

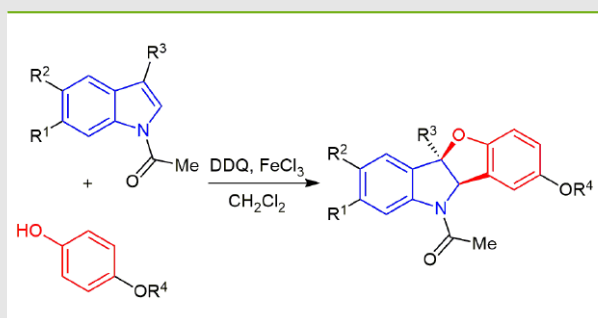
# SYNFORM

People, Trends and Views in Chemical Synthesis

2015/02

## SYNSTORIES ■ ■ ■ ■

■ **Coupling of Indoles and Phenols in Oxidative Conditions for the Synthesis of Benzofuro[3,2-*b*]indolines**



■ **Mild and Versatile Nitrate-Promoted C–H Bond Fluorination**

■ **Catalytic Enantioselective Alkylation of Sulfenate Anions to Chiral Heterocyclic Sulfoxides Using Halogenated Pentanidium Salts**

■ **Young Career Focus:  
Dr. Jonathan Sperry (University  
of Auckland, New Zealand)**

**CONTACT +++++**

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**Dear Readers,**

Although this Editorial will be published in the February issue of **SYNFORM**, the truth is that I am writing it soon after the Christmas and New Year celebrations, which I have spent in Italy. Like most of you, I have eaten

and drunk way too much and I suspect I have put on quite some weight as a consequence of the many lunches and dinners with relatives and friends. Now I am facing a period whereby I will necessarily have to keep my gastronomic exuberance under control, which doesn't make me too happy... Let's try to put aside food and drinks for a while then, and focus on something else, if possible. Let's concentrate on good chemistry, such as that described in this new issue of **SYNFORM**. We start with a novel fluorination procedure discovered by D.-Q. Xu and Z.-Y. Xu (P. R. of China) and continue with a Young Career Focus where J. Sperry (New Zealand) is the protagonist. A novel catalytic enantioselective synthesis of heterocyclic sulfoxides developed by C.-H. Tan (Singapore) comes next, and the issue is closed by the oxidative coupling of indoles with phenols discovered by G. Vincent (France). There is undoubtedly excellent science in this issue, but now I am starting to feel a bit hungry, wondering what's for dinner... I have just decided that the diet can wait...

Enjoy your reading!

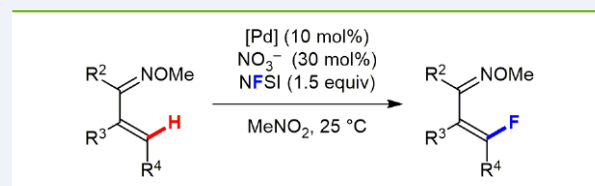
**Matteo Zanda**

*Editor of SYNFORM*

## IN THIS ISSUE

### SYNSTORIES ■ ■ ■ ■

**Mild and Versatile Nitrate-Promoted C–H Bond Fluorination** .....A20



**Young Career Focus: Dr. Jonathan Sperry (University of Auckland, New Zealand)** .....A23

**Catalytic Enantioselective Alkylation of Sulfenate Anions to Chiral Heterocyclic Sulfoxides Using Halogenated Pentanidium Salts** .....A25

