

# SYNFORM

People, Trends and Views in Synthetic Organic Chemistry

2014/06

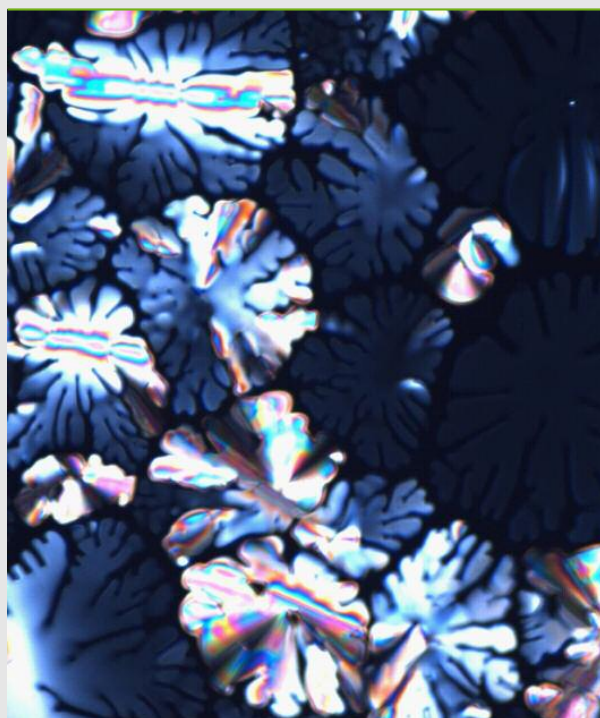
## SYNSTORIES ■ ■ ■ ■

■ Palladium/Copper-Catalyzed Oxidative Arylation of Terminal Alkenes with Aroyl Hydrazides

■ Young Career Focus: Dr. Ken Maly (Wilfrid Laurier University, Waterloo, Canada)

■ Direct Synthesis of 1,4-Diols from Alkenes by Iron-Catalyzed Aerobic Hydration and C–H Hydroxylation

■ Organocatalytic Enantioselective Synthesis of 2,3-Allenates by Intermolecular Addition of Nitroalkanes to Activated Enynes



### CONTACT ++++

Your opinion about SYNFORM is welcome, please correspond if you like:  
[marketing@thieme-chemistry.com](mailto:marketing@thieme-chemistry.com)



### Dear Readers,

Have you ever experienced a total lack of inspiration? That's exactly what is occurring to me today with this Editorial. I've been sitting here for more than one hour, I started three times on three different topics, but none of them has progressed further than a handful of lines. I guess all of them were reasonably interesting, I've tried first with the recent upsurge of mergers and acquisitions in the pharmaceutical industry, then I switched to the growing tendency to sensationalism in scientific publishing, finally I have even tried to play the card of the looming World Cup 2014 in Brazil and its potential effect on the research activity of our groups. But no way, it's just hopeless, words are not flowing today, inspiration is playing hide and seek with me, as soon as I come up with an idea, in the next five minutes I realize that I won't be able to write anything decent on that. So, I've just decided to make a public confession: today I have no inspiration, I am sorry but this Editorial is going to be rubbish. That's it! I feel better now... Luckily for me, the four articles in this new issue of **SYNFORM** are really interesting and featuring top quality science, so I hope I will be forgiven for the "rubbishness" of my Editorial. We start with the very clever idea of using aroyl hydrazides for performing oxidative arylations of terminal alkenes successfully developed by S.-K. Tian (P. R. of China). We continue with the direct synthesis of 1,4-diols from alkenes by using a "reagent kit" consisting of Fe(II)/phthalocyanine NaBH<sub>4</sub> and O<sub>2</sub> developed by T. Taniguchi (Japan). Then we look at the impressive construction of molecules containing contiguous all-carbon quaternary stereocenters via metal-catalyzed cycloadditions devised by T. Ooi (Japan). Finally we move to Canada where we meet K. Maly, who is the protagonist of our Young Career Focus.

Phew, I've made it...

**Matteo Zanda**

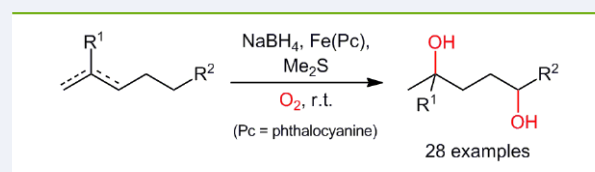
Editor of **SYNFORM**

## IN THIS ISSUE

### SYNSTORIES ■ ■ ■ ■

**Palladium/Copper-Catalyzed Oxidative Arylation of Terminal Alkenes with Aroyl Hydrazides.....A77**

**Direct Synthesis of 1,4-Diols from Alkenes by Iron-Catalyzed Aerobic Hydration and C-H Hydroxylation.....A79**



**Ligand-Enabled Multiple Absolute Stereocontrol in Metal-Catalyzed Cycloaddition for Construction of Contiguous All-Carbon Quaternary Stereocenters .....A81**

