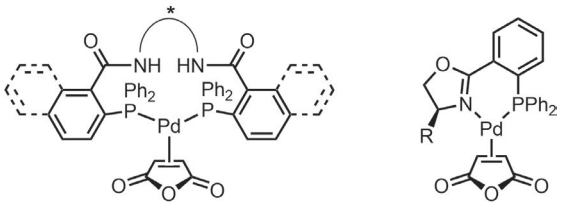
Synform

People, Trends and Views in Chemical Synthesis

2024/03

Chiral, Air Stable, and Reliable Pd(0) Pre-catalysts Applicable to Asymmetric Allylic Alkylation Chemistry

Highlighted article by J. J. Huang, T. Keenan, F. Richard, J. Lu, S. E. Jenny, A. Jean, S. Arseniyadis, D. C. Leitch



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Dear Readers,

This is going to be a brief editorial, because I am one of the lucky guys who can have a holiday in winter, and – as I wrote recently – I strongly believe holidays are only meant for resting and relaxing, so I will keep this one and only work-related task (even though SYNFORM is always a great pleasure for me) to a minimum. Which means that I will go straight to the contents featured in this March issue. As opposed to its Editor, SYNFORM is all but on holiday, as demonstrated by the exciting range of articles that follows. The first is very original and covers the discovery of a novel and sustainable method developed by the group of J. J. Weigand (Germany) for the synthesis of organo-phosphorus compounds. The second article is a Young Career Focus interview with one of the 2023 Thieme Chemistry Journal Awardees, B. Thirupathi (India) who tells SYNFORM about his work and interests, both scientific and personal. The third article covers a recent literature contribution by the group of Y. Sumida and H. Ohmiya (Japan), which addresses the traditional issue in organic chemistry of achieving the meta-selective acylation of electron-rich arenes, for which the authors found a novel solution using an organic photoredox-catalysed process. Last but not least, another Literature Coverage article, this time of S. Arseniyadis (UK) – with whom I had the pleasure to share one year during my postdoc in the lab of the late C. Mioskowski in Strasbourg (France) – and David C. Leitch (Canada), who jointly devised a novel class of Pd(0) precatalysts that can be very effectively used to perform asymmetric allylic alkylation chemistry.

Enjoy your reading! And back to my holiday!!

In this issue

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If you have any questions or wish to send feedback, please write to Matteo Zanda at:
synform@outlook.com

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Redox-Neutral Conversion of Ubiquitous P^V Sources to a Versatile PO_2^+ Phosphorylation Reagent

Nat. Synth. **2023**, *2*, 972–979

Phosphorus plays a pivotal role in organic and biological chemistry; furthermore, it is an essential element in a number of vitally important biological molecules, such as the nucleotides forming DNA and RNA biopolymers. In addition, phosphorus-containing molecules are endowed of countless applications, such as flame retardants, pharmaceuticals, food additives, pesticides, catalysts and many more. The production of most phosphorus-containing fine chemicals relies on the use of white phosphorus (P_4) derived from natural phosphate deposits (e.g. phosphate ores, like apatite), which causes their progressive depletion. In particular, industrial production of phosphorus compounds generally makes use of white phosphorus (P_4) – which is in turn obtained by reduction of phosphate ores in an arc furnace – that is (oxy)chlorinated to environmentally hazardous bulk chemicals such as PCl_3, PCl_5 and $OPCl_3$. It is therefore important to find novel, more sustainable methods for the synthesis of phosphorus-containing organic compounds, especially on a large scale.

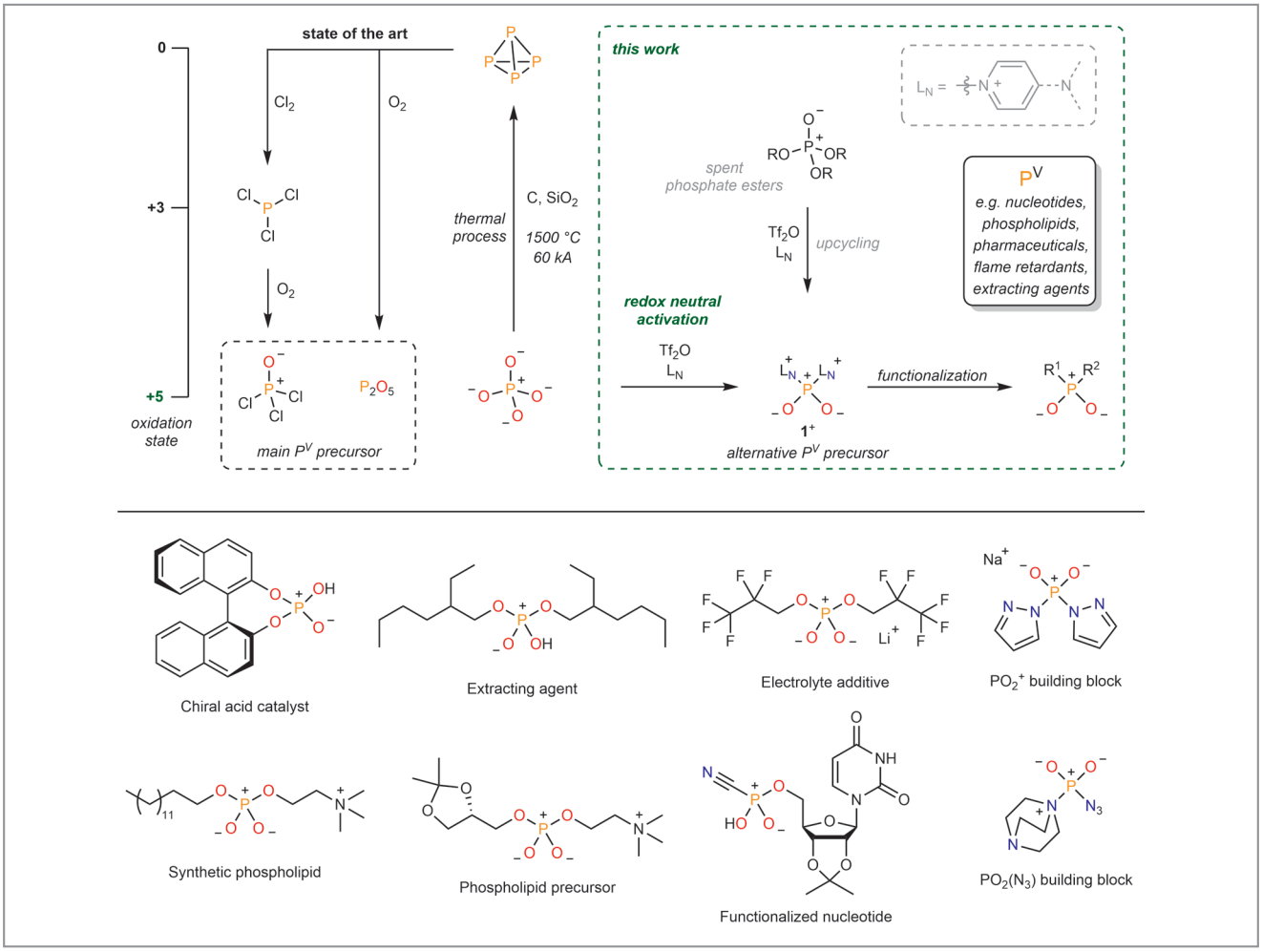

Figure 1 Redox-neutral activation of phosphate sources facilitates synthesis of a broad range of value-added P^V fine chemicals