**Coupling of Indoles and Phenols in Oxidative Conditions for the Synthesis of Benzofuro [3,2-*b*]indolines** .....A28

**COMING SOON** .....A31

**CONTACT + + + +**

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

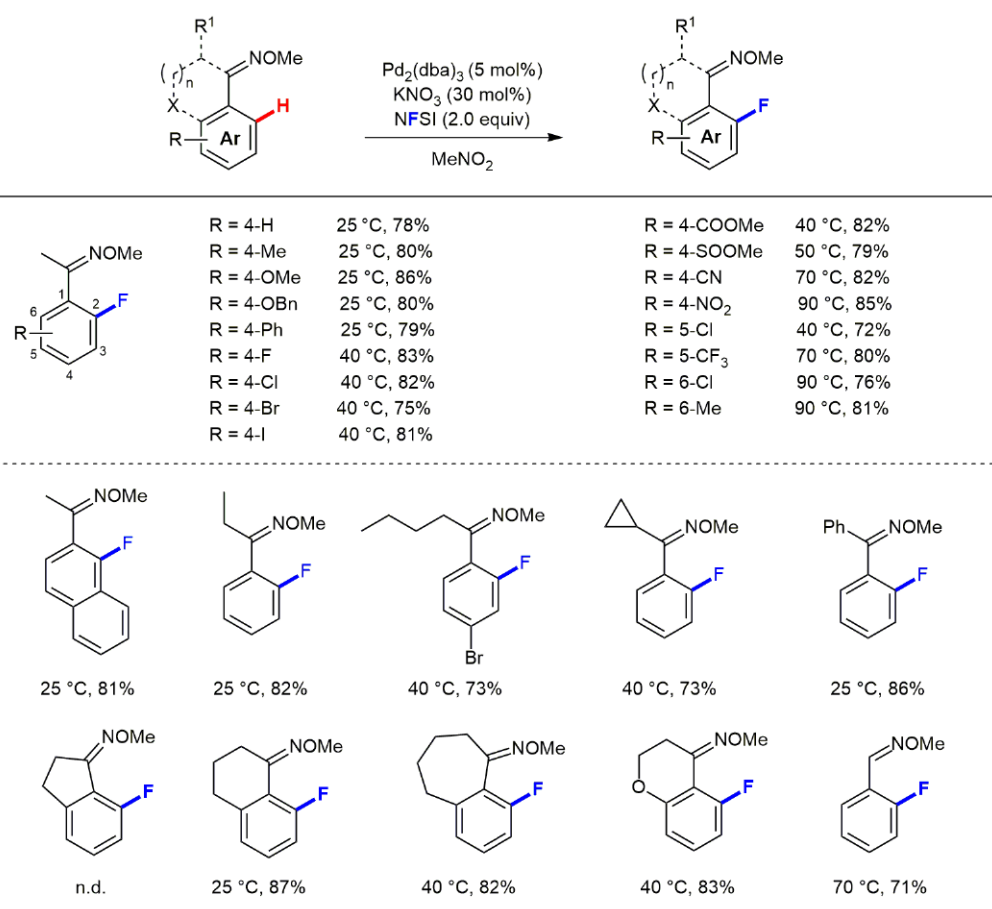
# Mild and Versatile Nitrate-Promoted C–H Bond Fluorination

*Angew. Chem. Int. Ed.* **2014**, *53*, 10330–10335

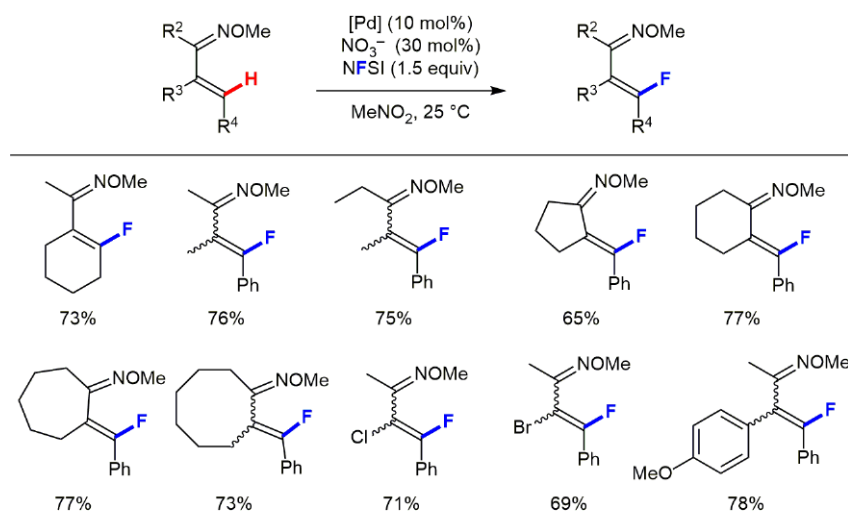
Carbon–fluorine bond construction has consistently been of great interest to chemists due to the unique characteristics of fluorinated molecules and the synthetic challenges connected with the introduction of fluorine into organic molecules. Apart from the *ipso*-fluorination of pre-functionalized substrates, C–H bond fluorination is a prospective alternative and has received a great deal of attention in recent years. However, several challenges, for example, relatively harsh conditions, excess amounts of fluorinating agents (oxidants), narrow substrate scopes and poor selectivity still need to be addressed for this emerging area. Given the broad application of fluorinated

