E. coli*, *Bacillus subtilis* and *Mycobacterium tuberculosis*. They were indeed found to inactivate MenD in a time-dependent manner. The structures of the enzyme-inhibitor complexes will be determined by protein crystallography in order to confirm the inhibition mechanism. This will pave the way for new antibiotics development targeting bacterial pathogens in the future.

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Acknowledgement: This work was financially supported by RGC of the HKSAR Government.

Structural and kinetic investigation of the thiamine-dependent MenD from the *Escherichia coli* menaquinone biosynthetic pathway

Mingming Qin, Haigang Song, Zhihong Guo*

Department of Chemistry and State Key Laboratory for Molecular Neuroscience, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China

**chguo@ust.hk*

MenD, or 2-succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexadiene-1-carboxylate (SEPHCHC) synthase, is a thiamin diphosphate (ThDP) dependent enzyme involved in menaquinone (Vitamin K2) biosynthesis pathway in *Escherichia coli*. Traditional views about THDP dependent enzymes assumed enamine as a universal intermediate. However, after solving a MenD complex binding with THDP adduct, it was revealed that a unique tetrahedral intermediate is involved in a new mode of catalysis of the THDP dependent enzyme [1]. Besides, two highly conserved arginine residues were found to interact with the succinyl group to serve crucial roles in the catalytic process.

To further understand the catalytic mechanism and the function of the highly conserved residues Arg395 and Arg413, we have overexpressed and purified MenD mutants characterized both the wild-type enzyme and the mutants by crystallographic and kinetic methods. Results from steady-state and pre-steady-state kinetic studies showed that the α-ketoglutarate binding is the rate determining step [2]. Moreover, the intermediate in reaction process is stable enough after decarboxylation and not affected by the electrophilic substrate, isochorismate, which is quite different when compared with previous reports for other ThDP dependent enzyme. Both kinetic data and crystal structures showed that the catalytic efficiency and substrate affinity is reduced significantly by alteration of interactions at the two highly conserved arginine residues. Surprisingly, an alternative binding site was observed in both R395A and R413A mutant structure with highly conserved residues. These results have provided new insights into the new catalytic mechanism of MenD.

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Acknowledgement: This work was financially supported by GRF601413 from the HKSAR Government.

Intrinsic Cleavage of RNA Polymerase II Adopts a Nucleobase-independent Mechanism Assisted by Transcript Phosphate

Carmen Ka Man Tse[1,+], Jun Xu[2,+], Liang Xu[2,4], Fu Kit Sheong[1], Shenglong Wang[3], Hoi Yee Chow[5], Xuechen Li[5], Peter Pak-Hang Cheung[1*], Dong Wang[2*], Yingkai Zhang[3,6*], Xuhui Huang[1*]

[1]Department of Chemistry, Center of Systems Biology and Human Health, State Key Laboratory of Molecular Neuroscience, The Hong Kong University of Science and Technology, Kowloon, Hong Kong
[2]Department of Cellular and Molecular Medicine, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, La Jolla, California 92093, United States
[3]Department of Chemistry, New York University, New York, New York 10003 United States
[4]Department of Chemistry, Sun Yat-Sen University, Guangzhou, China
[5]Department of Chemistry, State Key Lab of Synthetic Chemistry, The University of Hong Kong, Hong Kong
[6]NYU-ECNU Center for Computational Chemistry at NYU Shanghai, Shanghai 200062, China
*Email: ppcheung@ust.hk or dongwang@ucsd.edu or yz22@nyu.edu or xuhuihuang@ust.hk
[+] These authors contribute equally to this work.

ABSTRACT

RNA polymerase II (Pol II) utilizes the same active site for polymerization and intrinsic cleavage. Pol II proofreads the nascent transcript by intrinsic nuclease to maintain high transcriptional fidelity critical for cell growth and viability. The detailed catalytic mechanism of intrinsic cleavage remains unknown. Here, we combined *ab initio* quantum mechanics/molecular mechanics studies and biochemical cleavage assays to show that Pol II utilizes downstream phosphate oxygen to activate the attacking nucleophile in hydrolysis, while the new 3'-end is protonated through active site water without a defined general acid. Experimentally, alteration of downstream phosphate oxygen either by 2'-5' sugar linkage- or stereo-specific thio-substitution of phosphate oxygen drastically reduced cleavage rate. We showed by N7-modifiion that guanine nucleobase does not directly involved as acid-base catalyst. Our proposed nucleobase-independent cleavage mechanism suggests that the sequence-dependence of transcription proofreading rate is not due to intrinsic cleavage but likely backtracking.

