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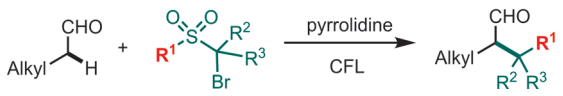
2024/10

# Radical-Mediated α-*tert*-Alkylation of Aldehydes by Consecutive 1,4- and 1,3-(Benzo)thiazolyl Migrations

*Highlighted article by J. Liu, J. Ma, T. Wang, X.-S. Xue, C. Zhu*



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# Dear Readers,

This October issue of SYNFORM is kicked off by a Literature Coverage article on a novel and ingenious strategy – conceived and developed by the group of J. E. Hein (Canada) – for performing Suzuki–Miyaura cross-couplings in biphasic systems, utilizing phase-transfer catalysis for achieving the key transmetalation step. The next article is a Young Career Focus interview with the 2024 Thieme Chemistry Journals awardee Shibdas Banerjee (India), who talks about his interests in organic chemistry, as well as those outside the lab. The next Literature Coverage article covers a recent method published by the groups of C. Zhu and X.-S. Xue (P. R. of China) for achieving the radical-mediated α-*tert*-alkylation of aldehydes by taking advantage of consecutive 1,4- and 1,3-(benzo)thiazolyl group migrations. The issue is closed by the third Literature Coverage article, which features a brilliant work from the group of C. Kammerer (France) for achieving the efficient synthesis of hexaarylcyclopentadienes through the copper-catalysed perarylation of cyclopentadiene.

Enjoy your reading!

## In this issue




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  • Published online: September 13, 2024 • DOI: 10.1055/s-0043-1763996

# Phase-Transfer Catalysts Shift the Pathway to Transmetalation in Biphasic Suzuki–Miyaura Cross-Couplings

*Nat. Commun.* **2024**, *15*, 5436

Since its initial reports in 1979 by Miyaura and Suzuki, the Suzuki–Miyaura coupling (SMC) reaction has become an indispensable tool for carbon–carbon bond formation, earning a share of the 2010 Nobel Prize in Chemistry. Its mild reaction conditions and broad substrate scope have led to widespread applications in pharmaceutical synthesis, medicinal chemistry, natural product synthesis, and polymer synthesis. Despite its broad utility, the dominant mode of transmetalation in SMC reactions remains controversial and highly dependent on the specific reaction conditions employed.

A recent paper published by the group of Professor Jason Hein's group at the University of British Columbia (Vancouver, Canada) represents a significant advancement in the field of SMC reactions. The study explores the mechanistic intricacies of SMC under biphasic conditions and highlights the pivotal role of phase-transfer catalysts (PTCs) in enhancing the reaction rate and shifting the transmetalation pathway and addresses a longstanding controversy in the SMC mechanism, particularly regarding the mode of transmetalation. Traditional studies have proposed two primary pathways: oxo-palladium and boronate-based.

"Our *Nature Communications* paper addresses a longstanding controversy in the SMC mechanism regarding the mode of transmetalation," said Professor Hein. He explained: "Two major pathways are typically proposed: a Pd-OH based pathway or a boronate-based pathway. Under traditional biphasic reaction conditions, the Pd-OH pathway was found to dominate. This results in sluggish reactivity as the halide byproduct builds up over time and inhibits the catalyst. The introduction of readily available PTCs dramatically improved reactivity under the biphasic conditions. This was found to result from shifting the dominant mode of transmetalation towards a boronate-based system by manipulating the speciation of both the catalyst and nucleophile. Under these conditions, the build-up of the halide salt byproduct benefits the overall reaction. Finally, the impact of organic and aqueous layer proportions was probed. Contrary to typical SMC conditions, minimizing the proportion of the organic layer was found to benefit reactivity."

Professor Hein explained that by favoring the boronate pathway, PTCs enhance both catalyst and nucleophile speciation, transforming the halide salt byproduct from an inhibitory to a beneficial role, thereby substantially improving reaction rates and efficiency. Professor Hein remarked: "The addition of PTCs not only enhances the reaction rate by a notable 12-fold, but also shifts the transmetalation pathway from the oxo-palladium pathway to the boronate-based pathway. This finding challenges the prevailing emphasis on organoboron species optimization and highlights the critical influence of water content and PTCs in the reaction medium."

Studying the mechanism of the SMC is an ongoing effort in the Hein lab. "We hope to shed light on how the specific conditions employed impacts which transmetalation pathway is favored and how that impacts side-product profiles," said Professor Hein, adding: "This will provide practitioners in the field with a rational approach towards optimization of SMC conditions."

The success of this project stemmed from the serendipitous combination of technological development with curiosity-driven research. Professor Hein told SYNFORM: "The development of the automated sampling platform leveraged in this study has been a longstanding focus of the Hein lab. Its robust performance under challenging heterogeneous conditions inspired us to explore its potential in one of the most important heterogeneous settings: the SMC under biphasic conditions."

The practical applications of this research are vast. Professor Hein explained: "The enhanced SMC process can be employed in the synthesis of pharmaceutically relevant compounds, natural products, and polymers." He concluded: "The demonstrated ability to achieve high yields with low catalyst loadings can lead to more sustainable and economical manufacturing processes in the chemical industry."



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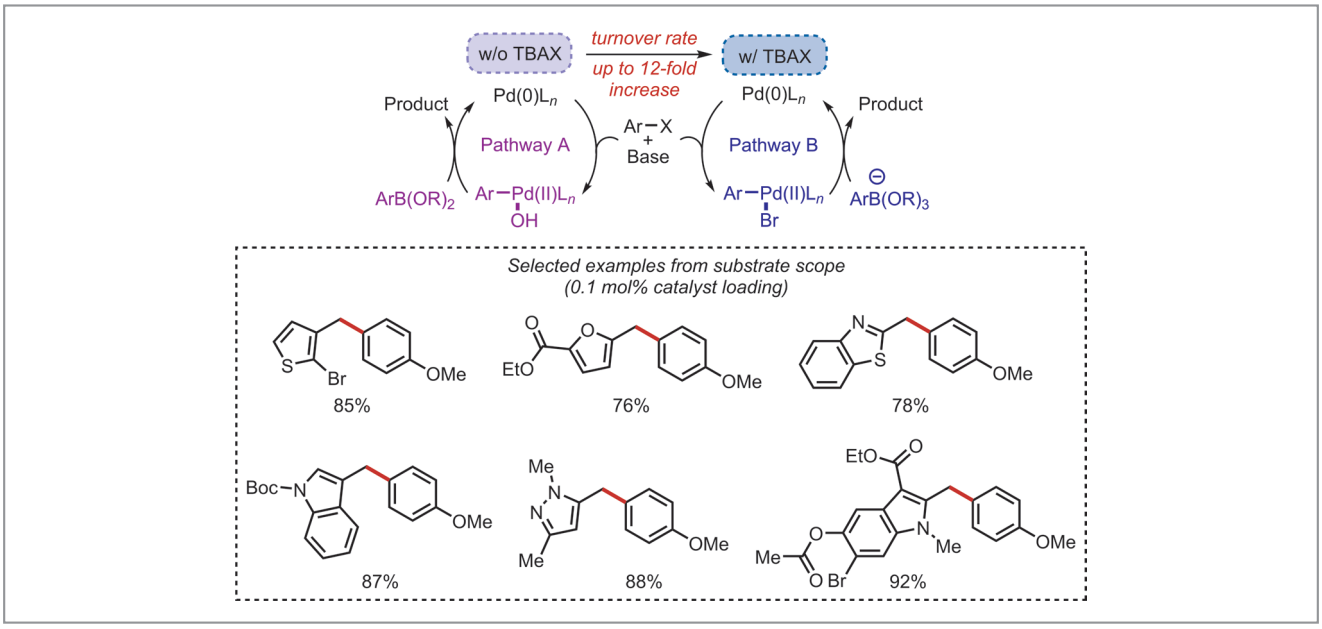