compounds in pharmaceuticals, agrochemicals and materials, a mild and versatile C–H bond fluorination protocol is highly desirable. Very recently, a novel and facile nitrate-promoted regioselective fluorination of aromatic and olefinic  $sp^2$ -C–H bonds under mild conditions was described by Professors Dan-Qian Xu and Zhen-Yuan Xu, and Dr. Shao-Jie Lou from Zhejiang University of Technology (P. R. of China).

Generally, the fluorination reactions took place under very mild conditions (close to room temperature in most cases). Professor D.-Q. Xu said: “Conventionally, C–H bond fluorination requires harsh conditions with respect to the great



**Scheme 1** Aromatic C–H bond fluorination



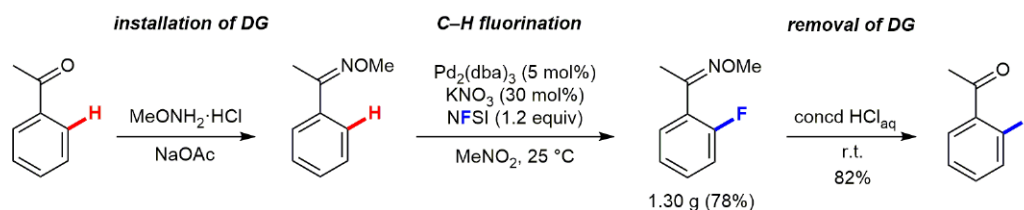
**Scheme 2** Olefinic C–H bond fluorination

strength of both C–H and C–F bonds, so we were delighted to find that the current palladium-nitrate catalytic system enabled the process in a much milder manner.”

“A catalytic amount of simple, non-toxic and cheap potassium nitrate served as a highly efficient promoter,” said Professor D.-Q. Xu. “Actually, silver nitrate was found to be an efficient additive for this transformation at the outset of this program,” she explained. Since silver salts were demonstrated to be incorporated in several C–F bond formation reactions, various silver salts were then screened. However, only silver nitrate and silver nitrite could successfully promote the reaction, whereas other silver salts were ineffective. Professor Z.-Y. Xu said: “The unique counter-anion effect led us to hypothesize that the nitrate anion might be the pivotal promoter. To our delight, nitrates were finally found to exhibit a unique ligand effect in this catalytic fluorination protocol.” He continued: “Though the actual role of the nitrate is still not clear at this stage, we proposed that a highly active cationic  $\text{Pd}(\text{NO}_3)^+$

was generated in situ and initialized the C–H activation under mild conditions. Meanwhile, the poorly nucleophilic nitrate additives might also be responsible for the selective reductive elimination of the C–F bond from the Ar–Pd(IV)–F intermediate (*Angew. Chem. Int. Ed.* **2011**, *50*, 1478).”