Background Error Model-coupled Precision Run-On Circular-sequencing (emProc-seq) discovers transcriptional mutational hotspots

Author' names:

Tin Hang Chong, Peter Pak-Hang Cheung, Biaobin Jiang, Gregory T. Booth, Ilona Christy Unarta, Yuqing Wang, Jiguang Wang*, John T. Lis*, Xuhui Huang*

Postal address:
jgwang@ust.hk or jtl10@cornell.edu or xuhuihuang@ust.hk

Abstract

Transcriptional mutation had been suggested to have influence on aging or cancer. Existing method, such as Cir-seq[1] are not able to provide information of nascent RNA and baseline for mutation call. Background Error Model-coupled Precision Run-On Circular-sequencing (EmPRO-Cseq) is newly developed method for accurate sequencing of nascent RNA produced by RNA polymerase I. The foundation of this approach is by combination of two existing technique, PRO-seq[2] and Cir-seq, which PRO-seq provides source of nascent RNA while Cir-seq provide accurate sequencing of RNA species. We present the initial development of EmPRO-Cseq and identification error hotspots and features of RNA polymerase I transcribed region by introducing a background baseline. Mismatch rate are greatly reduced from $1.43\pm0.11\times10^{-3}$(PRO-seq) to $3.79\pm0.81\times10^{-5}$ (EmPRO-Cseq), which imply that EmPRO-Cseq can successfully remove noise generated mainly in reverse transcription. One feature of RNA polymerase I is that the error tends to cluster at 3' end. EmPRO-Cseq may be further extend to study different transcriptional error spectrum of pre-mRNA (RNA polymerase II transcribed), siRNA, regulatory RNA between normal and disease cell, such as cancer.

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Dynamics of Opening and Closing Motions of the Clamp of Bacterial RNA Polymerase

Ilona Christy Unarta [2] **and Xuhui Huang**[1,2]

[1]Department of Chemistry, The Hong Kong University of Science and Technology

[2]Department of Chemical and Biomedical Engineering, The Hong Kong University of Science and Technology

xuhuihuang@ust.hk

Abstract

RNA Polymerase (RNAP) structure resembles a pair of crab claw, which is divided into the rigid and flexible are shown in Fig.1. The clamp domain of RNAP can open and close (Fig. 1) depending on the transcription step. Bacterial RNAP with σ factor in solution without nucleotides (holoenzyme) may adopt 3 states, i.e.: open, closed, collapsed, with the open state being the predominant one. Other than that, clamp domain motion is very important in other steps of transcription, i.e.: initiation step and hairpin-induced pausing. To understand how RNAP regulates the clamp domain motion in atomistic resolution, we employed MD simulation and Markov State Model. We observed that the two slowest mode of RNAP motion is the clamp opening and closing (clamp swinging), as well as clamp swiveling motion, which is a motion perpendicular to the clamp swinging. In addition, these two motions seem to be highly correlated with the switch region, a region at the base of clamp domain. With this observation, we may be able to look further into the specific residues that regulates the clamp domain.

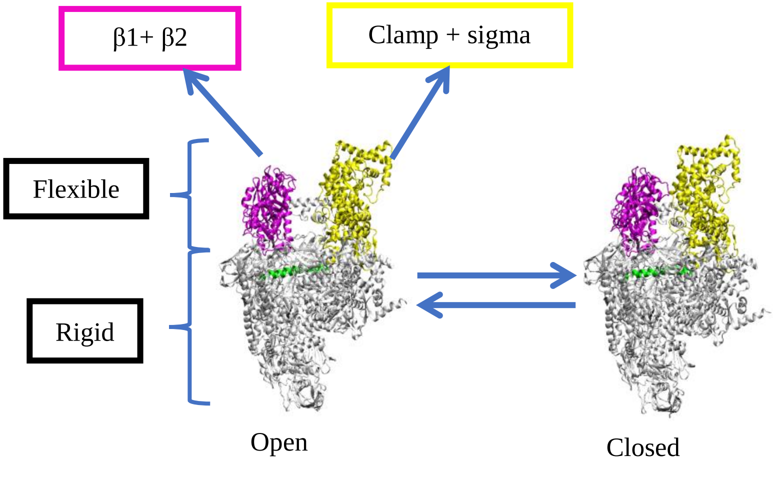

Fig. 1 Visualization of Open and Closed states of RNAP

Dynamics of Asymmetric DNA Partial Unwrapping in Nucleosomes at Atomic Resolution