**Scheme 1** Addition of a phase-transfer catalyst modifies the catalyst and arylboron speciation, favouring the Ar-Pd(II)X/boronate transmetallation pathway under biphasic conditions. This gives a 12-fold rate enhancement and enables challenging substrates to be accessed while maintaining exceptionally low catalyst loading.

## About the authors

*Y. Shi*

**Yao Shi** received her M. Phil. degree in chemistry from the Chinese University of Hong Kong (P. R. of China) under the supervision of Prof. Yeung Ying Yeung. She is currently pursuing her Ph.D. in chemistry under the supervision of Prof. Jason Hein at the University of British Columbia (Canada), focusing on reaction kinetics, employing online monitoring techniques to observe and analyze reactions in real time.

*Dr. J. S. Derasp*

**Joshua S. Derasp** began his postsecondary studies at the University of Prince Edward Island (Canada), where he received his B.Sc. in chemistry with honours. He then moved to Ottawa to join the group of Prof. André M. Beauchemin at the University of Ottawa (Canada) receiving his Ph.D in organic chemistry in 2019. He then joined the group of Prof. Jason E. Hein at the University of British Columbia (Canada) as a postdoctoral fellow having since taken on the role of research associate. His research interests are focussed on studying the mechanism of complex catalytic transformations.

*Dr. T. Maschmeyer-Tombs*

**Tristan Maschmeyer-Tombs** participated in marine natural products research with Prof. Philip Crews at the University of California, Santa Cruz (USA) and completed a B.Sc. in chemistry with honors in 2018. In 2019, he started his Ph.D studies with Prof. Jason E. Hein at the University of British Columbia (Canada) and completed his degree in 2023. His graduate research focused on the application of benchtop NMR for online reaction monitoring. Currently, he works as a Senior Scientist at Genentech Inc. in the Structure Elucidation Group of the Synthetic Molecule Pharmaceutical Sciences department.

*Prof. J. Hein*

**Jason Hein** is a Professor of Chemistry at the University of British Columbia (Canada), and an Adjunct Professor at the University of Bergen, Norway. Prof. Hein was the co-lead of Project ADA; the world's first autonomous discovery platform for thin film materials, supported by Natural Resources Canada, co-PI of the MADNESS team supported by the DARPA Accelerated Molecular Discovery Program and the UBC lead for the Acceleration Consortium CFREF spearheaded by the University of Toronto (Canada). He received his B.Sc. in biochemistry in 2000 and Ph.D. in asymmetric reaction methodology in 2005 from the University of Manitoba, Canada (NSERC PGS-A/B, Prof. Philip G. Hultin). In 2006, he became an NSERC postdoctoral research fellow with Prof. K. Barry Sharpless and Prof. Valery V. Fokin at the Scripps Research Institute in La Jolla, CA (USA). In 2010, he became a senior research associate with Prof. Donna G. Blackmond at the Scripps Research Institute. He began his independent career at the University of California, Merced (USA) in 2011, employing in situ kinetic reaction analysis to rapidly profile and study complex networks of reactions. In 2015, he moved to the University of British Columbia and was promoted to Associate Professor and then full Professor in 2019 and 2024 respectively. His research has resulted in a collection of prototype modular robotic tools and integrated analytical hardware which create the first broadly applicable automated reaction profiling toolkit geared toward enabling autonomous research and discovery.



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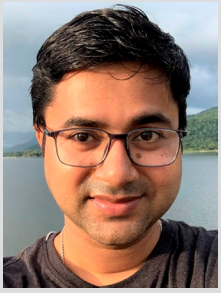
# Young Career Focus: Dr. Shibdas Banerjee (Indian Institute of Science Education and Research (IISER) Tirupati, India)

**Background and Purpose.** SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents Dr. Shibdas Banerjee (Indian Institute of Science Education and Research (IISER) Tirupati, India).

## Biographical Sketch



*Dr. S. Banerjee*

**Shibdas Banerjee** received his Master of Science in chemistry from the Indian Institute of Technology (IIT) Roorkee (India) in 2008. He then pursued his PhD in chemical sciences at the Tata Institute of Fundamental Research (TIFR), Mumbai (India), graduating in 2014 under the mentorship of Prof. Shyamalava Mazumdar. His PhD research was centered around exploring the gas-phase properties of analytes using electrospray ionization mass spectrometry, specifically targeting applications in protein engineering for cytochrome P450 biocatalysis.

Following his PhD, Dr. Banerjee joined the laboratory of Prof. Richard N. Zare at Stanford University (USA) as a postdoctoral fellow, where he advanced his expertise in microdroplet chemistry and clinical mass spectrometry.

In 2017, Dr. Banerjee accepted a position as an Assistant Professor at the Indian Institute of Science Education and Research (IISER) Tirupati, India. He was later promoted to Associate Professor, a role he currently holds. His current research at IISER Tirupati is at the forefront of developing microdroplet-based mass spectrometric methodologies and imaging techniques. These initiatives are particularly geared towards the discovery of disease biomarkers through the correlation of molecular and biological abnormalities, which are pivotal in advancing diagnostic capabilities for various diseases. Moreover, his group is recognized for discovering several unusual properties and reactivities at the air–water interface, significantly influencing the burgeoning field of microdroplet chemistry. Dr. Banerjee's contributions continue to push the boundaries of chemical and biomedical sciences, making substantial impacts on both academic and practical applications.

## INTERVIEW

**SYNFORM** *Which field of organic chemistry are you interested in the most and why?*

**Dr. S. Banerjee** Our interests are multidirectional, but all are centering on an important analytical approach involving ambient mass spectrometry, which we often use to (a) capture reactive intermediate species from the reaction vial, (b) map the biomolecular distribution in human tissue or blood for development in diagnostics, and (c) induce the unusual chemical transformation in microdroplets for producing value-added chemicals. My research team is also heavily engaged in developing new synthetic strategies at the air–water interface just by spraying the aqueous solution of reactants, circumventing the need for any catalyst or reagents, an upcoming green approach in organic synthesis.