**Young Career Focus: Dr. Ken Maly (Wilfrid Laurier University, Waterloo, Canada) ....A85**

**COMING SOON.....A87**

**CONTACT + + + +**

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

## NEWS AND VIEWS ■ ■ NEWS AND VIEWS ■ ■ NEWS AND VIEWS ■ ■

## Palladium/Copper-Catalyzed Oxidative Arylation of Terminal Alkenes with Aryl Hydrazides

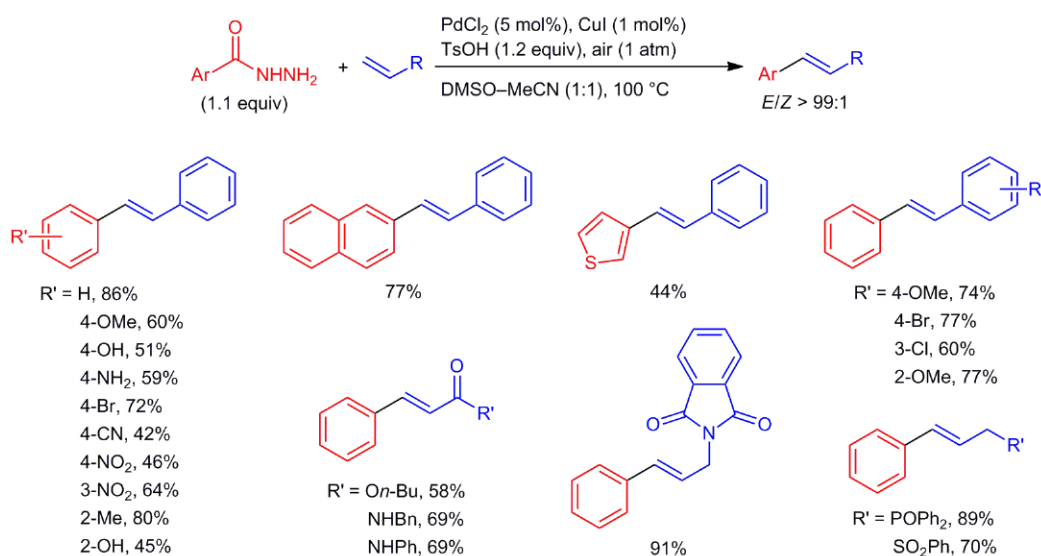
*Chem. Eur. J.* **2014**, *20*, 2765–2769

■ The traditional decarboxylative Mizoroki–Heck reaction requires *ortho*-substituents on benzoic acids and suffers from the use of excess terminal alkenes and expensive oxidants. Although some benzoic acid derivatives, such as acid chlorides, anhydrides, and active esters (vinyl or *p*-nitrophenyl carboxylates), without *ortho*-substituents have been reported to serve as aryl sources in the decarboxylative Mizoroki–Heck reaction, they are sensitive to moisture, are usually difficult to prepare and/or require an elevated reaction temperature of up to 160 °C.

In early 2011, Professor Shi-Kai Tian at the University of Science and Technology of China (Anhui, P. R. of China) conceived an idea of developing a possible Mizoroki–Heck-type reaction of aryl hydrazides with alkenes, wherein palladium was envisioned to catalyze the oxidative removal of the CONHNH<sub>2</sub> group from aryl hydrazides to generate arylpalladium intermediates, which in turn would couple with vinylic

C–H bonds. At that time, no method was available for using aryl hydrazides as aryl sources in cross-coupling reactions. Professor Tian explained: “This idea was substantially inspired by our previous success in the aerobic removal of the SO<sub>2</sub>NHNH<sub>2</sub> group from sulfonyl hydrazides (*Chem. Eur. J.* **2012**, *18*, 1582). Mr. Yong-Gang Zhang and Mr. Xiang-Lei Liu, two graduate students, carried out most of the experiments, and three other co-workers, including two undergraduate students, carried out a small portion of the experiments.” Although molecular oxygen was initially proposed by Professor Tian to serve as the terminal oxidant, Mr. Yong-Gang Zhang later demonstrated that both molecular oxygen and dimethyl sulfoxide served as terminal oxidants. Eventually, Professor Tian and Mr. Yong-Gang Zhang analyzed the data and wrote the manuscript together.

Professor Tian said: “Gratifyingly, the reaction proceeded well, open to air in the presence of 5 mol% PdCl<sub>2</sub>, 1 mol%



**Scheme** Professor Tian's decarboxylative Mizoroki–Heck reaction variant

CuI, and 1.2 equivalents of TsOH to afford a range of structurally diverse 1,2-disubstituted alkenes in moderate to excellent yields with excellent regio- and *E*-selectivity (see Scheme)."

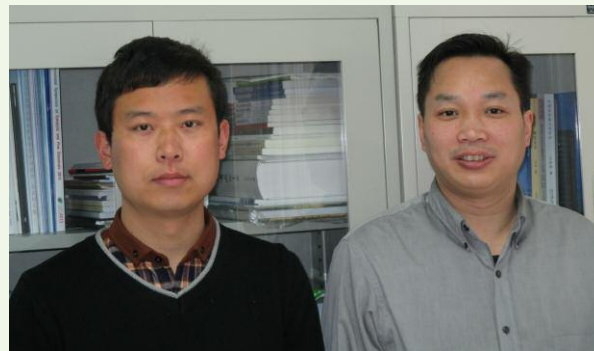
Professor Tian remarked: "When compared to previously reported Mizoroki–Heck-type reactions of arenecarboxylic acids and their derivatives, our reaction employs inexpensive reagents, is compatible with moisture and oxygen, and avoids the use of excess terminal alkenes and expensive oxidants. More importantly, it shows broader scope with regard to terminal alkenes through oxidative arylation of the vinylic C–H bonds in the *N*-allyl, *S*-allyl, and *P*-allyl groups and tolerates a wide variety of functional groups, such as hydroxy, amino, halo, cyano, nitro, ester, amide, imide, phosphine oxide, and sulfone groups. These features permit us to conclude that our reaction is synthetically useful for the preparation of a wide range of functionalized 1,2-disubstituted alkenes."

Currently, the research of Professor Tian's group focuses on the chemical transformations of nitrogenous organic compounds, such as alkylamines and monosubstituted hydrazines, through N–X bond cleavage. Professor Tian said: "The successful conversion of aroyl hydrazides into arylpalladium intermediates under aerobic conditions gives us an outstanding opportunity to further develop some oxidative cross-coupling reactions of acyl hydrazides with carbon or sulfur nucleophiles."

Professor Tian continued: "Our reaction has a very broad functional group tolerance, and is thus suitable for the synthesis of a variety of 1,2-disubstituted alkenes. Moreover, the application of our reaction is greatly facilitated by the fact that many aroyl hydrazides are commercially available solids and there is no need to exclude moisture and oxygen during the reaction." He concluded: "Although we are thoroughly satisfied with the usefulness of the synthetic methodology we have developed, there are a few limitations too: in fact, our reaction is incompatible with ketone and aldehyde groups, and it is not applicable to alkanoyl and alkenoyl hydrazides." ■

**Matteo Zanda**

### About the authors



From left: Y.-G. Zhang, Prof. S.-K. Tian

**Yong-Gang Zhang** was born in Henan (P. R. of China) in 1983. He received his B.S. degree in chemistry from Henan Normal University (P. R. of China) in 2008. He is currently a Ph.D. student in Professor Shi-Kai Tian's group at the University of Science and Technology of China.