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This paper describes the efforts of Professor Jan Weigand at the Technische Universität Dresden (Germany) and co-workers in rethinking traditional synthetic schemes for the production of phosphorus-containing chemicals. "Most compounds with direct applications, such as pharmaceuticals, flame retardants, or battery electrolytes, bear phosphorus in its most stable and naturally occurring oxidation state +5," said Professor Weigand. He continued: "However, their synthesis primarily relies on P_4 as an intermediate. Even simple esters of phosphoric acid are produced via this redox detour, despite the immense energy input required to break all the stable P–O bonds in mined phosphate minerals. The scientific community has recently questioned this approach (*ACS Cent. Sci.* **2020**, *6*, 848–860), and our work serves as a viable proof-of-concept for an alternative."

The group's approach originates from a previous contribution targeting the direct functionalization of white phosphorus. "We obtained one of the key reagents involved by deoxygenation of triphenylarsine oxide with triflic anhydride (Tf_2O), stabilizing the resulting highly reactive product with 4-dimethylaminopyridine (DMAP) as an *N*-donor base (*Nat. Chem.* **2022**, *14*, 384–391)," explained Professor Weigand. He went on: "This raised the question for us whether the same combination of reagents could activate phosphate by deliberate cleavage of P–O bonds. In our initial experiments, we aimed at the complete deoxygenation of phosphate $(PO_4)^{3-}$ and quickly realized that the thermodynamically preferred outcome of our approach is the P^V precursor 1^+ (Figure 1). We then used different phosphate sources and optimized the reaction conditions accordingly. This project turned out to be very much straightforward."

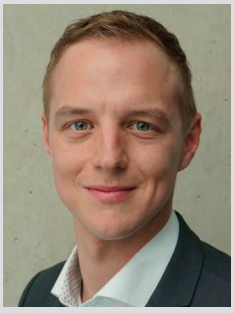
The versatility and simplicity of this approach stands out. With only pyridine and triflic anhydride required, the reagents are standard laboratory chemicals accessible to the majority of the scientific community. Professor Weigand remarked: "The range of usable phosphate sources is broad, enabling the use of both primary sources like phosphoric acid or phosphorus pentoxide, and secondary sources such as certain spent phosphate esters. Furthermore, the scope of possible target compounds is immense, spanning diverse applications, whose synthesis is simplified from five or six steps with state-of-the-art methods to just two (patent applications: EP4183742A1 and DE102022120599.1)."

Professor Weigand concluded: "We are currently further developing the synthetic application of **1**[OTf] as a universal building block in phosphorus chemistry, the full potential of which has yet to be discovered."

About the authors

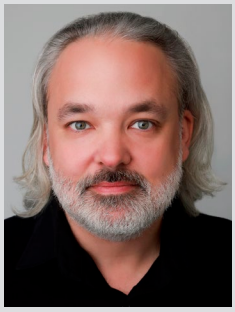
T. Schneider

Tobias Schneider received his B.Sc. in chemistry from the TU Dresden (Germany) in 2017. After interim research periods at the Hanoi University of Science and Technology (Vietnam) and Osaka University (Japan), he completed his M.Sc. degree in Dresden in 2020. He is currently working on his PhD thesis under the supervision of Prof. Jan J. Weigand, focusing on the development of alternative synthetic procedures for the production of phosphorus-containing fine chemicals.



Dr. K. Schwedtmann

Kai Schwedtmann received his diploma degree from the WWU Münster (Germany) in 2012 and started his PhD studies under the supervision of Prof. Jan J. Weigand. In 2013, he moved to TU Dresden (Germany) where he received his Dr.rer.nat. in 2016. During his PhD, he was a visiting researcher in the group of Prof. Neil Burford in 2014 at the University of Victoria (Canada). Today, he is senior researcher at TU Dresden with focus on reactive phosphorus compounds and sustainable phosphorus chemistry.



Prof. J. J. Weigand

Jan J. Weigand obtained his diploma in chemistry in 2002 and his Dr. rer. nat. in 2005 from the LMU in Munich (Germany). Awarded with the Bavarian Culture Prize in 2005, he obtained a Lynen Scholarship from the AvH Foundation for postdoctoral research at Dalhousie University in Halifax (Canada). He returned to Germany with a Lynen Return Fellowship and started his habilitation at WWU Münster in 2007 under Prof. Hahn's supervision. Shortly after, he was awarded the Liebig scholarship of the FCI, allowing him to start his independent career in 2008. In April 2010, he became a fellow of the prestigious Emmy Noether research program awarded by the DFG and received the Wöhler Research Award for Young Scientists. In July 2012, he obtained an ERC Starting Grant from the European Commission. Since January 1, 2013, he has been a Professor at TU Dresden (Germany). His research activities focus on molecular inorganic and phosphorus chemistry, the development of sustainable methods in extraction, technical applications, and novel recycling strategies. This includes innovative catalyst systems for application in the petrochemical industry and resource change to biogenic and fossil residues. In 2023, he received a Reinhardt Koselleck funding from the DFG for the project "Blueprint for a Modern Sustainable Phosphorus Chemistry".

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Young Career Focus: Assistant Professor Barla Thirupathi (Indian Institute of Science Education and Research Berhampur, 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 Assistant Professor Barla Thirupathi (Indian Institute of Science Education and Research Berhampur, India).