Junhui Peng, Xiaowei Wang, Wei Wang and Xuhui Huang*

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

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

xuhuihuang@ust.hk

Abstract

Nucleosomes, the basic unit of DNA packaging in eukaryotic genomes, undergo spontaneous DNA unwrapping and rewrapping. Although numerous experiments and simulations have been carried out to characterize this dynamic process, the detailed conformational dynamics of DNA partial unwrapping from nucleosomes remain unresolved. Here, we performed extensive all atom MD simulations and Markov State Models to study the conformational dynamics of nucleosomal DNA partial unwrapping. Our results show several different stages of asymmetric DNA unwrapping. Mean first passage time for the nucleosome to unwrap ~25-30 bp of DNA was estimated to be ~3-50 milliseconds, which agrees with previous FRET experiments. We have identified several key histone protein-DNA interactions in DNA unwrapping. In addition, we find that the asymmetric DNA unwrapping can be regulated by histone tails, histone post-translational modifications (PTMs) and local DNA sequences.

Translocation of Alkylpurine Glycosylase D(AlkD) at all-atom resolution

Xiaowei Wang[1], Xuhui Huang[1]

[1]Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong; xuhuihuang@ust.hk

Abstract

Alkylpurine Glycosylase D(AlkD) shows a unique base excision scheme which interact with non-lesion DNA stand instead of contacting with alkylated base. Although the mechanism of AlkD to capture and to excise lesions improve the progress of understanding the dynamics, the translocation of AlkD on intact DNA without any lesion is unclear. Here, through molecular simulation with atomic resolution, we observe the mechanism of AlkD's translocation on perfect DNA without any lesion. The result shows that AlkD translocates spirally upon DNA axis stepwise with the decorrelation between directly upon DNA axis and rotational move, on a microsecond timescale along one pair of DNA. Gln38, Thr39, Pro40 and Arg43 forming stable interactions with one strand of DNA benefit rotational move. These results provide insight into the dynamics of AlkD at atomic precision.

The NTP incorporation mechanism of Influenza A virus polymerase and anti-flu compounds

Xinzhou Xu, Zixi Dai, Hoishan Kei, Xuhui Huang, Peter Cheung

Address: xuhuihuang@ust.hk & ppcheung@ust.hk

Abstract:

Influenza A virus (IAV) can cause influenza in birds and mammals. Some of the IAV strains, like H1N1, H5N1, H7N9, have led to severe pandemic influenza infections which significantly affected the world. The IAV RNA-dependent RNA polymerase (RdRp) complex acts as a core of the virus infection and is much similar among different influenza strains. The highly conserved sequences of the IAV polymerase make itself a perfect target for drugs design, by interfering which could lead to termination of virus viability. Natural compounds and their derivatives have shown many advantages in developing new drugs. In this work, we demonstrated some of the polymerase mechanisms by comparing the wild-type and mutant polymerases in the core regions(K235, R239, I241 on PB1), as well as the discovery of novel anti-flu drugs from natural compound derivatives.

An AIEgen with Anion-π^+ Interactions for Selective Wash-Free Imaging and Photodynamic Killing of Bacteria

Qiyao Li, Jacky W. Y. Lam and Ben Zhong Tang*

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

Clear Water Bay, Kowloon, Hong Kong, China. Email: tangbenz@ust.hk

Abstract

Recently, a new aggregation-induced emission (AIE) system with anion-π^+ interactions was first developed and demonstrated a novel strategy to develop inherently charged AIE luminogens (AIEgens). AIEgens with charges possess unique advantages, such as enhanced biocompatibility and subcellular targeting ability resulted from electrostatic interactions between biomacromolecules and AIEgens. Therefore, they are expected to find wide biological applications. Unfortunately, the introduction of charges to AIEgens often suffers from complicated synthetic route, tedious purification and low yield.

Herein, a new AIEgen, namely TTPABQ, with anion-π^+ interactions was designed and obtained via a one-pot synthetic procedure. TTPABQ possesses a high specificity to bacteria and high photostability. It can image both Gram-positive and negative bacteria in a wash-free manner. This greatly simplify the imaging process. Furthermore, TTPABQ can also work as a promising photosensitizer to kill bacteria through efficient generation of reactive oxygen species upon white light irradiation.