**Shi-Kai Tian** received his B.S. degree from Lanzhou University (P. R. of China) in 1993 and Ph.D. from Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences (P. R. of China) in 1998 under the supervision of Professors Zhi-Min Wang and Min Shi. In 1999 he began conducting postdoctoral research with Professor Li Deng at Brandeis University (USA), and in 2002 he joined Vertex Pharmaceuticals Inc. (USA) as a medicinal investigator. Three years later he moved to the University of Science and Technology of China as a professor of chemistry. His research interests lie in the chemical transformations of nitrogenous organic compounds through N–X bond cleavage.

# Direct Synthesis of 1,4-Diols from Alkenes by Iron-Catalyzed Aerobic Hydration and C–H Hydroxylation

*Angew. Chem. Int. Ed.* **2014**, *53*, 2730–2734

Hydroxyl groups frequently emerge in many useful organic compounds such as natural products, pharmaceuticals and industrial materials. Therefore, hydroxylation reactions are fundamental and important chemical transformation of organic molecules. Among numerous methods for introducing a hydroxyl group into an organic molecule, direct hydroxylation reactions of inert C–H bonds have recently drawn considerable attention as a convenient and straightforward method for producing alcohols.

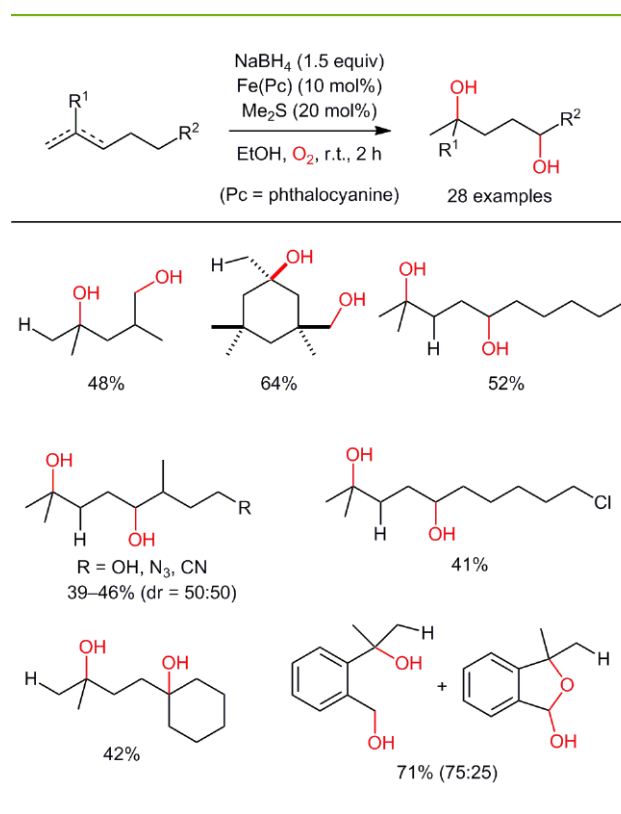
The group of Dr. Tsuyoshi Taniguchi at Kanazawa University (Japan) is interested in developing complex transformations of simple molecules using user-friendly reaction conditions. According to Dr. Taniguchi, in fact, one of the ultimate purposes of organic synthesis is to convert common materials into valuable products using convenient procedures that minimize costs. This work may be considered the representative example of Dr. Taniguchi's research philosophy because simple unsaturated hydrocarbons (alkenes) can be converted into 1,4-diols, that are considerably more functionalized compounds, by using an inexpensive reagent kit consisting of iron phthalocyanine, sodium borohydride and molecular oxygen.

“This reaction can introduce two hydroxyl groups into alkenes in one chemical step,” confirmed Dr. Taniguchi. “One hydroxyl group is introduced by known iron-catalyzed redox hydration of olefins with a hydride reagent and oxygen, and another is done by direct C(sp<sup>3</sup>)–H hydroxylation.” The project started when Dr. Taniguchi noticed the possibility of forming an alkoxy radical in the course of studying cyclizations of 1,6-dienes by applying the iron-catalyzed redox hydration. Dr. Taniguchi said: “We hypothesized that the formed alkoxy radical might cause a 1,5-hydrogen transfer to transform an inert C–H bond into another functional group. I performed model experiments employing 2,4-dimethylpent-1-ene and obtained the corresponding 1,4-diol product in 26% yield. Encouraged with this preliminary result, graduate student Takuma Hashimoto made efforts to improve the yield of the 1,4-diol, but it was not easy,” recalled Dr. Taniguchi. “We discussed the reaction mechanism and decided to focus on an intermediate iron peroxide complex (see Scheme 2).” Dr. Taniguchi explained that the literature (e.g., *Inorg. Chem.*

**2000**, *39*, 5572) indicated that ligands strongly coordinating to the iron complex promoted homolytic cleavage of an O–O bond to form the alkoxy radical. Therefore, Mr. Hashimoto tested various Lewis bases and found that Me<sub>2</sub>S provided the best result.

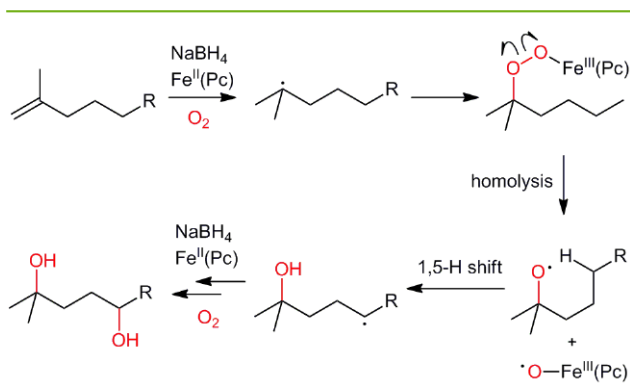
The reaction was applied to the synthesis of various 1,4-diols (Scheme 1). Tests of scope were performed by Mr. Hashimoto and Dr. Taniguchi. Dr. Taniguchi said: “In many cases, yields of products were still modest, but we believe that the impact of the unprecedented chemical transformation compensates for this drawback.”