The process shows a remarkably broad substrate scope for both aromatic and olefinic  $\text{sp}^2$ -C–H bonds. In general, both electron-donating and electron-withdrawing functional groups were well tolerated by cautiously adjusting the reaction temperature of the aromatic C–H bond fluorination. Moreover, good mono-/di-fluorination selectivity could also be achieved by controlling the reaction temperature. Professor D.-Q. Xu said: “Notably, the first example of chelation-assisted olefinic  $\text{sp}^2$ -C–H bond fluorination was also reported in this paper. Various functionalities, for example, alkyl-, halo-, and aryl-substituted  $\alpha,\beta$ -unsaturated oximes were well tolerated and furnished the  $\beta$ -fluorinated products in good yields at room temperature.



**Scheme 3** C–H fluorination of ketones

In addition, the oximyl directing group can be efficiently installed or removed, which would provide opportunities for further derivatization of the fluorinated ketone products. Gram-scale C–H bond fluorination proceeded smoothly with a reduced loading of fluorinating agent.

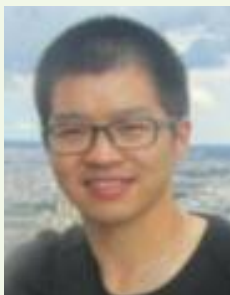
Professor Z.-Y. Xu said: “Given the mild conditions and universality of this method, the present fluorination protocol may enable the late-stage fluorination of more complex sub-

strates without touching the other functional groups. Attempts to apply this system to more substrates are ongoing in our lab.

In conclusion, we have developed a novel nitrate-promoted fluorination system, which features broad substrate scope, good functional group tolerance and simple operations,” said Professor D.-Q. Xu. “It should pave the way for mild and versatile C–H bond fluorination in synthetic and pharmaceutical chemistry.” ■

Matteo Zanda

### About the authors



Dr. S.-J. Lou

**Shao-Jie Lou** was born in Zhejiang (P. R. of China) in 1985. He received his BSc in 2008 and PhD in 2013 under the guidance of Professor Dan-Qian Xu at Zhejiang University of Technology (P. R. of China). Then he continued to work in the Catalytic Hydrogenation Research Center at Zhejiang University of Technology as a postdoctoral fellow with Professor Dan-Qian Xu in 2013. His research interest concerns transition-metal-catalyzed C–H bond functionalization.



Prof. D.-Q. Xu

**Dan-Qian Xu** was born in Zhejiang (P. R. of China) in 1963. She obtained her BSc in chemistry from East China Normal University (P. R. of China) in 1986 and her PhD in industrial catalysis under the guidance of Professor Yin-Chu Shen at Zhejiang University of Technology (P. R. of China) in 2005. In 2001, she was promoted to Professor. Her research interests include organocatalysis, transition-metal catalysis and fine chemicals. She has received several honors and awards, including the ‘Million Talents Projects’ (2007) sponsored by the Ministry of Personnel and two awards for National Progress in Science and Technology (2001 and 2005).



Prof. Z.-Y. Xu

After receiving his Bachelor’s degree at Beijing Agricultural University (P. R. of China) in 1963, **Zhen-Yuan Xu** directly joined the Faculty of the Beijing Agricultural University (P. R. of China). In 1976, he joined the faculty at Northwestern University (P. R. of China). Since 1985, he has been a member of the faculty of Zhejiang University of Technology (P. R. of China) where he was promoted to Professor of Chemistry in 1988. Professor Xu has received numerous awards, including one award for National Invention (1989), four awards for National Progress in Science and Technology (1991, 1997, 2001, and 2005), and one award for Chinese Outstanding Patented Invention (2009).

## Young Career Focus: Dr. Jonathan Sperry (University of Auckland, New Zealand)

■ **Background and Purpose.** From time to time *SYNFORM* 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 *SYNSTORY* with a Young Career Focus presents Dr. Jonathan Sperry (University of Auckland, New Zealand).

### BIOGRAPHICAL SKETCH



Dr. J. Sperry

**Jonathan Sperry** obtained his BSc (Hons) (2002) and PhD (2006, Professor Chris Moody) from the University of Exeter (UK). He spent 3.5 years as a postdoctoral researcher with Professor Margaret Brimble at the University of Auckland (New Zealand), before taking up a lectureship at the same institution in 2009, where he is currently a Senior Lecturer and a Rutherford Discovery Fellow.