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A Bifunctional Aggregation-Induced Emission Luminogen for Monitoring and Killing of Multidrug-resistant Bacteria

Ying Li, Zheng Zhao, Ryan T. K. Kwok, Jacky W. Y. Lam and Ben Zhong Tang

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

Abstract

Multidrug-resistant (MDR) bacteria pose serious threats to public health as currently there lacks effective and biocompatible drugs to kill them. Here, we report a bifunctional aggregation-induced emission luminogen (AIEgen) called triphenylethylene-naphthalimide triazole (TriPE-NT) capable of both staining and killing Gram-positive (G+) and Gram-negative (G-) bacteria. The intrinsic fluorescence nature of the TriPE unit enables TriPE-NT to monitor the drug-bacteria interactions. Meanwhile, the NT unit renders TriPE-NT the antibacterial activity. Furthermore, TriPE-NT can generate reactive oxygen species under light irradiation to drastically enhance its antibacterial efficacy by photodynamic therapy against wild bacteria and clinical-isolated MDR bacteria with a very low toxicity to mammalian cells. Moreover, the efficiency of TriPE-NT staining on bacteria closely correlates with its antibacterial efficacy. As an example of application, TriPE-NT is utilized in curing *E. coli*-, MDR *E. coli*-, *S. epidermidis- and* MDR *S. epidermidis*-infected wounds on rats with high efficacy and high safety. Thus, TriPE-NT could be used not only as a powerful antibiotic agent for treating MDR bacteria-infected diseases but also as a potential fluorescent agent for monitoring the bacterial infections and further exploring the related antibacterial mechanism.

Targeted Bioimaging and Theranostics Based on an AIEgen with Far Red/NIR Emission and Efficient ROS Generation

Haixiang Liu, Ryan T. K. Kwok, Jacky W. Y. Lam and Ben Zhong Tang*

Department of Chemical and Biological Engineering & Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China. E-mail: tangbenz@ust.hk

Abstract

Visualizing agents or photosensitizers (PSs) with strong long-wavelength emission are needed for efficient bioimaging and photodynamic therapy in real situations to avoid the auto-fluorescence of cells and penetrate skin or other biological barriers with a high depth. Among various emission color, far red/near infrared (NIR) is the most promising one to achieve such goals. However, traditional far red/NIR fluorophores suffers from the aggregation-caused quenching effect in the aggregate state, which weakens their fluorescence and ability to generate reactive oxygenic species (ROS) for practical applications.

In this work, we developed a novel carbazole-bridged push-pull fluorophore called DCQu with aggregation-induced emission characteristic, bright NIR solid-state emission, large Stokes shifts and large 2PA cross-section. DCQu shows specific mitochondria-targeting capability with good biocompatibility. Impressively, upon ultralow-power light irradiation, DCQu can readily generate ROS with a much higher efficiency than some popularly used PSs. DCQu can selectively differentiate cancer cells from normal cells without the aid of any extra targeting ligands. In vitro cancer cell death triggered by in-situ mitochondrial damage by PDT and in vivo melanoma ablation under ultralow-power light irradiation demonstrate the superior performances of DCQu in image-guided PDT with high safety.

Molecular Motion in Aggregates: Manipulating TICT for Boosting Photothermal Theranostics

Shunjie Liu, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

Planar donor (A)-acceptor (A) conjugated structures are generally believed as the standard for architecting highly efficient photothermal theranostic agents to restrict intramolecular motions in aggregates (nanoparticles). However, other channels of extra nonradiative decay may be blocked. Now this challenge is addressed by proposing an abnormal strategy based on “molecular motion in aggregates”. Molecular rotors and bulky alkyl chains are grafted to the central D-A core to lower the intermolecular interaction. The enhanced molecular motion favors the formation of dark twisted intramolecular charge transfer state, whose nonradiative decay enhances the photothermal properties. Result shows that small molecule called NIRb14 with long alkyl chains branched at the second carbon exhibits enhanced or much higher photothermal properties than NIRb6 with short branched chains, NIR6 with short linear chains and commercial gold nanorods. Both *in vitro* and *in vivo* experiments demonstrate that NIRb14 nanoparticles can be used as nano-agents for photoacoustic imaging-guided photothermal therapy. Moreover, NIRb14 specifically accumulates at the tumor site in the presence of charge reversal poly(β-amino ester). This study thus provides an excited molecular motion approach towards efficient phototheranostic agents.