**SYNFORM** *Following that, what is the focus of your current research activity?*

**Dr. S. Banerjee** We focus on the *in situ* analysis of chemical and biological transformations in real-time, pinpointing the chemical/biochemical species associated with the transformation route (Figure 1). This helps us decipher the organic reaction mechanism and understand the disease biology by correlating molecular and biological abnormalities during the disease progression. We employ high-speed (>100 m/s) micron-sized droplets to extract the chemical/biochemical information from the sample of interest (reaction mixture, human tissue or blood, etc.), which is subsequently studied by the ambient mass spectrometry approach (a new technology).

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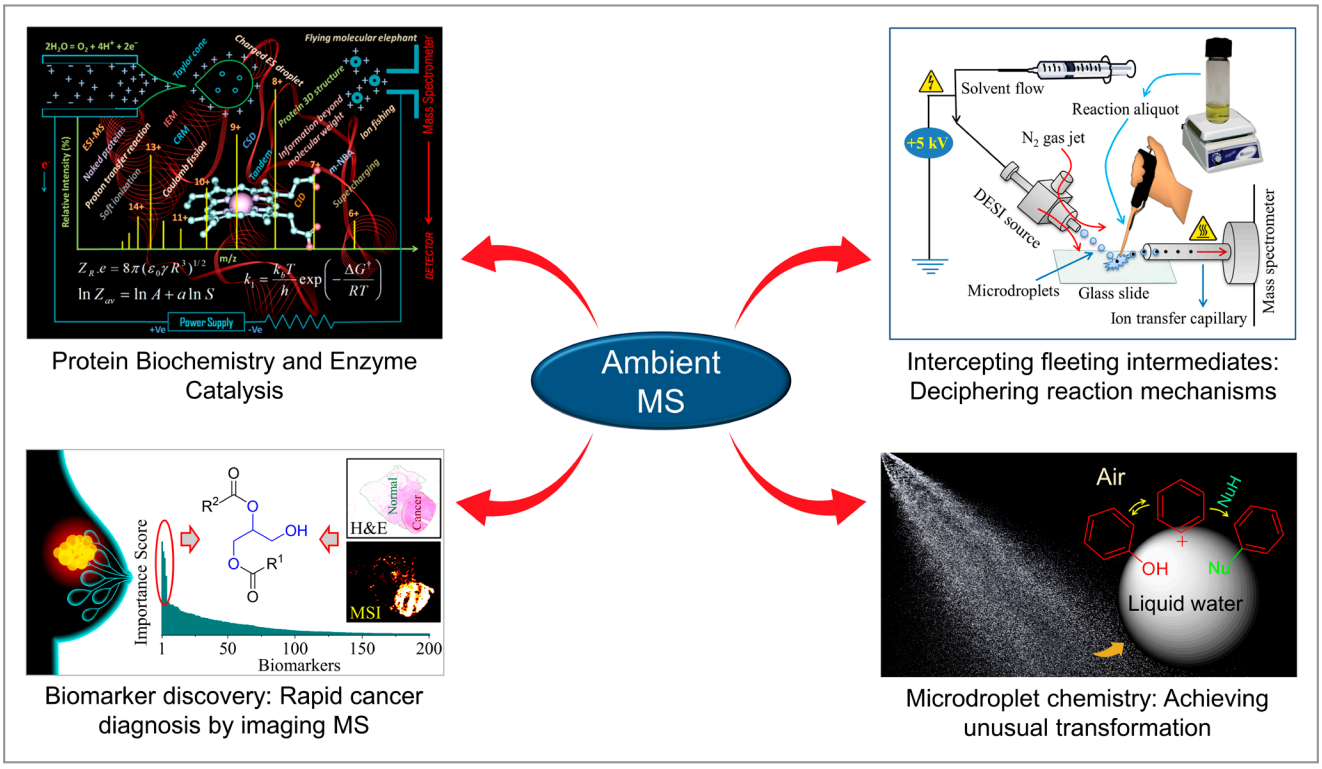



**Figure 1** Schematic overview of the research foci of Banerjee's group, centered on ambient mass spectrometry (MS). Figures are in part adapted from the following publications: *J. Am. Chem. Soc.* **2021**, *143*, 2459–2463; *J. Am. Chem. Soc.* **2023**, *145*, 15674–15679; *Anal. Chem.* **2023**, *95*, 8054–8062.

**SYNFORM** *What do you think about the modern role and prospects of organic chemistry?*

**Dr. S. Banerjee** Organic chemistry is abundant and lucrative in the modern age, whether in the medicine/pharma industry, energy, environment, agriculture, or fundamental understanding of natural and biological processes. It has transcended the boundary between the reaction vial and the living cell/organism. To advance in creating new drugs, laboratory medicines, biochemical tests, bioimaging techniques, and all that requires not only a strong understanding of the molecular makeup and mechanism of transformation of biological molecules *in situ*, but also the expansion of the efficient synthetic toolbox to deliver the need-based selectivity and specificity in the biological world. Another obvious prospect in organic chemistry is sustainable development, aiming to use natural resources in an environmentally benign fashion. This should be fostered by the upcoming revolution in green chemistry for making value-added chemicals.

**SYNFORM** *Which difficulties are there for young upcoming chemists in your field? Do you have any tips?*

**Dr. S. Banerjee** Young and enthusiastic minds are always the catalyst for any new advancement. Chemistry is now being applied beyond reaction vials to the living realm. For example, I see a bright future of biorthogonal chemistry. Sometimes, I find that the young chemists appear with preconceived notions and are reluctant to collaborate, or they are not much encouraged for interdisciplinary collaboration, which is much needed to bridge between different fields/techniques to solve a problem. Engaging in scientific endeavors is not a competitive situation with winners and losers but a collaborative effort where all participants benefit from each other's achievements. For example, we are developing a next-generation histopathology technique for intraoperative cancer margin analysis. This project is being pursued by strong synergistic efforts across different fields like mass spectrometry, biochemistry, surgical oncology, pathology, and machine learning. We cannot succeed without such collaboration.

I also want to mention that big scientific discoveries and breakthroughs are often accidental. The probability of meeting such accidental discoveries depends on persistent efforts, scientific temperament, and critical analysis of the data if unfavorable to the anticipated outcome.

**SYNFORM** *Could you tell us something about yourself outside the lab, such as your hobbies or extra-work interests?*

**Dr. S. Banerjee** Well, I enjoy outings in nature. When I get time, I do that with my family, research group, or friends. I enjoy watching films from different continents, as those expose me to a wide range of cultures and landscapes from various nations. I also enjoy music during my leisure time.