### INTERVIEW

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

**Dr. J. Sperry** | My research group focuses on three main areas: (1) organic synthesis, with particular emphasis on the total synthesis of alkaloids that possess unprecedented molecular architecture, biomimetic synthesis, C–H functionalization and novel reaction development; (2) medicinal chemistry, focusing on the development of novel antibiotics and small molecules that hinder the tumor metastasis process, and (3) sustainable synthetic processes and the use of biomass-derived building blocks in the construction of important structural motifs.

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

**Dr. J. Sperry** | At secondary school, when my chemistry teacher explained the important role of synthetic chemistry during both World Wars and in particular, Robinson's biomimetic synthesis of tropinone.

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

**Dr. J. Sperry** | I am optimistic about the future of organic synthesis as it will always play a pivotal role in the natural and technical sciences. Organic synthesis is constantly progressing and recent advances in areas such as organo- and photoredox catalysis, C–H functionalization and flow chemistry have contributed significantly to the ongoing evolution of the field. However, there is room for further innovation and I always enjoy reading reports that address our overreliance on protecting groups and toxic reagents. Biorenewable syntheses of commodity chemicals that are currently sourced from fossil fuels also draw my attention.

**SYNFORM** | *Your research group is active in the areas of organic synthesis, medicinal chemistry and green chemistry. Could you tell us more about your research and its aims?*

**Dr. J. Sperry** | We are currently working on the biomimetic synthesis of the alkaloids yuremamine,<sup>1</sup> dendridine A<sup>2</sup> and sciadole<sup>3</sup> (Figure 1, **A**). In these projects, we have proposed a biosynthesis for each of these natural products, which we are attempting to validate in the laboratory through synthesis. We are also interested in the synthesis of alkaloids using novel synthetic processes, three of which include iheyamine B,<sup>4</sup> bufoserotonin C<sup>5</sup> and spiroindimicin B<sup>6</sup> (Figure 1, **B**). In our medicinal chemistry research, we are involved in the development of novel antibiotics through selective inhibition of the bacterial enzyme pyruvate kinase<sup>7</sup> and we are also exploring ways small molecules can inhibit tumor metastasis processes. Incorporating biomass-derived building blocks during the synthesis of fine and commodity chemicals<sup>8</sup> is also under investigation.

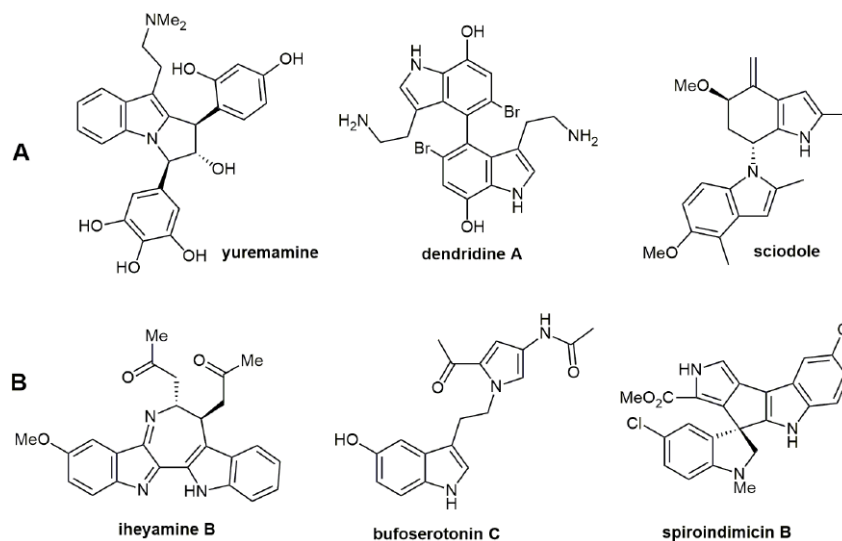
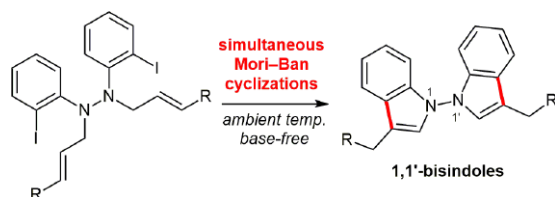