Exploration of AIE-Active Theranostic Material from Natural Herbs

Michelle M. S. Lee, Bingran Yu, Wenhan Xu, Ryan T. K. Kwok, Jacky W. Y. Lam,
Fujian Xu, Dong Wang,* Ben Zhong Tang*

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

Abstract

Aggregation-induced emission luminogens (AIEgens) show great performance in bioimaging and therapeutic applications, thanks to their intrinsic property including the capability to work at high concentration with bright fluorescence and good photostability. However, most of the AIEgens developed so far for biological applications are synthetic organic compounds, which pose the disadvantages of high cost, environmental unfriendly and potential cytotoxicity. In fact, many naturally-occurring compounds extracted from Chinese herbs exhibit AIE property. These materials are easy to access and show good biocompatibility, making their potential use in bioimaging and therapy applications. In this work, we demonstrated the use of Berberine chloride, an AIE-active natural isoquinoline alkaloid from Chinese herbal plants, as theranostic agent towards both cancer cells and bacteria. Berberine chloride could selectively target mitochondria in cancer cells over normal cells. It showed good biocompatibility under dark condition. However, upon light irradiation, it served as photosensitizers to generate reactive oxygen species to damage mitochondria followed by its migration to nucleus to kill the cancer cells by means of photodynamic therapy. Experiments proved that when mitochondrial potential was lost, the dye molecules could directly target the negatively charged nucleus. In the meantime, Berberine chloride successfully targeted and killed bacteria through photodynamic bacteria killing. It also demonstrated its capability to perform in vivo photodynamic wound bacterial killing.

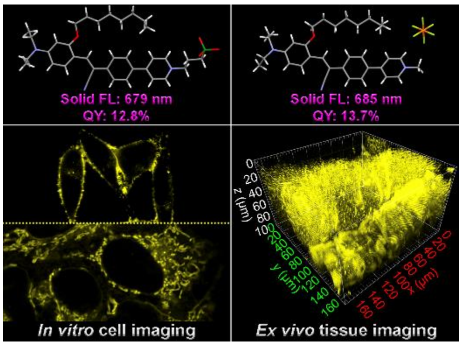
Highly Photostable Two-Photon NIR AIEgens with Tunable Organelle Specificity and Deep Tissue Penetration

Guangle Niu, Ryan T. K. Kwok, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

Photostability is a particularly important parameter for fluorescence imaging especially for long-term dynamic tracking in live samples. However, many organic fluorophores show poor photostability under one-photon and two-photon continuous irradiation. In addition, these traditional fluorophores also suffer from aggregation-caused quenching (ACQ) in the aggregate state or aqueous environment. Therefore, it remains challenging to develop photostable and ACQ-free fluorophores for biological imaging. In this work, we developed two highly photostable aggregation-induced emission luminogens (AIEgens) with cyanostilbene core for in vitro and ex vivo bioimaging. These AIEgens named CS-Py$^+$SO$_3^-$ and CS-Py$^+$ exhibit near-infrared solid-state emission, large Stokes shift (>180 nm), high fluorescence quantum yield (12.8%-13.7%) and good two-photon absorption cross section (up to 88 GM). CS-Py$^+$SO$_3^-$ and CS-Py$^+$ show specific organelle staining with high biocompatibility in membrane and mitochondria in live cells, respectively. In addition, selective two-photon visualization of mitochondria in skeletal muscle tissues of live rat with deep-tissue penetration (about 100 μm) is successfully realized by using CS-Py$^+$. Furthermore, these AIEgens especially CS-Py$^+$ exhibit remarkably high resistance to photobleaching under one-photon and two-photon continuous irradiation. These highly photostable AIEgens could be potentially utilized in visualizing and tracking specific organelle-associated dynamic changes in live systems.



Specific detection and quantitative analysis of serum albumin in biological fluids by tetrazolate-functionalized water-soluble AIEgens

Tu Yujie, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

The analysis of albumin has clinical significance in diagnostic tests of body fluids and is also of obvious value to researches on the serum albumin-mediated in vivo drug delivery and biological therapeutics. Since albumin, served as an endogenous carrier, can interact with many guest molecules, its analysis in biological fluids suffered from high variations and strong interferences from the background. Herein, we introduced a class of tetrazolate-tagged tetraphenylethylene derivatives (TPE-TAs) as novel fluorescent probes for albumin detection and quantification. These aqueous-soluble probes with aggregation-induced emission (AIE) characteristics offer a negligible background and by binding with the albumin, their fluorescence was turned on, leading to a general albumin assay with a low detection limit (0.21 nM), a broad tunable linear dynamic range (0.02~3000 mg/L) for quantification and a superior selectivity in aqueous solutions (pH = 6~9). These intriguing characteristics can be attributed to the tight and site-specific binding of tetrazolate functionality to albumin (K_D = 0.20~0.29 μM). The probe-albumin binding interactions were disclosed at three unusual sites: two in the polar inter-domain clefts and a third one in a polar cavity of Domain III. In this respect, the current analysis leaves the popular hydrophobic-carrying sites intact thus representing an alternative sensing method. Computational modeling implicated a key role of multiple lysine residues at the binding sites in the AIE-type detection, which was verified by the detection of poly-L-lysine macromolecules. Finally, we used the system to quantify the urinary albumin in clinic urine samples and found that it is a feasible and practical strategy for fluorogenic albumin analysis in complex biological fluids.