He continued: “Since we assumed radical species to be the principal intermediates in the reaction mechanism, Ph.D. student Daisuke Hirose tried to obtain data to support this



**Scheme 1**

assumption (Scheme 2).” The first carbon radical formed by hydration of the olefin was trapped by TEMPO. In addition, formation of the second carbon radical by the 1,5-hydrogen shift was supported by an experiment employing a radical clock. “Further to that, Mr. Hirose performed other important experiments to support the proposed mechanism,” said Dr. Taniguchi, who wrote the manuscript and directed the project. “I am proud that this project started from my experiments, and that the results obtained by my experiments occupied a good portion of the published paper,” he continued. “I personally believe that all authors including principal investigators should contribute to practical experiments, including set-up of the reaction, work-up, purification and NMR analysis. We can understand the essence of the reaction more deeply by watching experiments.”



**Scheme 2**

It is noteworthy that all the reagents used in this reaction are inexpensive and easily available. In particular, molecular oxygen is ideal as a source of hydroxyl groups. “The experimental operation is simple, and anybody including young students can reproduce the reaction as long as fresh reagents are always used,” emphasized Dr. Taniguchi. “The methods available for preparing 1,4-diols are still limited. If synthetic chemists need 1,4-diols as key intermediates or products, such as drug candidates, this method may provide them with ease.” Dr. Taniguchi concluded: “We consider that ‘advanced chemical transformation with a simple reaction system’ is a fundamental concept of organic synthesis. We would like to pursue the potential of this concept and expand it to develop additional valuable synthetic methods.”

**Matteo Zanda**

### About the authors



*T. Hashimoto*

**Takuma Hashimoto** was born in Kitakyusyu (Japan) in 1988. He received his B.Sc. degree from Kanazawa University (Japan) in 2012. He is currently a graduate student at Kanazawa University.



*D. Hirose*

**Daisuke Hirose** was born in Toyama (Japan) in 1988. He received his B.Sc. and M.Sc. degrees from Kanazawa University (Japan) in 2011 and 2013. He is currently a Ph.D. student at Kanazawa University and recipient of a JSPS Research Fellowship for Young Scientists.



*Dr. T. Taniguchi*

**Tsuyoshi Taniguchi** received his B.Sc. and M.Sc. degrees from Kanazawa University (Japan) in 2004 and 2006. He started his academic career as an assistant professor at Kanazawa University in 2006. He obtained his Ph.D. from Kanazawa University in 2009. He joined in the group of Professor Dennis P. Curran at the University of Pittsburgh (USA) as a visiting scholar for one year (2011–2012).

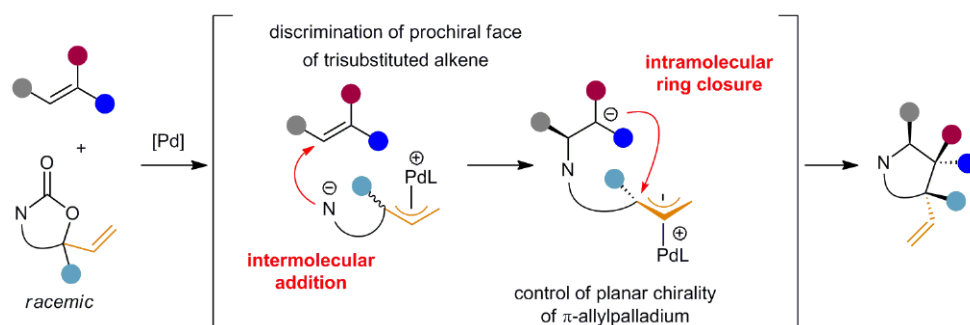
His research interests are the development of new synthetic methods and total synthesis of natural products.

# Ligand-Enabled Multiple Absolute Stereocontrol in Metal-Catalyzed Cycloaddition for Construction of Contiguous All-Carbon Quaternary Stereocenters

*Nat. Chem.* **2014**, *6*, 47–51

■ The prime research interests of Professor Takashi Ooi's group at Nagoya University (Japan) are focused on the molecular design of chiral organic ion pairs, particularly novel chiral quaternary onium salts, and understanding the relationship between their three-dimensional structures and functions as molecular catalysts in the development of challenging asymmetric transformations. As a part of this program, Professor Ooi and his co-workers recently introduced a conceptually new, multicomponent chiral ligand, named 'ion-paired chiral ligand', consisting of an ammonium-phosphine hybrid ligand and chiral anion (*Nat. Chem.* **2012**, *4*, 473). This type of chiral ligand has been proven to be effective for asymmetric palladium-catalyzed allylations of prochiral carbon nucleophiles, enabling the facile installation of all-carbon quaternary stereocenters (*J. Am. Chem. Soc.* **2013**, *135*, 590; *Chem. Commun.* **2014**, *50*, 4554). Professor Ooi said: "On the basis of these achievements, we set our next target on one of the most challenging objectives in asymmetric synthesis; that is, the development of a single-step catalytic methodology for the enantio- and diastereoselective construction of contiguous all-carbon quaternary stereocenters, which are found in many complex natural products and are often crucial for the expression of their biological activities."

The approach of the Nagoya researchers is based on the development of palladium-catalyzed enantio- and diastereoselective [3+2]-cycloaddition reactions of 5-vinylloxazolidinones and activated trisubstituted alkenes. Professor Ooi said: "The overall bond connection in this annulation is believed to take place in a stepwise manner, and the intramolecular ring-closing step would be advantageous for the coupling between sterically congested carbons (Figure)." He continued: "In addition, if the ring-closing bond formation is fast enough for the transiently generated carbanion to retain the stereochemical information originating from the parent alkene geometry, enantiofacial discrimination of the alkene in the initial intermolecular addition step would enable the stereoselective construction of not only the trisubstituted chiral center but also the adjacent quaternary stereocenter." At the same time, according to Professor Ooi, employment of a precursor having a tetrasubstituted chiral carbon for the generation of the 1,1-disubstituted allylpalladium species allows for the introduction of an additional quaternary stereocenter in the ring-closing step. "Importantly, the stereoselective construction of this chiral carbon center necessitates the control of isomerization of the planar chiral  $\pi$ -allylpalladium," he added.