Biographical Sketch

Dr. B. Thirupathi

Barla Thirupathi was born in Madavelli, Manchirial district, Telangana, India in 1984. After completing his M.Sc. (organic chemistry) from Osmania University, India (2006–2008), he worked as a research chemist at Aragen Life Sciences, formerly known as GVK-Biosciences, Hyderabad, India (2008–2009). In early 2009, he joined the CSIR-Indian Institute of Chemical Technology, Hyderabad (India) as a Junior Research Fellow (JRF), and undertook his doctoral studies with Dr. Debendra K. Mohapatra (2009–2014). Afterwards, he worked as an associate research scientist in the process R&D division at Sai Life Sciences, Hyderabad, India (2014–2015). Then he moved to Harvard University (USA) as a postdoctoral fellow to work with Nobel laureate Prof. E. J. Corey (2015–2018), where he worked on the development of highly active fluorinated second-generation oxazaborolidine catalysts and their application in enantioselective Diels–Alder reactions. In July 2018, he moved back to India and was appointed as an assistant professor of chemistry at one of India's premier institutes, the Indian Institute of Science Education and Research (IISER) Berhampur. He has already been recognized as an upcoming independent researcher and has received various accolades, including the 2023 Thieme Chemistry Journals Award.

INTERVIEW

SYNFORM *What is the focus of your current research activity?*

Dr. B. Thirupathi My research program emphasizes the development of novel methods for carbon–carbon bond formation reactions and their application in natural product synthesis. The primary emphasis of this research work is on designing and developing innovative reactions through a simple, cost-effective, environmentally friendly, and easy to automate approach, while using readily available starting materials. My area of research also includes the total synthesis of biologically active natural products or model compounds having potential bioactivities.

SYNFORM *When did you get interested in synthesis?*

Dr. B. Thirupathi As an undergraduate student studying mathematics, physics and chemistry as three major subjects, I was attracted to chemistry by considering its job opportunities in the pharmaceutical industry and academia. When I joined a pharmaceutical company after my Master's degree in organic chemistry, I decided to pursue my PhD in organic synthesis because of the way people were involved in and influenced by research and developmental activities in an industry setting. Accordingly, I joined the CSIR-Indian Institute of Chemical Technology, Hyderabad, for doctoral studies. The opportunities I have had throughout my post-graduate and doctoral studies helped me to pursue a research career in synthesis further.

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

Dr. B. Thirupathi Organic synthesis is one of the most exciting and vital fields of research in modern science. It plays

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a significant role in improving human welfare, health care and developing new drugs to prevent and treat high-priority diseases. Due to its universality and pervasive nature across science and technology, it has also influenced other fields of science and engineering. Many fields like chemical biology, medicinal chemistry, biology and biotechnology, physics, materials science, and nanotechnology overlap with the area of organic synthesis. This understanding of the centrality and significance of organic synthesis demands and requires its ongoing improvement, encompassing both method development and total synthesis.

SYNFORM *Could you tell us more about your group's areas of research and your aims?*

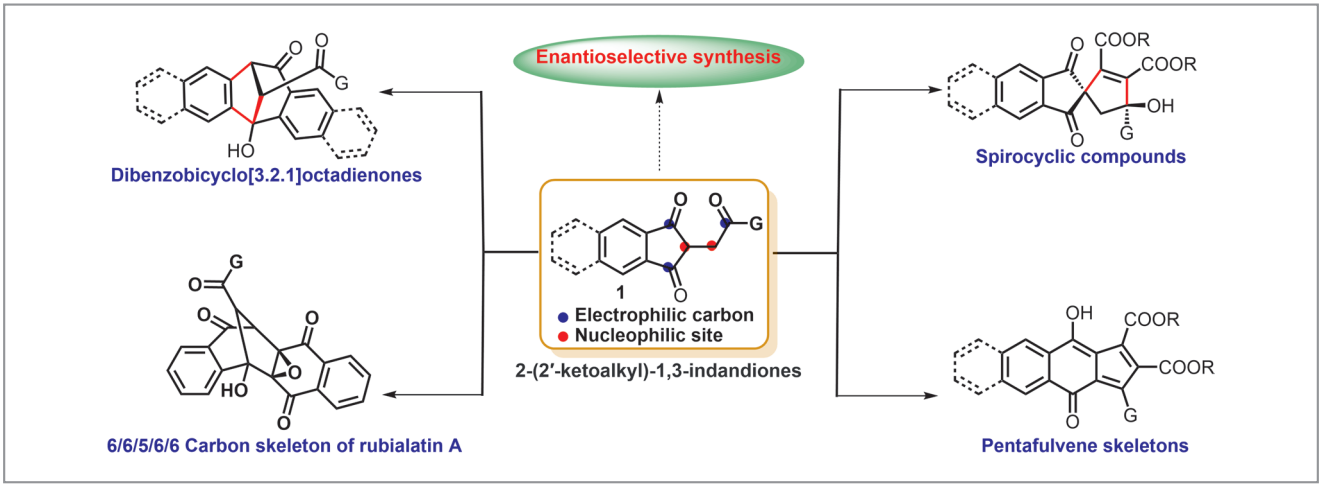
Dr. B. Thirupathi Our research program emphasizes the development of new synthetic methodologies for novel C–C bond formation reactions. Achieving multiple bond formations in a single operation is currently one of the main challenges in the search for cost-effective syntheses. Ideal organic syntheses require a process that is simple, cost-effective, environmentally friendly, and easy to automate while using readily available starting materials and producing products that incorporate substantial portions of all the components. We aim to develop synthetic methods by considering the best possible organic synthesis approach. Accordingly, I have chosen 2-(2′-ketoalkyl)-1,3-indandione as a crucial starting material for method development, as it has the unique characteristics of having two sets of nucleophilic and electrophilic sites within the molecule. So much interesting and exciting chemistry is going on in my laboratory using 2-(2′-ketoalkyl)-1,3-indandione as one of the key, intriguing, starting materials (Scheme 1). Furthermore, we also work on the total synthesis of biologically active natural products or model compounds with potential bioactivities. The targeted molecules pose unique challenges in asymmetric bond construction. An endeavour towards complex multistep synthesis affords a target-oriented setting to engage in reaction innovation and design. Our research aims to facilitate and make significant contributions to the synthesis of important organic molecules, like natural products and heterocyclic compounds, and make these processes more environmentally friendly.

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

Dr. B. Thirupathi I was delighted with our recent achievements in developing new synthetic methods using 2-(2′-ketoalkyl)-1,3-indandiones as a key substrate. These recent accomplishments were published in *Chemistry A European Journal* (*Chem. Eur. J.* **2023**, *29*, e202301976), and *The Journal of Organic Chemistry* (*J. Org. Chem.* **2022**, *87*, 11925–11938) and showcased on these journals' cover pages. These accomplishments gave me immense pleasure, because my initial hypothesis was materialized in the form of publications.