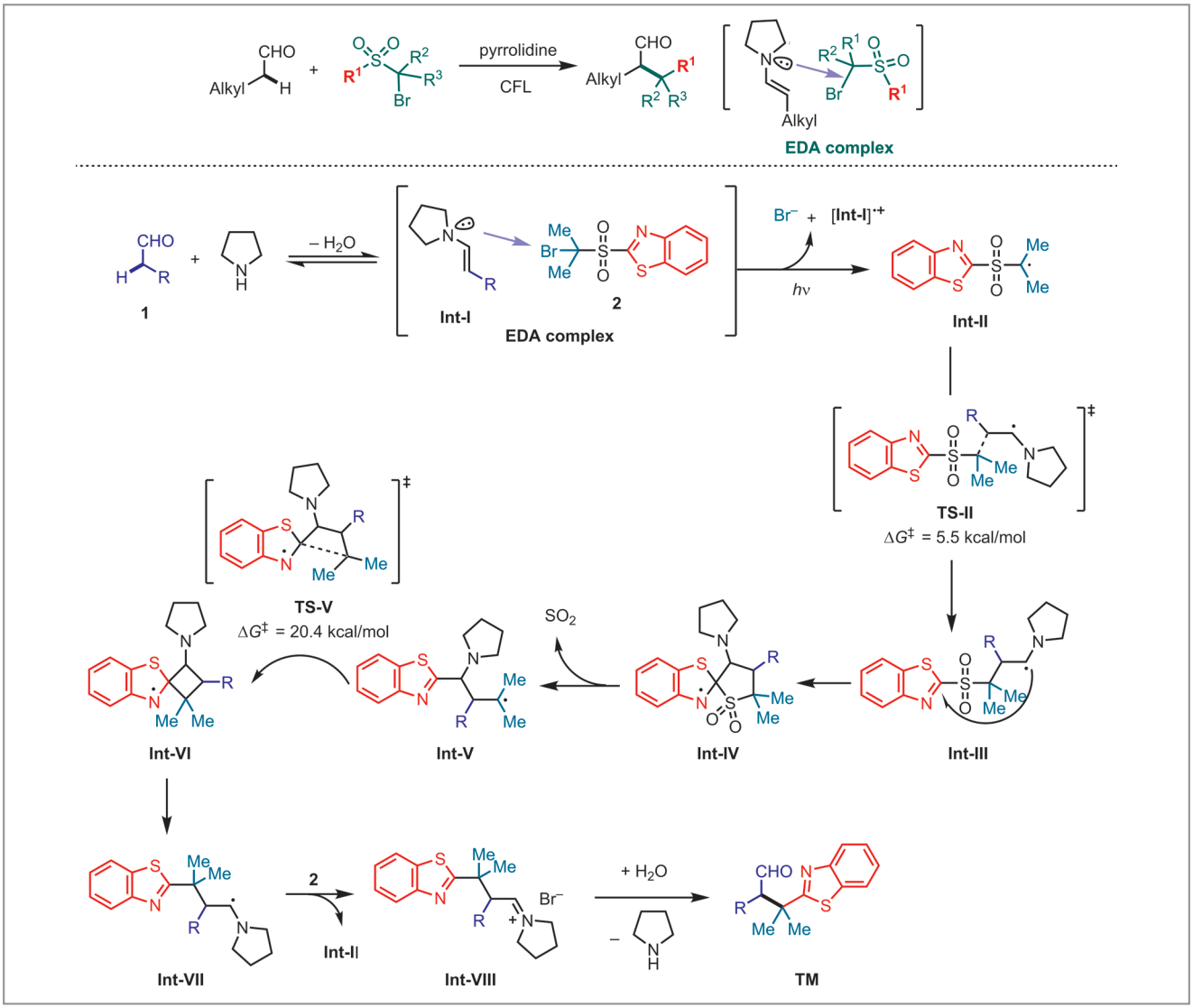
**SYNFORM** *What is your most important scientific achievement to date and why?*

**Dr. S. Banerjee** I think I have participated in the pioneering process of an emerging field called microdroplet chemistry. Back in 2011, during my PhD, we revealed that microdroplets in the air can cause unusual chemical reactions that may not be possible by conventional bulk-phase chemistry (*J. Am. Soc. Mass Spectrom.* **2011**, *22*, 1707–1717). In the same year, a report from the Cooks lab (Purdue University) showed the acceleration of chemical reactions in microdroplets (*Chem. Sci.* **2011**, *2*, 501–510). These two reports mark the beginning of the field. After that, I moved to the Zare lab (Stanford University) and continued working in the field along with others. After starting my independent research career at IISER Tirupati in 2017, my research group focused on taming micron-sized water droplets to capture and stabilize reactive intermediate species such as carbocations, carbanions, and protein-unfolding intermediates, followed by detecting those species using mass spectrometry. Generally, transient intermediate species in the reaction medium have such a short lifetime that conventional spectroscopic techniques fail to detect them because the measurement duration is longer than their lifespan. However, our finding that the air–water interface of microdroplets can enhance the lifetime of reactive intermediate species for their direct detection represents an important milestone of microdroplet chemistry, which is now apparently multifaceted with diverse applications. We are now translating this success to utilize the chemistry of such reactive species in aqueous microdroplets, especially for advancing sustainable organic synthesis in aqueous medium. As we have discovered that water microdroplets facilitate unusual reactions at the air–water interface, we are also currently exploiting such interfacial reactions for advancements in disease detection (diagnosis). I am very much optimistic about the promising future of microdroplet chemistry. It will likely significantly impact molecular/material synthesis, comprehension of reaction mechanisms, disease diagnostics, disinfections, environmental studies, and other areas in the future.

# Radical-Mediated α-*tert*-Alkylation of Aldehydes by Consecutive 1,4- and 1,3-(Benzo)thiazolyl Migrations

*JACS Au* **2024**, *4*, 2108–2114

The direct alkylation of aliphatic aldehydes in the α-position represents a common strategy for the preparation of complex functionalized aldehydes, which are present in numerous natural products and functional molecules. The precedents are mainly limited to the incorporation of primary and secondary alkyl groups by electrophilic alkylation, while the *tert*-alkylation of aldehydes remains challenging due to steric hindrance and halide elimination often occurring with tertiary alkyl halides. A recent article in *JACS Au* from the groups of Professor Chen Zhu at Shanghai Jiao Tong University and Professor