A New Strategy towards “Simple” Water-soluble AIE Probes for Hypoxia Detection

Changhuo Xu, Hang Zou, Jacky W. Y. Lam and Ben Zhong Tang*

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

Abstract

Hypoxia-responsive fluorescent probes have been emerging as a novel scaffold for tumor diagnosis. However, dilemma often exists between simple synthesis and high water-solubility in traditional probes. Owing to the intrinsic property of N-oxides, we herein proposed a new strategy to design and synthesize probes for in vitro hypoxia imaging. Three tetraphenylethene (TPE)-containing N-oxides were synthesized with good water solubility. The zwitterionic N-oxide groups not only enabled the molecules to dissolve in water but also endowed them with sensitivity to reducing species. The neutral nature of the N-oxides also made them inert to positively or negatively charged interferences. Because of the active intramolecular motion, the water-soluble N-oxides were non-emissive in aqueous medium. The N−O covalent bond of one molecule could be specifically cleaved by cellular reductase overexpressed under hypoxic conditions. The aggregation of the hydrophobic TPE residue restricted the intramolecular motions of the molecule, which turned on its fluorescence. The new strategy to design hypoxia imaging probes is extremely valuable and has great potential for application in tumor diagnosis.

Rational design of a unique probe for imaging mitochondria and lipid droplets in dual colors

Ruoyao Zhang[1], Jacky W.Y. Lam[2], Ryan T.K. Kwok[2], Ben Zhong Tang[1,2]*

[1]Department of Chemical and Biological Engineering and [2]Department of Chemistry,
The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon,
Hong Kong, China. E-mail: tangbenz@ust.hk

Abstract

Subcellular organelles involve in many cellular functions to maintain the normal physiological functions of cells. Organelle-targeting bioimaging can illuminate the way how the organelles function and can further guide the treatment of a variety of related diseases. Due to their properties of excellent photostability, large Stokes shift, high signal-to-noise ratio and free of aggregation-caused quenching effect, luminogens with aggregation-induced emission characteristic (AIEgens) serve as superior contrasting agents for bioimaging. Thus in this work, a novel organelle-targeting AIEgen abbreviated as DSQA was developed. Interestingly, instead of targeting one specific organelle, DSQA can target both mitochondria and lipid droplets in dual color (red and blue). In addition, in vivo imaging experiments demonstrate its ability to image mitochondria (red channel) and lipid droplets (blue channel) simultaneously in HeLa cells. Therefore, DSQA is a promising candidate to investigate the mutual effect of mitochondria and lipid droplet and their associated physiological and pathological processes in live biological samples.

In Situ Self-Reporting Photodynamic Therapy System based on a Positive-Charged AIEgen

Tianfu Zhang, Yuanyuan Li, Jacky W. Y. Lam, Ben Zhong Tang*

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

Abstract

Although photodynamic therapy thrived as a promising disease treatment, highly active photosensitizers (PSs) and intense light power could cause treatment overdose. To mitigate the problem, real-time in situ monitoring its therapeutic response is important and urgent. Herein, we design a cationic PS with aggregation-induced emission (AIE) characteristic, named TPE-4EP+, which not only exhibits extremely high $^1O_2$ generation efficiency, but also undergoes mitochondrial-to-nucleus translocation during apoptosis induced by photodynamic therapy (PDT), enabling in-situ real-time self-reporting the therapy process. Adjusting the charge number to double and triple positive charges generates TPE-2EP+ and TPE-3EP+, which retains the PDT effect but without translocation. Moreover, we prove that the in situ translocation of TPE-4EP+ is mainly attributed to its high positive charge, which interacts straongly with DNA. The ability of PS to introduce photodynamic therapy with real-time diagnosis helps control the treatment dose that can avoid excessive phototoxicity and minimize potential side effect. Future development of new generation of PS is envisioned.