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

Dr. B. Thirupathi Outside the lab, I enjoy watching movies and cooking for myself and my family.



Scheme 1 Synthesis of intriguing carbon skeletons involving 2-(2′-ketoalkyl)-1,3-indandiones

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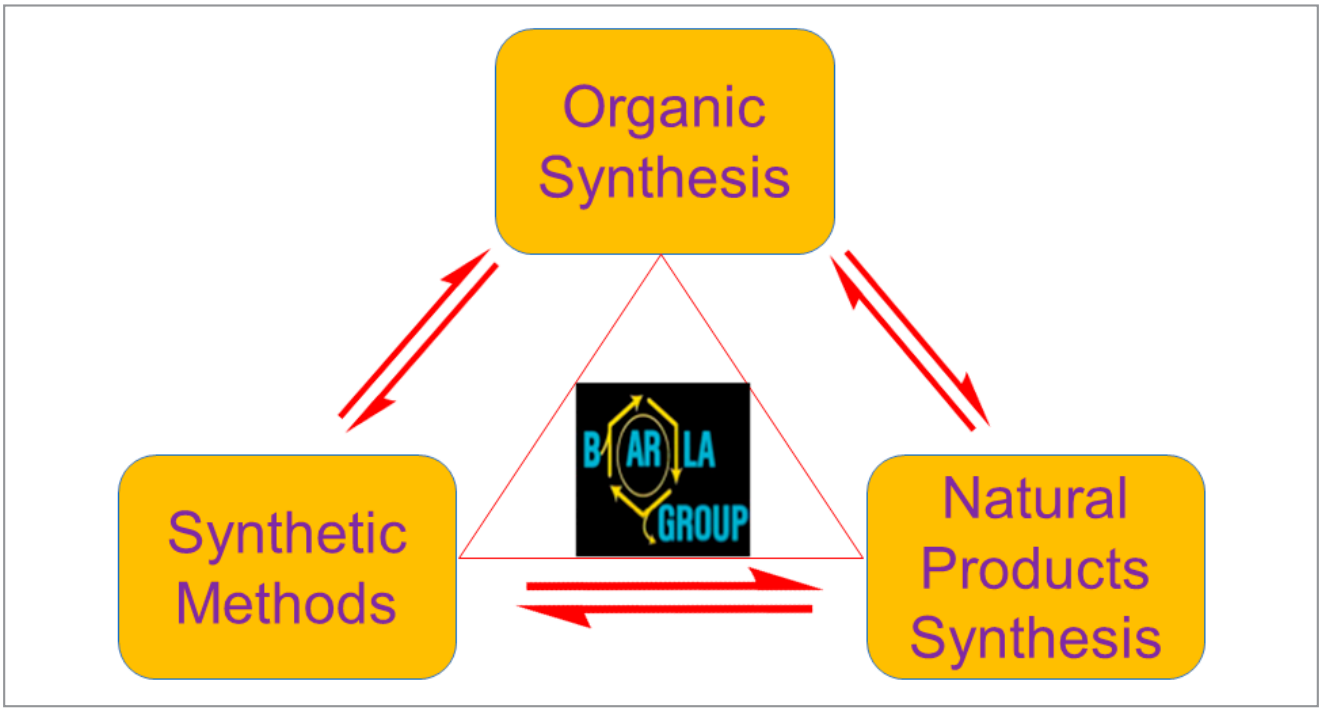

Figure 1 Schematic representation of Dr. Thirupathi's research

Twitter id: @ThirupathiBarla
Group Twitter id: @BarlaLab
Group web page: https://bthirupathi56.wixsite.com/website
Email: thirupathibarla@iiserbpr.ac.in

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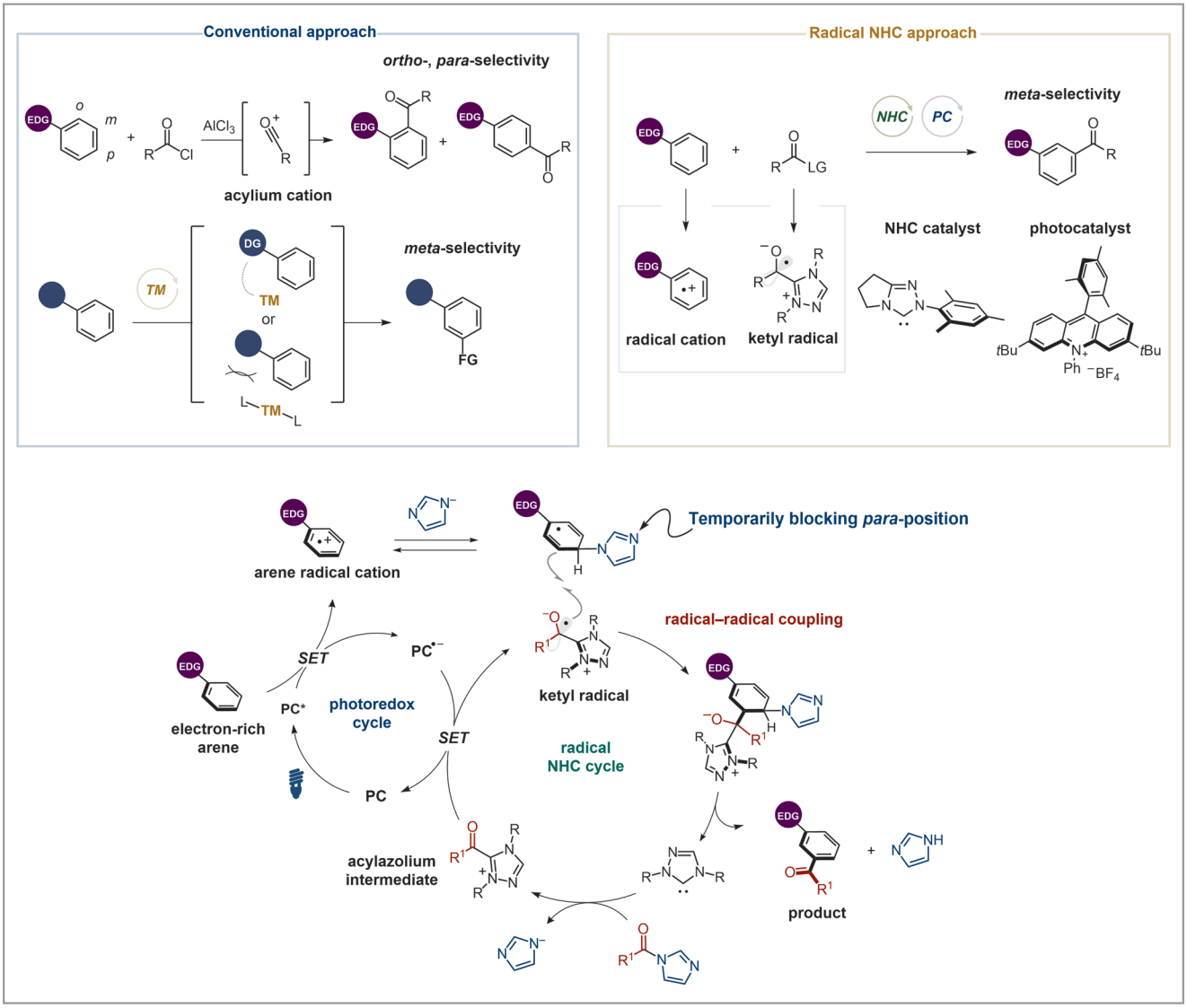
N-Heterocyclic Carbene- and Organic Photoredox-Catalysed *meta*-Selective Acylation of Electron-Rich Arenes