**Scheme 1** Radical *tert*-alkylation of the α-position of aldehydes

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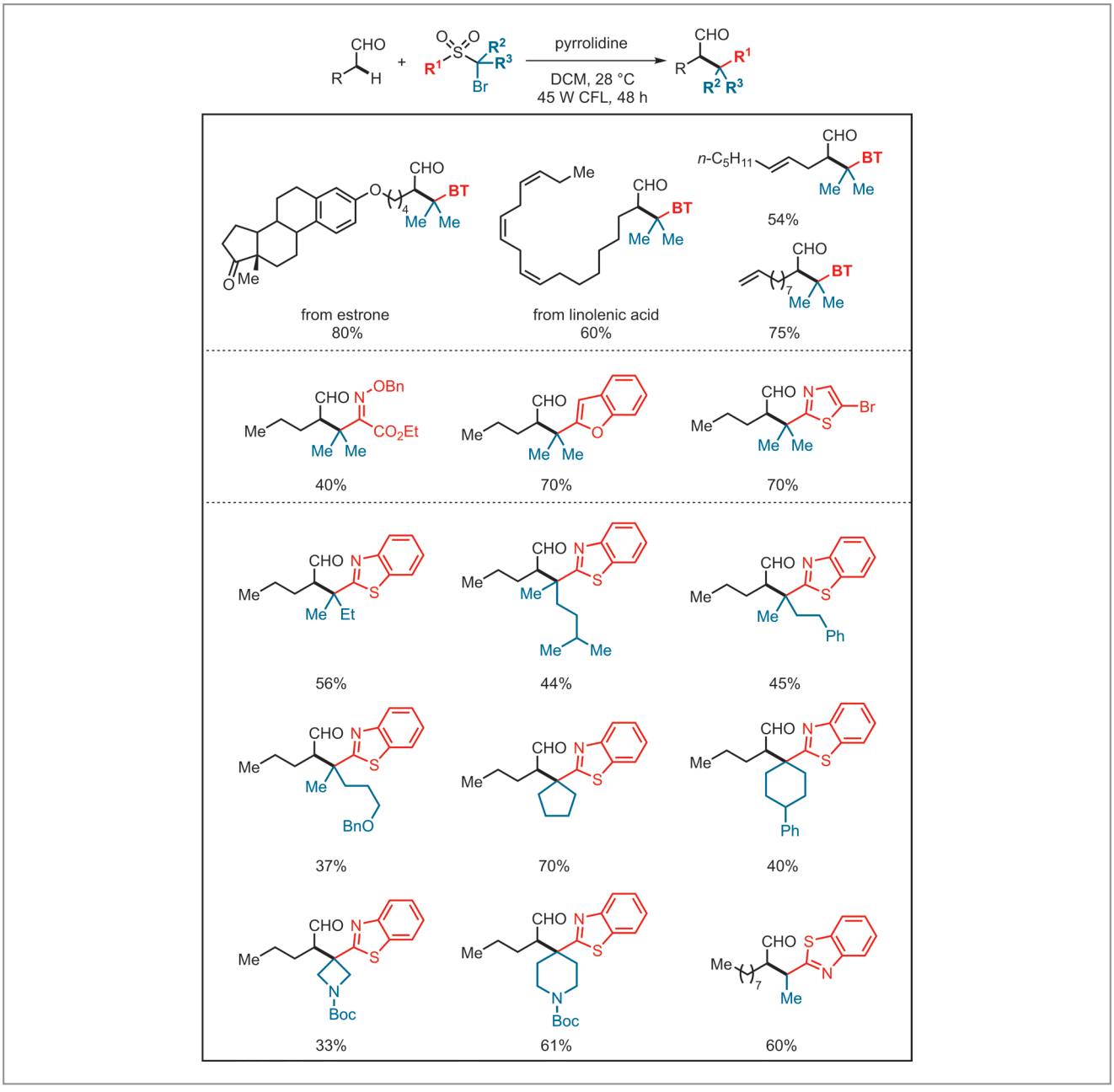
Xiao-Song Xue at Shanghai Institute of Organic Chemistry (both P. R. of China) describes a novel radical cascade for the elusive *tert*-alkylation of aldehydes, leading to structurally diverse aldehydes. "Initially, the reaction of pyrrolidine and aldehyde generates an enamine intermediate, which interacts with the strategically designed sulfone reagent to form an electron donor–acceptor (EDA) complex, which in turn produces a radical species that triggers the ensuing consecutive 1,4- and 1,3-functional group migrations (Scheme 1)," explained Professor Zhu. Professor Xue continued: "Consecutive functional group migrations, especially the 1,3-group migration via four-membered cyclic transition state, are uncommon. However, our density functional theory (DFT) calculations revealed that such a process has a feasible barrier of 20.4 kcal/mol under




**Scheme 2** Product diversity and reaction scope

the used experimental conditions. Compared with the three-membered cyclic transition state in a competing pathway, the lower strain arising from its four-ring transition state makes the proposed mechanism kinetically favored."

The process entails the formation of an EDA intermediate through the interaction of enamines with bifunctional reagents, followed by a single electron transfer and subsequent 1,4-heteroaryl migration. "Remarkably, it also includes an atypical 1,3-heteroaryl group migration," added Professor Zhu. "This innovative mechanism enables the concurrent incorporation of heterocycles and bulky alkyl groups at the α-position of the aldehyde. Furthermore, this protocol exhibits excellent functional group compatibility. Additionally, the resultant products can be further transformed into more valuable compounds, such as alcohols, amines, carboxylic acids, olefins, and alkynes."

The Zhu group has a long-term interest in radical-mediated functional group migration reactions, which have been successfully applied to the difunctionalization of various alkenes and alkynes (*Acc. Chem. Res.* **2020**, *53*, 1620–1636). "Differently from previous contributions, this report targeted the difunctionalization of enamines," Professor Zhu explained, continuing: "Surprisingly, the reaction did not afford the multi-substituted aliphatic amines via routine 1,4-benzothiazolyl intermediate, as expected. Instead, it resulted in the serendipitous finding of the unusual 1,3-benzothiazolyl migration."

What particularly stands out with this method are the mild reaction conditions and broad product diversity. "The reaction proceeds under photochemical conditions and works with a broad range of aliphatic aldehydes (Scheme 2)," said Professor Zhu. He added: "It is worth noting that when the substrate contains olefinic fragments, the reaction exclusively targets the right α-position, and the olefin remains unaltered, thus demonstrating excellent chemoselectivity. Complex natural product aldehyde derivatives can also be effectively modified. Furthermore, varying the alkylating agents allows for diverse alkylation modifications, including heterocycles and even oxime esters. Chain alkyl groups, cyclic alkyl groups, and alkyl groups containing heteroatoms have been successfully applied in this reaction. Secondary alkyl groups are also well-suited for this process."

Professors Zhu and Xue remarked that this process represents a useful approach to achieve α-site alkylation of aldehydes, characterized by excellent functional group compatibility and a broad substrate scope. "Looking forward, we aim to use catalytic conditions instead of the current stoichiometric pyrroline, and to design chiral amines for the asymmetric alkylation reaction," they concluded.

## About the authors

*Dr. J. Liu*

**Jige Liu** obtained his BS degree from Ludong University (P. R. of China) in 2017 and his Master's degree from Soochow University (P. R. of China) in 2020 under the supervision of Prof. Chen Zhu. He obtained his PhD in the same group in January 2024.

*J. Ma*

**Jiangshan Ma** received his BS degree from Shandong University (P. R. of China) in 2019, and obtained his Master's degree from Shanghai Institute of Organic Chemistry (P. R. of China) in 2023 under the supervision of Guo-Qiang Lin. He then joined Prof. Chen Zhu's group at Shanghai Jiao Tong University (P. R. of China). His current research focuses on asymmetrical radical-mediated functional group migrations.