References

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2. Zheng, Z.; Zhang, T.; Lam, J. W. Y.; Tang, B. Z. *ACS Nano* **2018**, *12*, 8145–8159.

Engineering Sensor Arrays Using Aggregation-Induced Emission Luminogens for Pathogen Identification

Chengcheng Zhou, Ryan T. K. Kwok, Jacky W. Y. Lam, Ben Zhong Tang*

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

Abstract

Fast and reliable identification of pathogens is crucial for the effective treatment of infectious diseases. However, even some advanced technologies applied in hospitals and other authorized organizations such as automated biochemical instrumentation and MALDI-TOF MS, the accuracy rate of pathogen identification is only 90–95% and several hours of operation are still needed. Without rapid and reliable pathogen diagnostic platforms, a suboptimal prescription could be made, which greatly threatens human life and accelerates the emergence of bacterial resistance.

In this work, we created a series of simple and reliable sensor arrays based on a tetraphenylethylene (TPE) derivative called TPE-AR for fast identification of pathogens. Each sensor array consists of three TPE-ARs based on the criterion of balancing the simplicity of sensor array and the diversity of fluorescence response. TPE-ARs bear the cationic ammonium group with different hydrophobic substituents, providing tunable logP (*n*-octanol/water partition coefficient) values to enable different multivalent interactions with pathogens. Meanwhile, TPE-ARs also show diverse aggregate behaviors, further enriching the multivalent interactions of TPE-ARs and pathogens. Thanks to the diverse interactions of TPE-ARs with the pathogens, each sensor array can provide a unique fluorescence response pattern for different pathogens. By recognizing the fluorescence pattern of pathogens with assistance of LDA, our sensor arrays can identify different kinds of pathogens including normal and drug-resistant bacteria, with nearly 100% accuracy. Also, blends of pathogens can be identified accurately. The identification procedure of our sensor arrays is time-saving (about 0.5 h), easy-to-operate without washing steps and high-throughput, showing a great potential to offer timely and reliable pathogen information for clinical decisions.

Summary of Presentation and Participant Distribution

		Presentations								**Participants**
		Poster (in different subject areas*)						**Oral**	**Sub-total**	
		A&E	INORG	ORG	PHYS	MAT	BIO			
Institution**	CITYU	1	17	1	4	3	20	1	47	90
	CUHK	1	8	22	8	1	3	1	44	122
	HKBU	15	4	5	1	2	0	1	28	60
	HKU	5	22	9	8	7	19	1	71	195
	HKUST	23	13	17	7	22	21	1	104	153
	POLYU	3	6	2	3	5	14	1	34	62
	Macau U	0	0	0	0	0	0	0	0	2
	SIOC	0	0	2	0	0	0	0	2	2
	SUST	0	0	0	0	0	0	0	0	1
	Sub-total	48	70	58	31	40	77	6	330	687
No. of awards		2	3	2	1	2	3	1	14	----

***	Subject area codes:**

A&E	Analytical and Environmental Chemistry
INORG	Inorganic Chemistry
ORG	Organic Chemistry
PHYS	Physical Chemistry
MAT	Material Chemistry
BIO	Biochemistry and Chemical Biology

****	Institution abbreviations:**

CITYU	City University of Hong Kong
CUHK	The Chinese University of Hong Kong
HKBU	Hong Kong Baptist University
HKU	The University of Hong Kong
HKUST	Hong Kong University of Science and Technology
POLYU	The Hong Kong Polytechnic University
Macau U	University of Macau (Macau)
SIOC	Shanghai Institute of Organic Chemistry (Shanghai)
SUST	Southern University of Science and Technology (Shenzhen)