Nat. Synth. **2023**, *2*, 1037–1045

The Friedel–Crafts reaction serves as a highly useful chemical process, featured prominently in organic chemistry literature and textbooks. Since the initial report from Friedel and Crafts on the acylation of aromatic rings in 1877 (see also the Name Reaction Bio article, *Synform* **2018**, A49–A52), this methodology has found widespread applications, extending seamlessly from the laboratory to industrial level, for the synthesis of materials, natural products, and pharmaceutical agents.

According to Professor Hirohisa Ohmiya (Kyoto University, Japan), the Friedel–Crafts acylation reaction, specifically, demonstrates high efficiency in the case of electron-rich arenes, which is achieved through the induction of acylium cations.



Scheme 1 NHC- and organic photoredox-catalysis enabling *meta*-selective acylation

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"Electrophilic aromatic substitution reactions typically introduce acyl groups to the *ortho*- and *para*-positions to electron-donating groups on aromatic rings," he explained. "This *ortho*- and *para*-selectivity has enabled the construction of complex aromatic compounds. However, challenging this norm by achieving *meta*-selective aromatic substitution reactions on electron-rich arenes is a difficult yet powerful process, offering a valuable toolbox for organic synthesis."

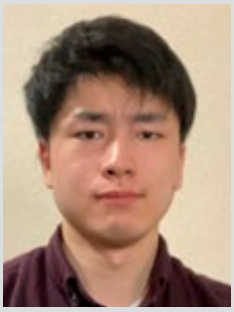
This *Nature Synthesis* paper by Goto, Sano, Sumida and Ohmiya described the N-heterocyclic carbene (NHC) and organic photoredox cooperative catalytic *meta*-selective acylation of electron-rich arenes. "The catalytic system involves a nucleophilic addition of an azolide anion to the radical cation species produced by single-electron oxidation of the electron-rich arenes," said Professor Ohmiya, corresponding author of this paper. He continued: "The nucleophile, the azolide anion, is delivered from the acylation reagent, acyl imidazole, via addition/elimination with an NHC catalyst. The desired *meta*-acylation was achieved based on the cross-selective radical–radical coupling of the cyclohexadienyl radical formed by the nucleophilic addition with the persistent radical, the ketyl radical, via single-electron reduction of the acyl azolium intermediate (Scheme 1)."

Dr. Yuto Sumida, co-corresponding author on the paper, told SYNFORM: "This reaction pathway involves a unique route of functionalization to aromatic rings by radical–radical coupling via attaching and detaching of azolide anion. This catalytic pathway opens up the possibility of radical NHC catalytic systems." Dr. Sumida went on: "This project was accomplished by two promising students: Yamato Goto discovered the reaction through extensive experiments and demonstrated the validity of the plausible mechanism using computational chemistry. Masaki Sano also greatly accelerated the project with countless experiments and analyses."

Dr. Sumida added that the developed method enables modification of a broad range of substances from *meta*-acylation of simple electron-rich arenes, such as anisole, to biologically active molecules having complex structures, such as SN-38, that are difficult to achieve via the conventional approach.

Prof. Ohmiya commented: "In recent years, several *meta*-functionalizations of arenes have been reported using transition-metal catalysts with directing groups or specially designed ligands, but most of them yield products with a small amount of mixed regioisomers. Conversely, our reaction is innovative because it proceeds with almost perfect selectivity based on the mechanistic principle of radical NHC catalysis." Prof. Ohmiya concluded: "We hope that this discovery will be a stepping stone for further regioselective functionalization of aromatic rings."

About the authors



Y. Goto

Yamato Goto received his B.S. degree from Kanazawa University (Japan) in 2021. He then started his MS degree studies under the supervision of Professor Hirohisa Ohmiya. His research interests focus on the development of novel methodology based on radical process under N-heterocyclic carbene catalysis.

M. Sano

Masaki Sano is an undergraduate student at Graduate School Medical Science, Kanazawa University (Japan). His research interests focus on the development of radical chemistry with organic photoredox catalysts and cancer theranostics through radiochemical strategies.

Assoc. Prof. Y. Sumida

Yuto Sumida received his PhD from Kyoto University (Japan) in 2010 under the supervision of Professor Koichiro Oshima. He spent nine months as a JSPS postdoctoral fellow in the group of Professor Daniel Kahne at Harvard University (USA). In 2011, he became an Assistant Professor at Tokyo Medical and Dental University (TMDU, Japan) working with Professor Takamitsu Hosoya. He moved to RIKEN Kobe (Japan) as a Research Scientist in 2014. He became an Assistant Professor at Kanazawa University (Japan) working with Professor Hirohisa Ohmiya in 2019. He has been an Associate Professor at TMDU working with Professor Takamitsu Hosoya since 2023.

Prof. H. Ohmiya

Hirohisa Ohmiya is a Professor at Kyoto University (Japan). He received his Ph.D. from the same university in 2007 under the supervision of Professor Koichiro Oshima. He spent one year as a JSPS postdoctoral fellow in the group of Professor Timothy F. Jamison at Massachusetts Institute of Technology (USA). In 2008, he became an Assistant Professor at Hokkaido University (Japan) working with Professor Masaya Sawamura. He was promoted to Associate Professor in 2010. He began his professorial career at Kanazawa University (Japan) in 2017 before moving to Kyoto University in 2022.