*Dr. T. Wang*

**Tongkun Wang** obtained his PhD in chemistry from University of Massachusetts, Amherst (USA) in 2023 under the supervision of Prof. Scott Auerbach. He then joined Prof. Xiao-song Xue's group at Shanghai Institute of Organic Chemistry (P. R. of China) for postdoctoral research. His research interests include dynamic effect and quasi-classical simulations in fluorine chemistry.

*Prof. X.-s. Xue*

**Xiao-song Xue** received his Ph.D. at Nankai University (NKU, P. R. of China) in 2013 with Jin-Pei Cheng. He joined the College of Chemistry at NKU as an assistant professor and was promoted to associate professor in 2016. He was a visiting scholar at the Department of Chemistry and Biochemistry at UCLA (USA) with K. N. Houk from 2017 to 2020. In 2021, he moved to SIOC (Shanghai Institute of Organic Chemistry), Chinese Academy of Sciences (P. R. of China) as a professor. His current research interest focuses on physical organofluorine chemistry.

*Prof. C. Zhu*

**Chen Zhu** received a BS degree from Xiamen University (P. R. of China) in 2003, and earned his PhD from the Shanghai Institute of Organic Chemistry (P. R. of China) in 2008 under the supervision of Guo-Qiang Lin. After postdoctoral research in Gakushuin University (Japan) with Takahiko Akiyama, he moved to the University of Texas Southwestern Medical Center (USA), working with John R. Falck and Chuo Chen as postdoctoral fellow. He was appointed as full professor at Soochow University (P. R. of China) in 2013 and moved to Shanghai Jiao Tong University (P. R. of China) as tenured full professor in 2021. His current research interests include radical-mediated functional group migrations and the applications in the construction of functional small molecules and polymers.



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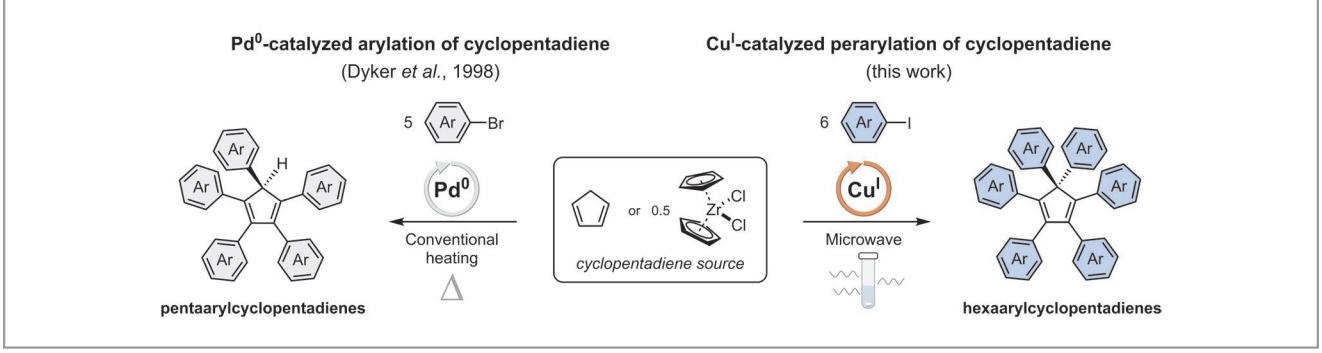
# Copper-Catalysed Perarylation of Cyclopentadiene: Synthesis of Hexaarylcyclopentadienes

*Chem. Sci.* **2024**, *15*, 9127–9137

Silacyclopentadienes (siloles) have attracted the attention of the scientific community for decades, for their remarkable electronic properties coupled with excellent photo- and electroluminescence. In particular, in line with their propeller shape, polyarylsilacyclopentadienes exhibit Aggregation-Induced Emission (AIE) leading to widespread applications as materials in high-performance OLEDs, chemosensors for analyte detection, biological probes, and smart materials. The parent hydrocarbon-based polyarylcyclopentadienes $Ar_nH_{(6-n)}Cp$ also display AIE activity up to pentasubstituted derivatives (n = 3–5), but, strikingly, hexaarylcyclopentadienes (n = 6) had not been investigated until now, despite their structural similarity with the archetypal AIE luminogen hexaphenylsilole.

In a recent article in *Chemical Science*, the group of Prof. G. Rapenne and Dr. C. Kammerer at the University of Toulouse and CEMES-CNRS (France) introduced a groundbreaking method for the synthesis of hexaarylcyclopentadienes in a single step, relying on the copper-catalyzed direct perarylation of cyclopentadiene (Scheme 1, right). "The synthesis of hexaarylcyclopentadienes poses significant challenges and only the hexaphenyl derivative had been reported once in the early 1940s by Allen and VanAllan (*J. Am. Chem. Soc.* **1943**, *65*, 1384–1389), with a revision of the mechanism 30 years later by Youssef and Ogliaruso (*J. Org. Chem.* **1972**, *37*, 2601–2604)," explained Dr. Kammerer, adding: "Besides, this early synthetic route appeared both lengthy (four steps from tetraphenylcyclopentadienone) and tedious, with limited functional group compatibility and a low modularity."

Dr. C. Kammerer went on by explaining how this project started: "In the frame of our research aiming at the design, synthesis and single-molecule investigations of rotary molecular machines based on pentaarylcyclopentadienyl ruthenium(II) complexes as core scaffold (*Nat. Commun.* **2019**, *10*, 3742; *Chem. Sci.* **2021**, *12*, 4709–4721; *Chem. Eur. J.* **2021**, *27*, 16242–16249), we became interested in the development of more straightforward methods for the synthesis of pentaarylcyclopentadienes. Indeed, the 'classical' tetracyclone route is a multistep process, displaying limited modularity. We came across the work by Dyker and co-workers (*Chem. Commun.* **1998**, 1889–1890) reporting the direct arylation of cyclopentadiene to yield pentaarylcyclopentadienes in a single step upon palladium catalysis (Scheme 1, left). In an attempt to transpose this reaction to the use of a cheaper, abundant and environmentally benign catalyst, we serendipitously discovered that copper(I) mediates not just five, but six consecutive arylations when cyclopentadiene reacts with iodobenzene. The resulting hexaphenylcyclopentadiene was not interesting as such for the elaboration of organometallic molecular machines, but its similarity with the AIE luminogen hexaphenylsilole associated to its straightforward synthetic accessibility drove our scientific curiosity. We thus initiated




**Scheme 1** Synthesis of polyarylcyclopentadienes upon direct arylation of cyclopentadiene: the palladium-catalyzed reaction under conventional heating affords pentaarylcyclopentadienes (left), whereas the copper-catalyzed microwave-activated process results in the formation of six new C–C bonds in a single synthetic operation to yield unprecedented hexaarylcyclopentadienes (right)

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a project aiming at the development of the copper(I)-catalyzed six-fold arylation of a single cyclopentadiene moiety as a streamlined and unprecedented process to obtain variously substituted hexaarylcyclopentadienes."