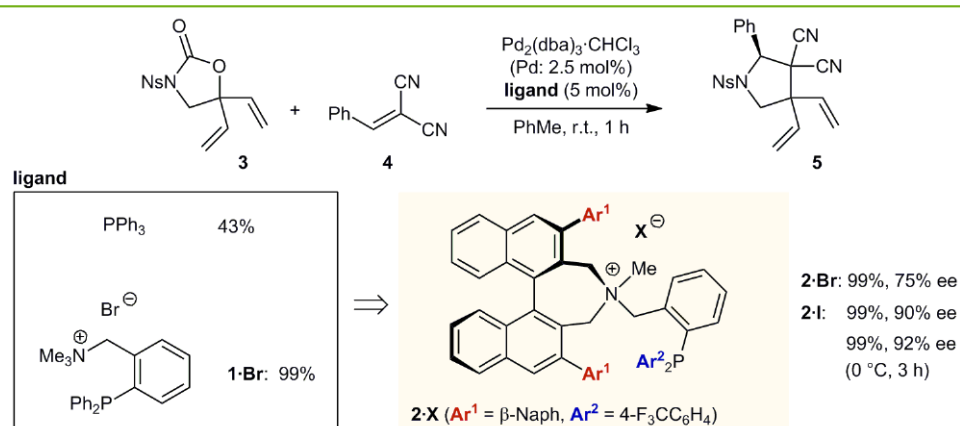


**Figure** Conceptual framework of multiple absolute stereocontrol in palladium-catalyzed cycloaddition for asymmetric construction of contiguous all-carbon quaternary stereocenters

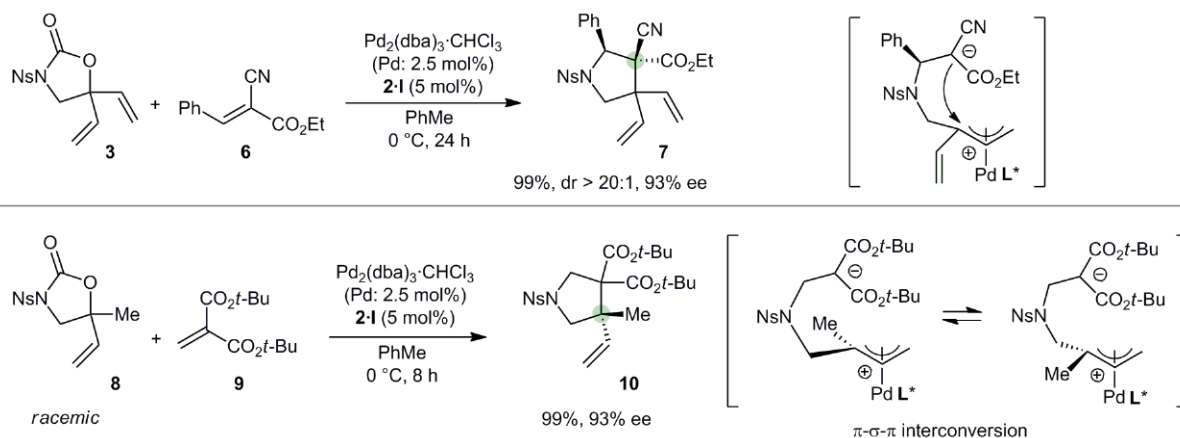
“To achieve such double absolute stereocontrol in a single cycloaddition process, we devised a new phosphine ligand with a pendant chiral ammonium salt **2·X**,” explained Professor Ooi. “The key idea for the design of this ligand came from the remarkable reactivity enhancement observed when we used ammonium phosphine **1·Br** as a palladium ligand instead of triphenylphosphine ( $\text{Ph}_3\text{P}$ ) in the cycloaddition of vinyloxazolidinone **3** with 2-benzylidenemalononitrile (**4**) (Scheme 1).” The evolution of achiral **1·Br** into chiral **2·Br** allowed the discrimination of the prochiral face of the alkene to afford the protected pyrrolidine **5** enantioselectively. Professor Ooi revealed that the optimization of the structure of **2·X** with regard to the aromatic substituents on the binaphthyl skeleton ( $\text{Ar}^1$ ) and phosphorus center ( $\text{Ar}^2$ ) was particularly challenging and the perseverance of the Japanese researchers was thoroughly tested. Finally, the identity of the halide ion ( $\text{X}$ ) was also found to be critical in enantiocontrol

and the use of **2·I** delivered the highest selectivity. Professor Ooi said: “We were very pleased with this finding because it showed that the cooperative participation of all the structural components of **2·I** in the stereodetermining event was essential, which clearly demonstrates the advantage of employing chiral organic ion pairs as metal ligands.”

With this new class of ion-paired chiral ligand in hand, the authors evaluated its potential for achieving individual absolute stereocontrol in two reaction settings that involve the construction of quaternary carbon stereocenters. Professor Ooi explained: “The enantiofacial discrimination of geometrically defined 2-cyano-3-phenylacrylate **6** under the influence of the palladium complex bearing **2·I** as a ligand also made it feasible to establish the adjacent quaternary stereocenter, as we initially expected.” He continued: “Moreover, ammonium phosphine **2·I** was capable of rigorously controlling the isomerization of the planar chiral  $\pi$ -allylpalladium intermediate

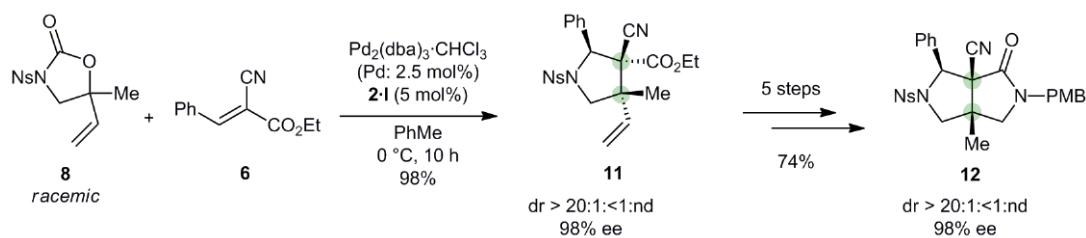


**Scheme 1** Development of new ion-paired chiral ligand



**Scheme 2** Examination of individual absolute stereocontrol





**Scheme 3** Asymmetric construction of contiguous all-carbon quaternary stereocenters via palladium-catalyzed [3+2] cycloaddition

through  $\pi$ - $\sigma$ - $\pi$  interconversion to install an additional quaternary stereocenter with a vinyl substituent (Scheme 2)."