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Chiral, Air Stable, and Reliable Pd(0) Precatalysts Applicable to Asymmetric Allylic Alkylation Chemistry

Nat. Commun. **2023**, *14*, 8058

In the realm of homogeneous catalysis for organic synthesis, there are two major methods for generating catalytically active species, according to Professor David Leitch, from the University of Victoria in Canada, who told SYNFORM: "Most common for organopalladium catalysis is the in situ assembly of an active complex through combination of a metal precursor compound and the ancillary ligand, both added separately to the reaction mixture. While this is arguably convenient, it is also often inefficient and unreliable as ligand metalation rates may be slow and multiple species can be generated, while changes of the metal–ligand stoichiometry can greatly affect performance. There are two approaches to this problem: either design advanced metal precursor compounds able to rapidly and reliably generate active species, or use single-component precatalysts where the appropriate ancillary ligand is already installed to give a stable complex."

Prior work from Professor David Leitch's group, spearheaded by one of the PhD students, Jingjun Huang, sought to take both approaches by designing stable palladium(0) species able to function as *in situ* precursors and as a platform for generating single-component catalysts. The key compound, ^{DMP}DAB-Pd-MAH (Figure 1), was first reported in 2021 in the context of cross-coupling catalysis (*ACS Catal.* **2021**, *11*, 5636–5646). Professor Leitch said: "Literally the day after this initial work was posted to *ChemRxiv* in January 2021, Dr Stellios Arseniyadis from Queen Mary University of London (UK) reached out to us via email to inquire if ^{DMP}DAB-Pd-MAH could be used to replace common Pd(0) catalysts, in particular $Pd_2(dba)_3$, in the context of asymmetric allylic alkylation (AAA) chemistry. After a few discussions and a transatlantic shipment, a collaboration was born to build better catalysts for this family of enantioselective reactions."

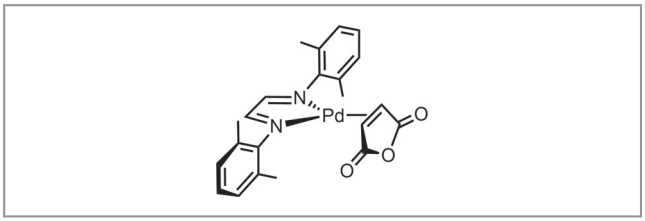

Figure 1 ^{DMP}DAB-Pd-MAH

The first reaction, run by François Richard, PhD student in the Arseniyadis group, showed great promise. "Indeed, applying ^{DMP}DAB-Pd-MAH as an *in situ* precursor in a late-stage Pd-AAA reaction enabled the total synthesis of three *O*-terpenoidal natural products, namely excavacoumarin B, D and E, concluding a tremendous collaborative campaign to develop a unique C5-selective Pd-AAA of butenolide derivatives (*Nat. Synth.* **2022**, *1*, 641–648)," said Dr Arseniyadis. Emboldened by this early success, the Leitch and Arseniyadis groups then sought to address a key gap in AAA chemistry: the lack of single-component precatalysts.

"Despite the long and fruitful history of the Trost chiral ligands in AAA chemistry (*J. Am. Chem. Soc.* **1992**, *114*, 9327–9343), including many natural product total syntheses (*Chem. Rev.* **2003**, *103*, 2921–2944), accessing discrete palladium complexes with these ligands has proved surprisingly difficult (Scheme 1A)," explained Professor Leitch. He continued: "Trost, Breit, and Organ observed rapid oxidative decomposition of the catalyst to form an inactive tetradentate [PNNP] Pd complex (*Tetrahedron Lett.* **1994**, *35*, 5817–5820). Furthermore, extensive work from the Lloyd-Jones group established the complexities of Pd(II) coordination with the Trost ligands, observing multiple coordination modes and oligomeric species in solution (*Chem. Commun.* **1999**, 1707–1708; *Chem. Commun.* **2000**, 2447–2448; *Chem. Sci.* **2015**, *6*, 5793–5801). The Leitch/Arseniyadis hypothesis was that the favorable ligand substitution chemistry of ^{DMP}DAB-Pd-MAH and the stabilizing influence of the maleic anhydride ligand, would lead to well-defined complexes."

To test their hypothesis, a thorough investigation began in collaboration with their industrial partner, Servier. "While Jingjun Huang explored the synthesis and all the organometallic chemistry aspects of the precatalysts in Victoria, Thomas Keenan and François Richard evaluated the catalyst on a variety of AAA reactions in London, and the advantages of these new systems quickly became apparent," remarked Professor Leitch. He continued: "The Pd(0) complexes generated from simple combinations of chiral ligands and ^{DMP}DAB-Pd-MAH proved easily isolable as discrete, stable species (Scheme 1B). As hypothesized, the maleic anhydride ligand renders these complexes air stable, both as solids and in solution. This means that the precatalysts can easily be used without the