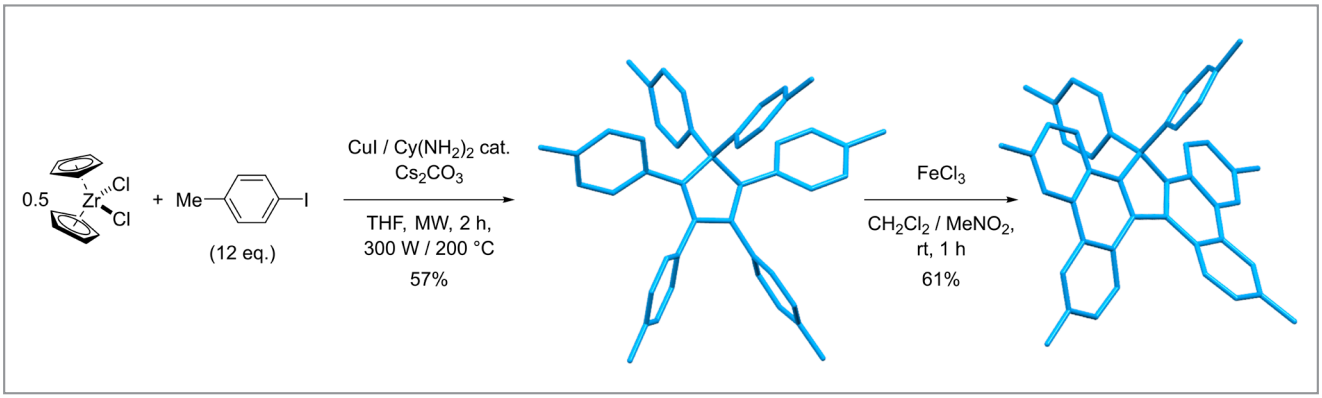
The targeted transformation involves six sequential copper-catalyzed cross-couplings in a single synthetic operation, which are reminiscent of the Hurtley reaction: each new C–C bond results from the coupling of an aryl halide with a cyclopentadienide species acting as stabilized nucleophile. Interestingly, the freshly distilled cyclopentadiene obviously used as a source of cyclopentadienide in the initial catalytic cycle can be advantageously replaced with the easy-to-handle zirconocene dichloride. "Preliminary investigations revealed that the use of aryl iodides as coupling partners and microwave irradiation as thermal activation mode are crucial for the success of the cyclopentadiene perarylation," said Dr. Kammerer. "Further optimization highlighted that maximal yield and purity of hexaarylcyclopentadienes are reached with copper(I) iodide and *trans*-1,2-cyclohexanediamine as catalytic system, cesium carbonate as base and THF as solvent (Scheme 2). Finally, an assessment of the scope showed that a variety of aryl iodides, including relatively bulky ones, are tolerated in this cross-coupling reaction, resulting in a series of hexaarylcyclopentadienes bearing diverse substitution patterns," she added.

"With our method, the synthesis of hexaarylcyclopentadienes gains in simplicity and efficiency compared to the previous multi-step approach, with a straightforward access to structural diversity, making this family of compounds readily accessible for further research and application," explained Dr. Kammerer.

After in-depth structural characterization confirming their propeller shape, optical investigations of hexaarylcyclopentadienes revealed that these compounds are virtually non-emissive in solution but intense photoluminescence is observed upon aggregation (Figure 1), as anticipated. "Hexaarylcyclopentadienes thus appear as promising AIE luminogens for the fabrication of high-performance optoelectronic devices," said Dr. Kammerer, adding: "We also demonstrated that the nature of the aryl substituents directly impacts the emission spectra, thus emphasizing the potential of the copper-catalyzed perarylation as a straightforward synthetic route to a variety of AIE luminogens with tailored properties."

Inspired by further possible applications for luminescent materials, Dr. Y. Gisbert envisioned to exploit hexaarylcyclopentadienes as direct precursors of extended π-conjugated polycyclic compounds (Scheme 2). He explained: "In an attempt to decrease the degrees of freedom in such molecules and possibly increase their luminescence properties in solutions, we performed Scholl-type oxidative cyclization on hexaarylcyclopentadienes. Upon cyclodehydrogenation, the propeller-shaped scaffolds underwent planarization to yield helicenic 17,17-diarylcyclopenta[*l*,*l*′]diphenanthrenes, displaying restored photoluminescence in solution. These structurally complex polyannelated fluorene derivatives are now readily prepared in only two synthetic steps from cyclopentadiene, and hold great promise for applications as organic semiconductors or fluorophores."

Looking ahead, the team plans to extend the copper-catalyzed perarylation methodology so as to build higher molecular complexity in cyclopentadiene derivatives. "On the one hand, in line with the preliminary result obtained in this work, the




**Scheme 2** Synthetic sequence involving the copper-catalyzed perarylation of cyclopentadiene in the presence of 4-iodotoluene to give the corresponding propeller-shaped hexaarylcyclopentadiene, and subsequent Scholl reaction yielding a helicenic 17,17-diarylcyclopenta[*l*,*l*′]diphenanthrene. The products of both steps are depicted using their X-ray crystal structure to highlight their 3D-shape (hydrogen atoms are omitted for clarity).