As anticipated from the results illustrated in Scheme 2, chiral ammonium phosphine **2-I** paved the way to the asymmetric construction of contiguous all-carbon quaternary stereocenters via the [3+2] annulations of racemic oxazolidinones **8** with 2-cyano-3-phenylacrylate **6**, thereby offering a straightforward access to the stereochemically pure, densely substituted pyrrolidine **11** (Scheme 3). "The synthetic versatility of this catalytic system was amply demonstrated through the exploration of the substrate scope, scalability, and the product derivatization," said Professor Ooi. "For instance, the reaction of **8** with **6** on a 10 mmol scale was found to be complete in 48 hours even with a reduced amount of catalyst, yielding 4.7 grams of cycloadduct **11** with almost complete stereochemical control." He continued: "Furthermore, product **11** was successfully converted into the densely substituted bicyclic lactam **12**, which is the core structure of the analogue of thrombin inhibitors."

Professor Ooi concluded: "We have developed a highly enantio- and diastereoselective [3+2]-annulation reaction of 5-vinyloxazolidinones and activated trisubstituted alkenes catalyzed by a palladium complex bearing a newly devised phosphine ligand with a chiral ammonium salt component, which allows for the single-step construction of three contiguous stereocenters, including vicinal all-carbon quaternary stereocenters, on the pyrrolidine core. This protocol relies on the remarkable ability of the chiral onium-phosphine hybrid ligand to facilitate the intermolecular cycloaddition with precise control of the individual absolute stereochemistry across multiple bond formations, and represents a reliable catalytic process for the asymmetric synthesis of densely functionalized pyrrolidines and their derivatives." ■

Matteo Zanda

### About the authors



Prof. K. Ohmatsu

**Kohsuke Ohmatsu** was born in 1980 in Wakayama (Japan) and received his Ph.D. (2008) from Kyoto University (Japan) under the direction of Professor Keiji Maruoka. He was granted a Fellowship of the Japan Society for the Promotion of Sciences (JSPS) for Japanese Junior Scientists (2005–2008). He was appointed as assistant professor at Nagoya University (Japan) in 2008 and promoted to lecturer (2013). He was awarded the Akasaki Prize (2013), the ITbM research award (2013), and Chemical Society of Japan Lecture Award for Young Chemists (2014).



N. Imagawa

**Naomichi Imagawa** was born in 1988 in Nagoya (Japan). He received his B.S. degree in engineering from Nagoya University, where he conducted research in the laboratory of Professor Takashi Ooi. In 2011, he began graduate school at Nagoya University, where he is currently a fourth-year student in the Ooi lab.

>>



*Prof. T. Ooi*

**Takashi Ooi** was born in 1965 in Nagoya (Japan). He received his Ph.D. (1994) from Nagoya University under the direction of Professor Hisashi Yamamoto. He was granted a Fellowship of the Japan Society for the Promotion of Sciences (JSPS) for Japanese Junior Scientists (1992–1995), during which he joined the group of Professor Julius Rebek, Jr. at MIT (USA) as a postdoctoral fellow (1994–1995). He was appointed as an assistant professor at Hokkaido University (Japan) in 1995 and promoted to lecturer in 1998. He moved to Kyoto University (Japan) as an associate professor (2001), and became a full

professor of Nagoya University in 2006. He was awarded the Chugai Award in Synthetic Organic Chemistry, Japan (1997), the Japan Chemical Society Award for Young Chemist (1999), the Thieme Chemistry Journal Award (2006), the JSPS Prize (2010), the IBM Japan Science Prize (2011), and the Inoue Prize for Science (2013).

## Young Career Focus: Dr. Ken Maly (Wilfrid Laurier University, Waterloo, Canada)

■ **Background and Purpose.** *SYNFORM* will from time to time meet 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 *SYNSTORY* with a Young Career Focus presents Dr. Ken Maly, Wilfrid Laurier University, Waterloo, Canada.

### BIOGRAPHICAL SKETCH



Dr. K. Maly

**Ken Maly** was born near Boston, Massachusetts (USA) and grew up in Montreal, Canada. He obtained his B.Sc. in chemistry at Queen's University in Kingston, Ontario, Canada in 1997. He then continued his studies at Queen's, conducting his Ph.D. with

Professor Robert Lemieux, where he worked on the synthesis of photochromic compounds for use in ferroelectric liquid crystals. After completing his Ph.D. in 2002, he held a Natural Sciences and Engineering Council of Canada (NSERC) Postdoctoral Fellowship at the Université de Montréal in Montreal, Quebec (Canada) with Professor James D. Wuest. His postdoctoral work focused on the design and synthesis of compounds that self-assemble in predictable ways using non-covalent interactions such as hydrogen bonding. In 2006, he started his independent career at Wilfrid Laurier University in Waterloo, Ontario (Canada). His current research focuses on the design and synthesis of novel aromatic compounds and the investigation into how these compounds self-assemble. His work has been recognized with an Ontario Early Researcher Award and a Thieme Chemistry Journal Award, and is also currently funded by the Natural Sciences and Engineering Research Council of Canada (NSERC) and the American Chemical Society Petroleum Research Fund.