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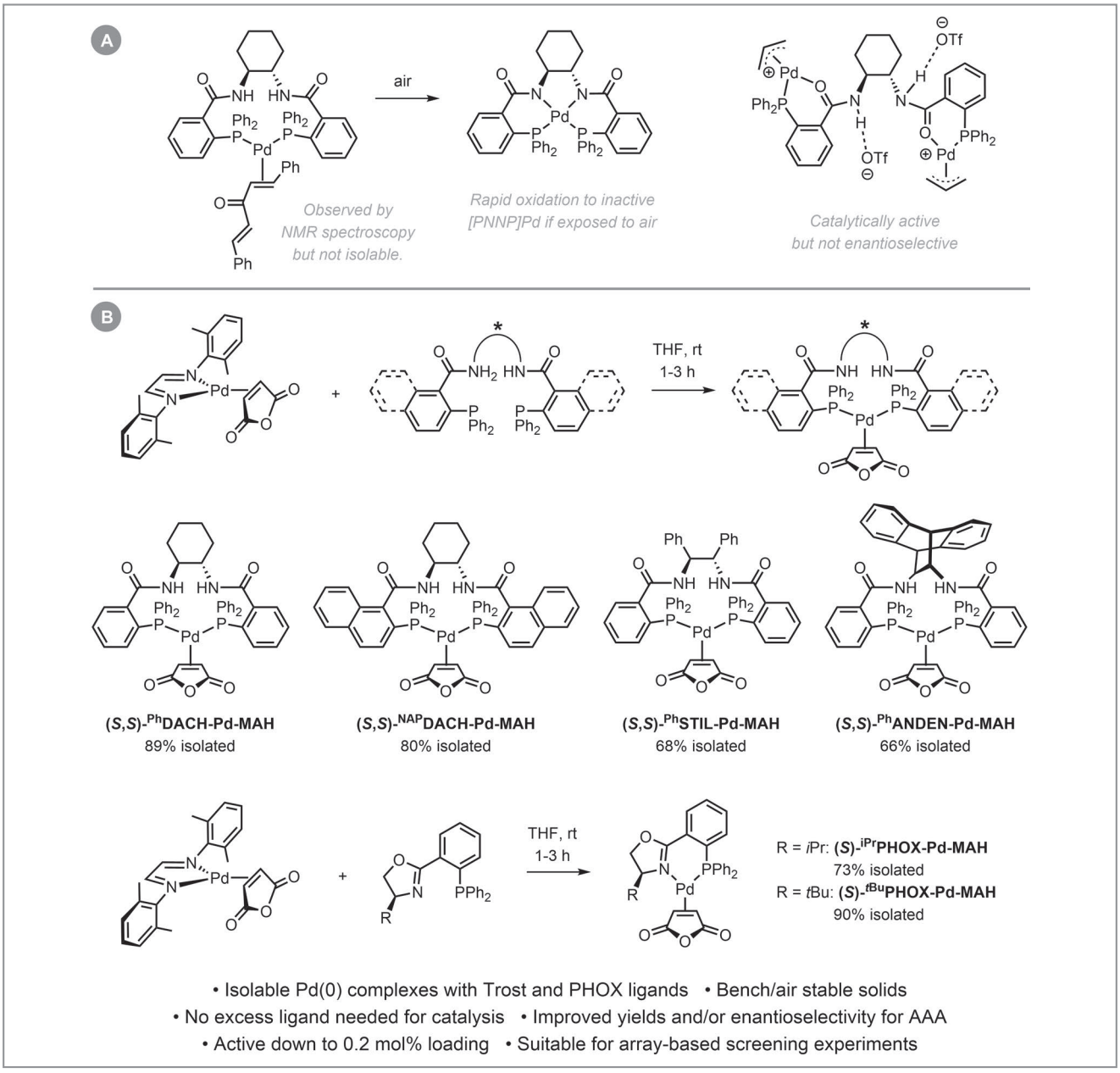

Scheme 1 (A) Challenges in accessing discrete Pd complexes with Trost modular ligands. (B) Chiral precatalysts derived from ^{DMP}DAB-Pd-MAH.

need for a glovebox. As a bonus, the well-behaved nature of these complexes enabled to characterize conformational effects in solution and in solid-state molecular structures from single-crystal X-ray diffraction, observing direct evidence of hydrogen bonding between the backbone N–H and a carbonyl group on the coordinated maleic anhydride. This type of ligand–substrate interaction was actually proposed to be a crucial element for stereochemical induction in Pd-AAA reactions (*J. Am. Chem. Soc.* **2009**, *131*, 9945–9957)."

A set of six representative chiral Pd(0) precatalysts, including four with Trost modular ligands and two with phosphinooxazoline (PHOX) ligands (*Acc. Chem. Res.* **2000**, *33*, 336–345) were assembled, characterized, and evaluated. Dr Arseniyadis said: "All six demonstrated their superiority

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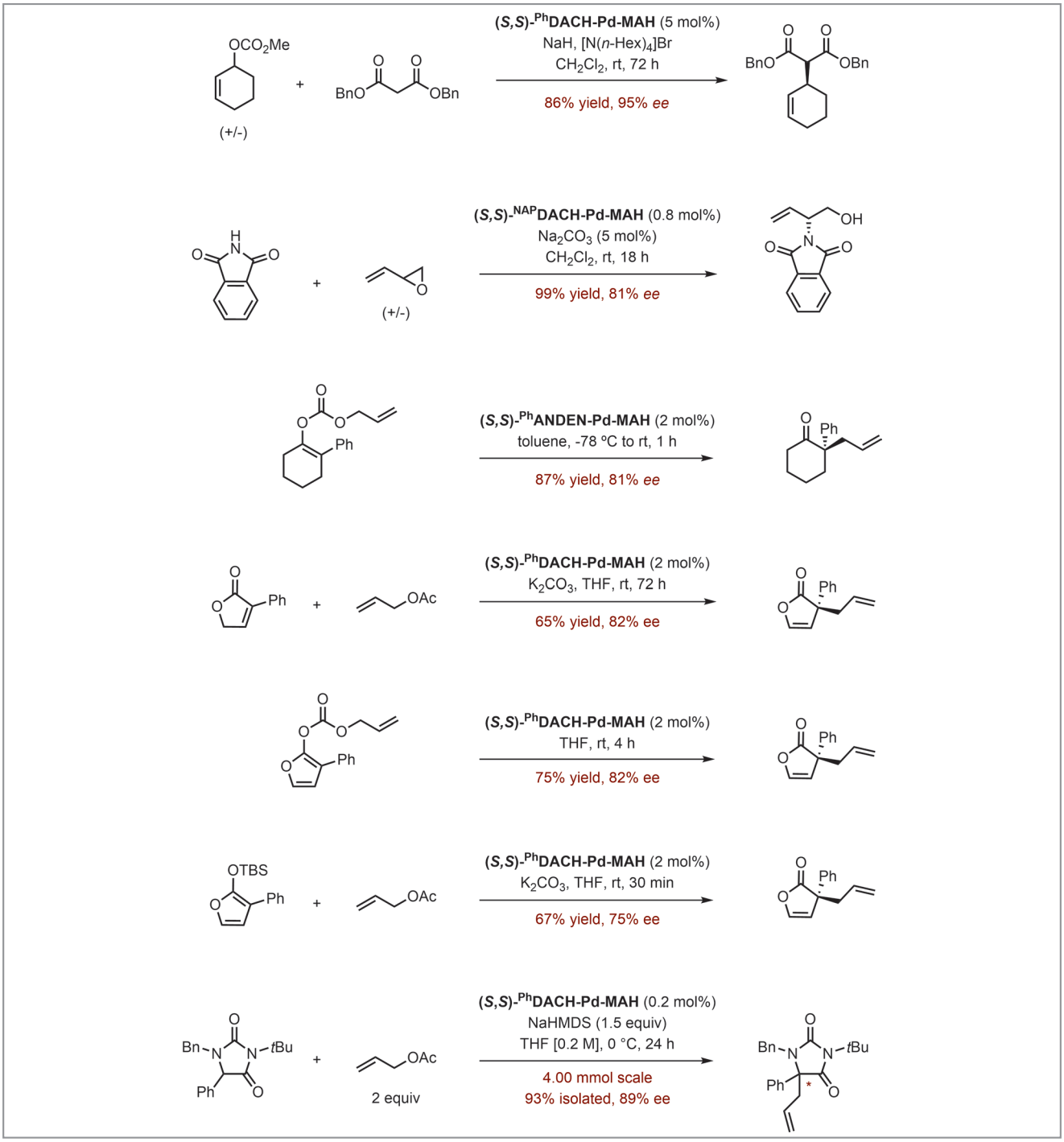
over established systems across nine distinct AAA reactions (Scheme 2). Because the chiral ligand is already installed, there is no need for premixing/incubation protocols to ensure complete ligand metalation before adding the substrates and the reagents. Furthermore, many existing protocols require excess chiral ligand to function; with a 1:1 Pd to ligand stoichiometry, the reactions outright fail. The single-component precatalysts obviate this failure mode."