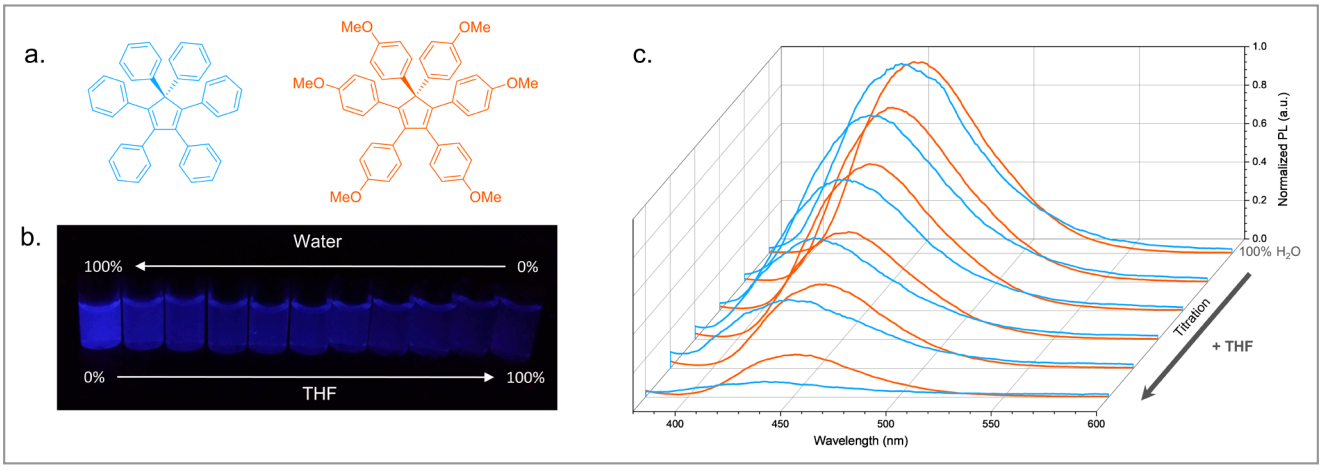


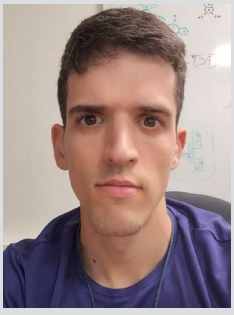

**Figure 1** Aggregation-induced emission properties of two hexaarylcyclopentadienes displaying different substitution patterns. (a) Structure of hexaphenylcyclopentadiene (in blue) and hexa(4-methoxyphenyl)cyclopentadiene (in orange). (b) Picture of hexaphenylcyclopentadiene solutions with varying $H_2O$/THF ratios. (c) Normalized photoluminescence spectra of hexaphenylcyclopentadiene (in blue) and hexa(4-methoxyphenyl)cyclopentadiene (in orange) in pure $H_2O$ ($10^{-7}$ M, $\lambda_{Ex}$ = 350 nm), and corresponding spectra after successive additions of small aliquots (20 µL) of THF.

direct synthesis of spirofluorenes using dihalogenobiphenyls as coupling partners will be further investigated. On the other hand, strategies to sequentially introduce different aryl substituents on one cyclopentadiene core will be explored," said Dr. Kammerer. She concluded: "Indeed, the ability to synthesize a wide range of hexaarylcyclopentadienes could open up new avenues in the design and development of advanced materials with unique properties."

## About the authors

*Dr. Y. Gisbert*

**Yohan Gisbert** graduated from Université Paul Sabatier (Toulouse, France). After internships in Prof. Nitschke's group at Cambridge University (UK) working on supramolecular cages and in Prof. Veige's group at the University of Florida (USA) synthesizing new supramolecular polymers, he joined the CEMES-CNRS (Toulouse, France) under the supervision of Dr. C. Kammerer and Prof. G. Rapenne for his Master's and PhD research, investigating the synthesis of dissymmetrized and long-chain-functionalized rotary molecular machines (including molecular winch prototypes) and copper-catalyzed arylation reactions. In February 2022 he joined Prof. Ben Feringa's research group at the University of Groningen (Netherlands) as a Marie Skłodowska-Curie postdoctoral fellow where he is currently investigating new molecular motors performing coupled motion and helicene chemistry.



*Dr. P. S. Marqués*

**Pablo Simón Marqués** received his BSc and MSc degrees from the University of Zaragoza and the Autonomous University of Madrid (Spain), respectively. In 2020, he obtained his PhD from the University of Angers (France) under the supervision of Dr. P. Blanchard and Dr. C. Cabanetos. Before joining the CEMES-CNRS in 2023, he completed two other postdoctoral experiences at the Max Planck Institute of Colloids and Interfaces (Germany) and the University of Calgary (Canada), where he obtained the Eyes-High Fellowship. His research interests focus on organic synthesis and molecular materials with potential application in organic electronics and on-surface synthesis.

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*C. Baccini*

**Caterina Baccini** studied chemistry at the University of Parma (Italy), where she obtained her MSc in materials chemistry in 2021 after a short research period at CEMES-CNRS (Toulouse) under the supervision of Dr. C. Kammerer and Prof. G. Rapenne. She is currently working as a third-year PhD student at the University of Parma, in the group of Prof. A. Secchi. During her PhD studies, she went to ISIS-University of Strasbourg (France) for a research stay with Prof. G. Ragazzon. Her main research activities regard the development of hybrid inorganic–organic materials and supramolecular chemistry.

*Dr. S. Abid*

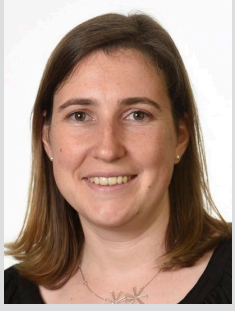
**Seifallah Abid** grew up in Bizerte, Tunisia, where he obtained his BSc and MSc degrees in organic chemistry from the University of Carthage. Then, he moved to France to earn a PhD in molecular and macromolecular chemistry from INSA Rennes under the supervision of Dr. C. Paul-Roth and Prof. B. Jamoussi. During his PhD, he synthesized organic and organometallic phthalocyanine dendrimers and studied their optical properties. In 2018, he joined the GNS Group at CEMES-CNRS (Toulouse, France) as a postdoctoral fellow to work with Dr. C. Kammerer and Prof. G. Rapenne on the design and synthesis of porphyrinic molecular cogwheels, with the aim of ultimately achieving controlled intermolecular gearing motions on surface. In 2021, he started a postdoctoral fellowship in the Stoddart group at Northwestern University (USA) to explore further the fascinating world of molecular machines. In 2022, he joined ICBMS Lyon in France to develop with Dr. A. Tlili new strategies in organometallic photocatalysis.

*Dr. N. Saffon-Merceron*

**Nathalie Saffon-Merceron** received her PhD in molecular chemistry in 2003 from Paul Sabatier University (Toulouse, France), working on carbene chemistry under the supervision of Dr. A. Baceiredo and Dr. G. Bertrand at the Laboratoire Hétérochimie Fondamentale et Appliquée. She is currently working as a research engineer, head of the X-ray diffraction service of the Institut de Chimie de Toulouse (France). She is an expert in structural determination using single-crystal X-ray diffraction, particularly on very reactive species.

*Prof. G. Rapenne*

**Gwénaël Rapenne** obtained his PhD in 1998 from Louis Pasteur University (Strasbourg, France) under the supervision of Prof. J.-P. Sauvage working on the synthesis and resolution of double helices and knots. After spending one year as a Lavoisier postdoctoral fellow working on fullerenes with Prof. F. Diederich at ETH Zürich (Switzerland), he joined the NanoSciences Group (CEMES-CNRS) as a Maître de Conférences at the University Paul Sabatier (Toulouse, France) to work in the field of single molecular machines and motors. Promoted to Full Professor in 2011 and Distinguished Professor in 2019, he is also Professor at Nara Institute of Science and Technology (NAIST, Japan, crossed-position) since 2018, where he is head of the Biomimetic and Technomimetic Molecular Science Laboratory.



*Dr. C. Kammerer*

**Claire Kammerer** obtained her PhD in 2009 from the University Pierre and Marie Curie (Paris, France) under the supervision of Prof. G. Poli and Prof. G. Prestat, working on transition-metal-catalyzed domino reactions and cycloisomerizations. Next, she joined Prof. T. Bach at Technische Universität München (Munich, Germany) as an A. von Humboldt fellow to work on the total syntheses of (+)-bretonin B and (–)-pulvomycin. In 2012, she was appointed Maître de Conférences at the University Paul Sabatier (Toulouse, France) and joined the NanoSciences Group at CEMES-CNRS. Her research interests span from the design and synthesis of functional molecules tailored for molecular mechanics or electronics, to the development of novel reactivities not only in solution but also on surfaces.

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