### INTERVIEW

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

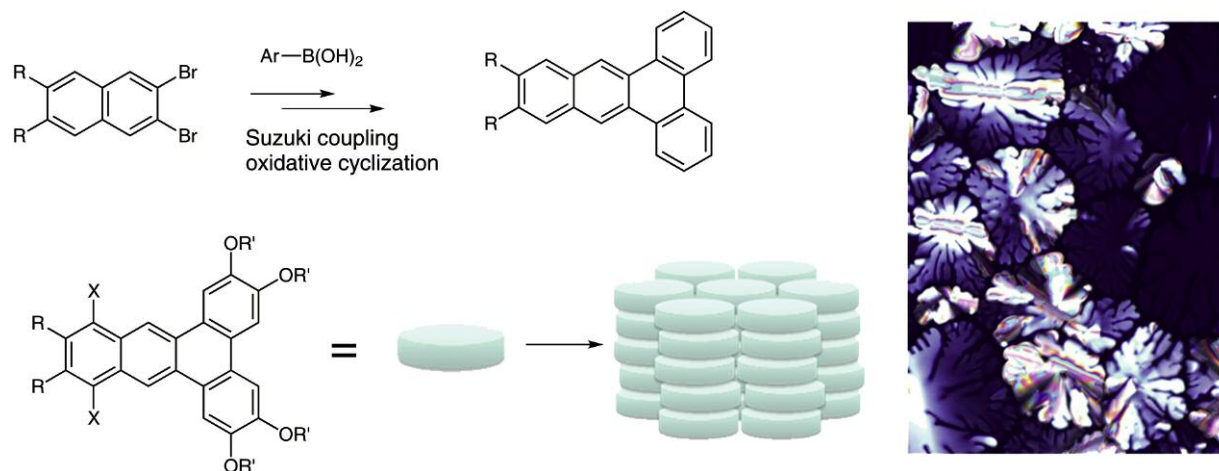
**Dr. Ken Maly** | My research focuses on the synthesis and studies of the self-assembly of new aromatic compounds. Specifically, my interests are in preparing substituted polycyclic aromatic hydrocarbons that can exhibit columnar liquid crystalline phases, as well as preparing microporous materials from rigid aromatic compounds. Both of these research areas involve extensive molecular design and multistep organic synthesis. I also seek to understand how these compounds self-associate, and hope to exploit this understanding for the preparation of functional materials.

**SYNFORM** | *When did you get interested in synthesis?*

**Dr. Ken Maly** | I became interested in synthesis when I took my first course in organic chemistry. I found all aspects of the subject fascinating, from fundamental structure and structure elucidation, to reaction mechanisms and multistep syntheses. As a graduate student, I found the design and construction of complex molecules using organic reactions to be intellectually appealing. At the same time, while the lab work was often challenging, the feeling of finally obtaining a target compound was incredibly rewarding.

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

**Dr. Ken Maly** | Organic synthesis has long focused on the total synthesis of natural products or the preparation of other biologically active compounds, and the development of methods related to these goals. While nature provides complex structural targets that will continue to challenge synthetic chemists, I believe that organic chemists have an increasingly important role to play in the preparation of new materials. Through organic synthesis, we have the opportunity to access tremendous structural diversity that is limited only by our imagination and to tune properties based on changes in molecular structure.



**SYNFORM** | *Your research group is active at the frontier of materials science, supramolecular chemistry, and organic synthesis. Can you tell us more about your research and its aims?*

**Dr. Ken Maly** | One of the main goals of my research is to prepare compounds that exhibit liquid crystalline phases. Liquid crystal phases are intermediate states of matter between crystalline solids and isotropic liquids that are characterized by some degree of order while maintaining fluidity and molecular motions that are characteristic of liquids. Specifically, I am interested in preparing disk-shaped compounds that stack in columnar liquid crystalline phases. These materials can often exhibit semiconducting properties that make them potentially useful for organic electronics. The disk-shaped compounds are typically polycyclic aromatic hydrocarbons that are substituted with several peripheral flexible chains. Despite the fact that these discotic liquid crystals have been known since 1977, the influence of molecular structure on liquid crystalline properties (such as the phase temperature range) is not well understood. One of the aims of my research is to understand the structure–property relationships in these systems through systematic structural variations. Recently, we have focused our attention on alkoxy-substituted trinaphthylenes and dibenz[a,c]anthracenes and shown that the liquid crystal phase range is remarkably sensitive to small structural variations. Our current efforts are directed at preparing derivatives of acenequinones and exploring their liquid crystalline properties.

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

**Dr. Ken Maly** | As a relatively junior researcher, I would like to think that my biggest achievements lie ahead of me. Indeed – some of our recent unpublished results appear to be very exciting and may be prime candidates. However, looking back, one of my most important achievements was the synthesis of some of the first substituted trinaphthylenes. Although the compounds themselves did not display any liquid crystalline properties, I am proud of the synthetic approach, which notably was done entirely with the assistance of an undergraduate student. These compounds were also significant because they encouraged me to look further into how structural changes influenced liquid crystallinity. ■

**Matteo Zanda**

COMING SOON ►► COMING SOON ►►

SYNFORM 2014/07

is available from June 16, 2014

In the next issues:

## SYNSTORIES ■ ■ ■ ■

■ **Extracellular Palladium-Catalyzed Dealkylation of 5-Fluoro-1-propargyl-uracil as a Bioorthogonally Activated Prodrug Approach**  
(Focus on an article from the current literature)

■ **Nickel-Catalyzed Reductive and Borylative Cleavage of Aromatic Carbon–Nitrogen Bonds in *N*-Aryl Amides and Carbamates**  
(Focus on an article from the current literature)

■ **Remote Activation of the Nucleophilicity of Isatin**  
(Focus on an article from the current literature)

## FURTHER HIGHLIGHTS + + + +

## SYNTHESIS

**Review on: [Dehydrogenative Heck Annulations of Internal Alkynes](#)**

(by J. Le Bras, J. Muzart)

## SYNLETT

**Account on: [Trifluoromethylated Internal Alkynes: Versatile Building Blocks for the Preparation of Various Fluorine-Containing Molecules](#)**

(by T. Konno)

## SYNFACTS

**Synfact of the Month in category “Metal-Mediated Synthesis”:  
[Enantioselective Allene Addition to Aryl and Alkyl Imines](#)**