Scheme 2 Representative AAA reactions catalyzed by single-component Pd(0) precatalysts

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Professor Leitch continued: "One of the most important features of these precatalysts is their compatibility with rapid screening protocols for improving product yield and enantioselectivity. Because existing procedures for AAA catalysis require pre-incubation of the Pd source and the ligand to generate the chiral catalyst, and because the resulting Pd species are very oxygen sensitive, microscale high-throughput screening becomes very challenging. Both ^{DMP}DAB-Pd-MAH and the single-component systems are ideally suited to array experiments, rapidly optimizing the unprecedented AAA of a hydantoin to achieve high yield and enantioselectivity with only 0.2 mol% catalyst."

One aspect of this work that became abundantly clear to the authors from speaking with others in the field is that precatalyst development and catalyst activation studies remain a significant gap in AAA reactions, especially compared to Pd-catalyzed cross-coupling and other transformations. "After I presented this work at OMCOS XXI in July 2023, several Trost group alumni remarked that many attempts were made to isolate discrete Pd complexes with the modular ligands, with not much success," said Professor Leitch.

The authors also want to make it as easy as possible for other researchers to use these catalysts in their own applications. "^{DMP}DAB-Pd-MAH is commercially available (and is also readily synthesized), and work is ongoing to commercialize the single-component chiral catalysts as well," remarked Professor Leitch, who concluded: "In the meantime, the Leitch and Arseniyadis groups are more than happy to provide samples – just reach out to Stellios or me via email."

About the authors

Dr. J.J. Huang

Jingjun Huang was born in Qingyuan, China. She obtained bachelor degrees in chemistry from the University of Cincinnati (USA) and in environmental engineering from South China Normal University (P. R. of China) in 2019. She then joined the Leitch group at the University of Victoria (Canada) as an MSc student in 2019, and transferred to PhD student in 2020. Her thesis research focused on the development of active, stable and high-throughput screening compatible palladium precatalysts for cross-coupling and asymmetric allylic alkylation reactions. She obtained her PhD degree in chemistry from the University of Victoria in November 2023.

T. Keenan

Thomas Keenan grew up on the Wirral (UK) a place that is home to the world's best chippy and ice-cream shop. He obtained his MSc in medicinal and biological chemistry from the University of Nottingham (UK) in 2019. His MSc project involved the design and synthesis of selective integrin antagonists for the treatment of idiopathic pulmonary fibrosis. After graduating, he joined the Arseniyadis group at Queen Mary University of London (UK) to start his PhD in collaboration with Servier focusing on several topics, including Pd-catalysed asymmetric alkylations, asymmetric organocatalysis and natural product synthesis.

Dr. F. Richard

François Richard received his MS in chemistry from the Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM), France. In 2017, he joined the Arseniyadis group at Queen Mary University of London (UK) to start his PhD in collaboration with Lilly, studying the Pd-catalysed asymmetric allylic alkylation of butenolides. He then joined the group of Prof. Andrew Lawrence at the University of Edinburgh (UK) for his postdoctoral studies, where his research focused on the development of stereoretentive enantioconvergent reactions. Recently, Francois joined the group of Prof. Matthew Gaunt at the University of Cambridge (UK) as a postdoctoral research associate.

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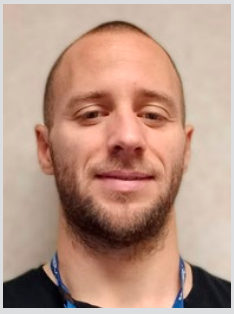

Dr. A. Jean

Alexandre Jean graduated from the University of Rouen (France) in 2010 and did his PhD under the joint supervision of Dr Jacques Maddaluno, Dr Jacques Rouden, Dr Michael De Paolis and Dr Jérôme Blanchet, in the field of asymmetric organocatalysis. He then joined the group of Prof. David Yu-Kai Chen at Seoul National University in South Korea for his postdoctoral studies, where his research focused on the total synthesis of communesin F and a putative member of the communesin family of bis-aminal alkaloid natural products. In 2015, he returned to Rouen to work with Dr Michael De Paolis on the development of new synthetic approaches towards γ-pyrone natural products. Finally in 2016, he joined Servier as a process chemist and has been collaborating with the Arseniyadis group since 2019.

L. Arseniyadis

Stellios Arseniyadis obtained his PhD in 2002 from the University of Strasbourg (France) under the guidance of Dr. C. Mioskowski. After various postdoctoral stints in industry (Rhodia Chirex, Boston, USA, in collaboration with Professor S. L. Buchwald, MIT) and in academia with Professor A. C. Spivey (Imperial College London, UK) and Professor K. C. Nicolaou (The Scripps Research Institute, USA), he started his academic career in France in 2005, first as a CNRS researcher and later as a CNRS Director. In 2015, he moved his group to Queen Mary University of London where he is mainly interested in developing new synthetic methods and applying them in natural product synthesis.

Prof. D. C. Leitch

David C. Leitch obtained both his BSc (2004) and PhD (2010) at the University of British Columbia, Vancouver (Canada). There he worked with Professor Laurel Schafer on organozirconium chemistry and hydroamination catalysis. He then held postdoctoral positions at McGill University (2010–2012, Arndtsen Group), and the California Institute of Technology (2012–2014, Bercaw Group). In 2014, he joined GlaxoSmithKline as a Process Chemist, becoming group leader of the Chemical Catalysis group (2016–2018), as well as the Continuous Primary group (2017–2018). In 2019, he accepted an Assistant Professor position at the University of Victoria (Canada), and was promoted to Associate Professor with tenure in 2023. His research group is focused on mapping chemical reaction space by using high-throughput experimentation, and developing new catalysts and catalytic reactions for complex-molecule synthesis.

Jingru Lu (PhD 2023, University of Victoria) and **Sarah E. Jenny** (PhD 2022, Temple University) made supporting contributions to this work (computational studies and X-ray crystallography, respectively).

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