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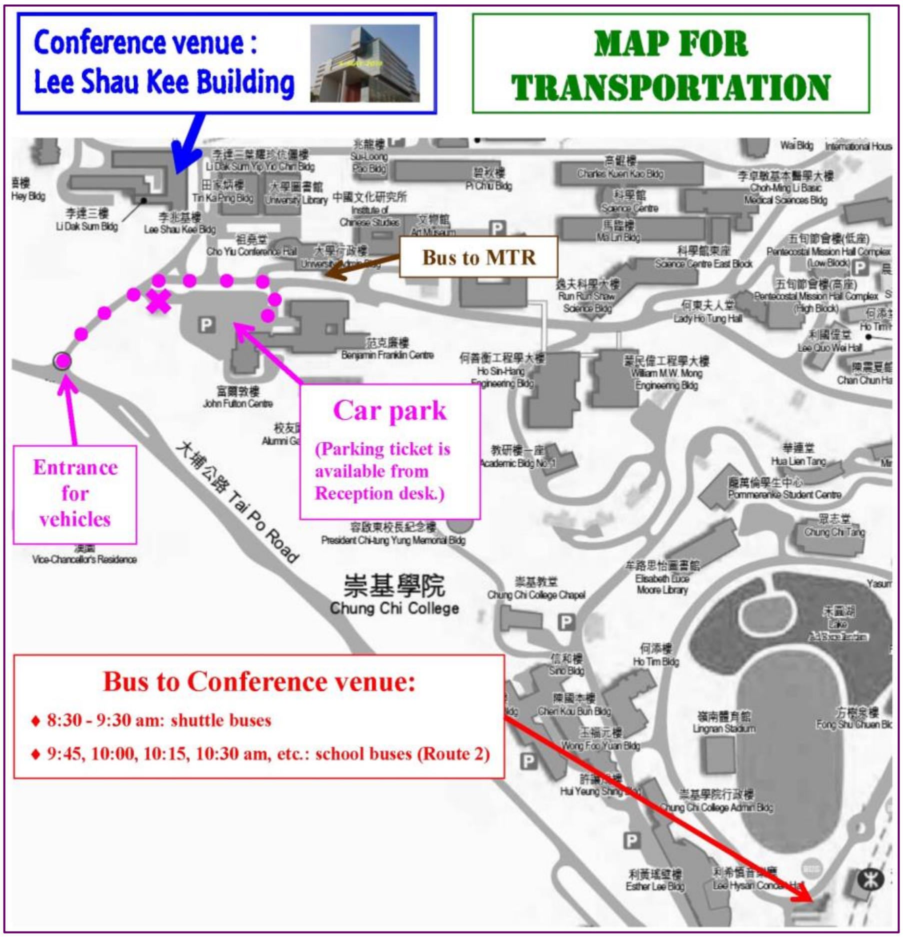
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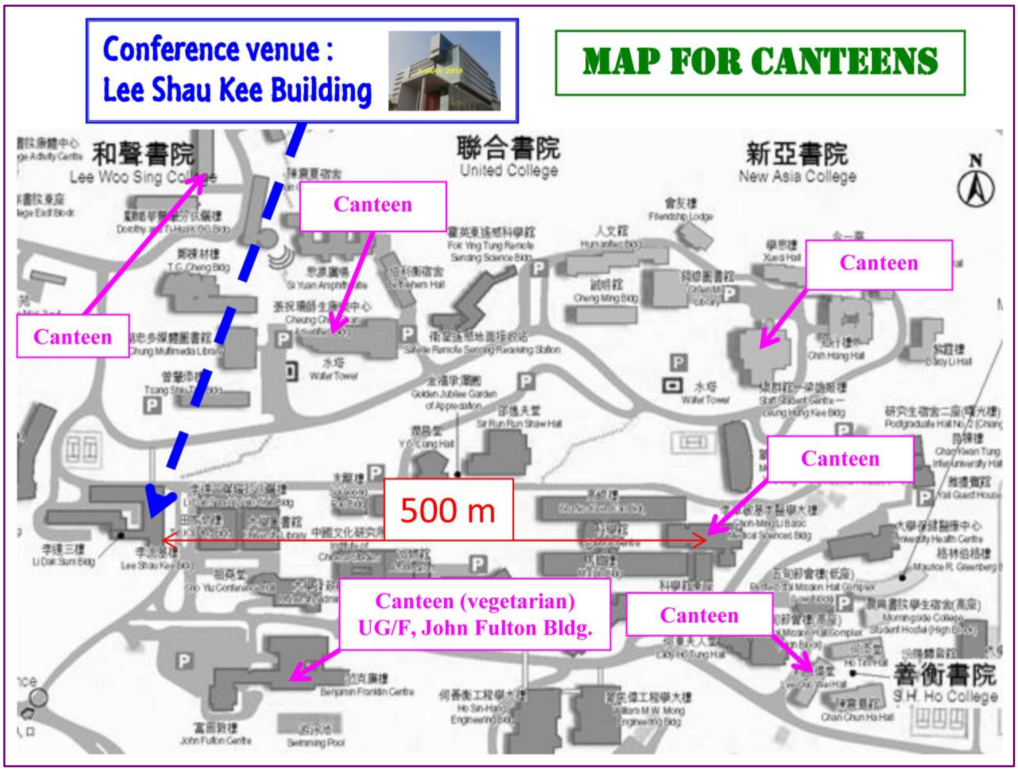
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