## CONTACT + + + +

Matteo Zanda,  
NRP Chair in Medical Technologies  
Institute of Medical Sciences  
University of Aberdeen  
Foresterhill, Aberdeen, AB25 2ZD, UK  
and

C.N.R. – Istituto di Chimica del Riconoscimento Molecolare,  
Via Mancinelli, 7, 20131 Milano, Italy,  
e-mail: [synform@outlook.com](mailto:synform@outlook.com), fax: +39 02 23993080

## Editor

Matteo Zanda, NRP Chair in Medical Technologies, Institute of Medical Sciences, University of Aberdeen, Foresterhill, Aberdeen, AB25 2ZD, UK and

C.N.R. – Istituto di Chimica del Riconoscimento Molecolare  
Via Mancinelli, 7, 20131 Milano, Italy  
Editorial Assistant: Alison M. Sage  
[synform@outlook.com](mailto:synform@outlook.com); fax: +39 02 23993080

## Editorial Office

- Managing Editor: Susanne Haak,  
[susanne.haak@thieme.de](mailto:susanne.haak@thieme.de), phone: +49 711 8931 786
- Scientific Editor: Selena Boothroyd,  
[selena.boothroyd@thieme.de](mailto:selena.boothroyd@thieme.de)
- Scientific Editor: Stefanie Baumann,  
[stefanie.baumann@thieme.de](mailto:stefanie.baumann@thieme.de), phone: +49 711 8931 776
- Assistant Scientific Editor: Michael Binanzer,  
[michael.binanzer@thieme.de](mailto:michael.binanzer@thieme.de), phone: +49 711 8931 768
- Assistant Scientific Editor: Christiane Kemper,  
[christiane.kemper@thieme.de](mailto:christiane.kemper@thieme.de), phone: +49 711 8931 785
- Senior Production Editor: Thomas Loop,  
[thomas.loop@thieme.de](mailto:thomas.loop@thieme.de), phone: +49 711 8931 778
- Production Editor: Helene Ott,  
[helene.ott@thieme.de](mailto:helene.ott@thieme.de), phone: +49 711 8931 929
- Production Editor: Thorsten Schön,  
[thorsten.schoen@thieme.de](mailto:thorsten.schoen@thieme.de), phone: +49 711 8931 781
- Editorial Assistant: Sabine Heller,  
[sabine.heller@thieme.de](mailto:sabine.heller@thieme.de), phone: +49 711 8931 744
- Marketing Manager: Julia Stötzner,  
[julia.stoetznern@thieme.de](mailto:julia.stoetznern@thieme.de), phone: +49 711 8931 771
- Postal Address: SYNTHESIS/SYNNLETT/SYNFACTS, Editorial Office,  
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany,
- Homepage: [www.thieme-chemistry.com](http://www.thieme-chemistry.com)

## Publication Information

SYNFORM will be published 12 times in 2014 by Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany, and is an additional online service for SYNTHESIS, SYNLETT and SYNFACTS.

## Publication Policy

Product names which are in fact registered trademarks may not have been specifically designated as such in every case. Thus, in those cases where a product has been referred to by its registered trademark it cannot be concluded that the name used is public domain. The same applies as regards patents or registered designs.

## Ordering Information for Print Subscriptions to SYNTHESIS, SYNLETT and SYNFACTS

The Americas: Thieme Publishers New York, Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.

To order: [customerservice@thieme.com](mailto:customerservice@thieme.com) or use the Web site facilities at [www.thieme-chemistry.com](http://www.thieme-chemistry.com), phone: +1 212 760 0888

Order toll-free within the USA: +1 800 782 3488

Fax: +1 212 947 1112

Periodicals postage paid at Hanover, PA 17331.

Europe, Africa, Asia, and Australia: Thieme Publishers Stuttgart, Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany.

To order: [customerservice@thieme.de](mailto:customerservice@thieme.de) or use the Web site facilities at [www.thieme-chemistry.com](http://www.thieme-chemistry.com).

Phone: +49 711 8931 421; Fax: +49 711 8931 410

Current list prices are available through [www.thieme-chemistry.com](http://www.thieme-chemistry.com).

## Online Access

The online versions of SYNFORM as well SYNTHESIS, SYNLETT and SYNFACTS are available through Thieme-connect ([www.thieme-connect.com/ejournals](http://www.thieme-connect.com/ejournals)) where you may also register for free trial accounts. For information on multi-site licenses and pricing for corporate customers as well as backfiles please contact our regional offices:

The Americas: [esales@thieme.com](mailto:esales@thieme.com), phone: +1 212 584 4695

Europe, Africa, Asia, and Australia: [eproducts@thieme.de](mailto:eproducts@thieme.de), phone: +49 711 8931 407

India: [eproducts@thieme.in](mailto:eproducts@thieme.in), phone +91 120 45 56 600

Japan: [brhosoya@poplar.ocn.ne.jp](mailto:brhosoya@poplar.ocn.ne.jp), phone +81 3 3358 0692

## Manuscript Submission to SYNTHESIS and SYNLETT

Please consult the Instructions for Authors before compiling a new manuscript. The current version and the Word template for manuscript preparation are available for download at [www.thieme-chemistry.com](http://www.thieme-chemistry.com). Use of the Word template helps to speed up the refereeing and production process.

## Copyright

This publication, including all individual contributions and illustrations published therein, is legally protected by copyright for the duration of the copyright period. Any use, exploitation or commercialization outside the narrow limits set by copyright legislation, without the publisher's consent, is illegal and liable to criminal prosecution. This applies translating, copying and reproduction in printed or electronic media forms (databases, online network systems, Internet, broadcasting, telecasting, CD-ROM, hard disk storage, microcopy edition, photomechanical and other reproduction methods) as well as making the material accessible to users of such media (e.g., as online or offline backfiles).

## Copyright Permission for Users in the USA

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by Georg Thieme Verlag KG Stuttgart · New York for libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that the base fee of US\$ 25.00 per copy of each article is paid directly to CCC, 22 Rosewood Drive, Danvers, MA 01923, USA, 0341-0501/02.