Figure 1

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

**Dr. J. Sperry** | Developing a general synthetic approach to 1,1'-bisindoles (Scheme 1).<sup>9,10</sup> This new methodology relied on several diallylated hydrazobenzenes undergoing two simultaneous Mori–Ban cyclizations to construct both heterocycles in a single step with minimal N–N bond cleavage. Despite the bisindolization being conducted under reductive conditions, the ‘normal’ Heck products were obtained, inferring that the  $\beta$ -hydride elimination occurs faster than the reduction step. We also constructed 1,1'-bistryptophan using this methodology, and showed that the 1,1'-bisindole is a sturdy heteroaromatic motif that is capable of surviving lengthy synthetic sequences and a variety of different reaction conditions.



Scheme 1

Matteo Zanda

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# Catalytic Enantioselective Alkylation of Sulfenate Anions to Chiral Heterocyclic Sulfoxides Using Halogenated Pentanidium Salts

*Angew. Chem. Int. Ed.* **2014**, *53*, 11849–11853

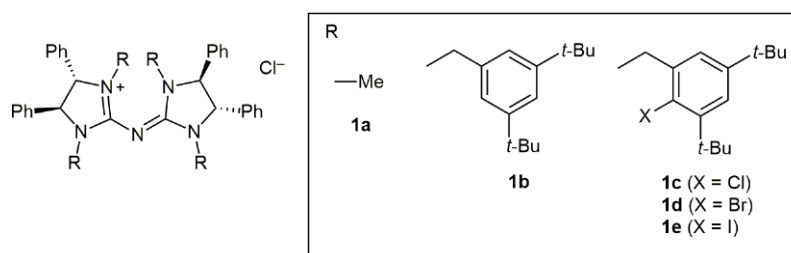


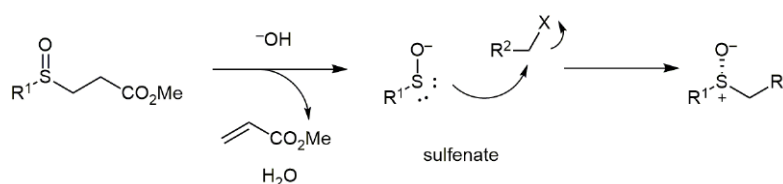
Figure 1

■ Sulfoxides of high stereochemical purity are widely used in organic synthesis as organocatalysts, ligands, and chiral auxiliaries. Molecules incorporating a sulfinyl group are also important in medicinal chemistry, as witnessed by the presence on the market of important drugs such as esomeprazole, armodafinil, and sulindac, which belong to the sulfoxide family.

The group of Professor C.-H. Tan at the Nanyang Technological University (Singapore) has been interested in Brønsted base catalyzed enantioselective reactions for many years. Professor Tan explained: “We have utilized bicyclic guanidine to demonstrate the wide applicability of this class of catalysts (*Synlett* **2010**, 1589). Building on this work, we became interested in creating a ‘super-guanidine’ and found that such moieties are efficient phase-transfer catalysts when fully alkylated (Figure 1).” The catalyst is highly amenable to variation by changing its R groups, and the term ‘pentanidium’ was coined to describe this new catalyst structure in the

initial report (*J. Am. Chem. Soc.* **2011**, *133*, 2828). “We were so excited when we found that this catalyst can work at low catalyst loading of 0.02 mol%! This is the most efficient catalytic system that we have found in our laboratory,” said Professor C.-H. Tan.

From a synthetic perspective, explained Professor C.-H. Tan, this work represents a breakthrough in exploiting nucleophilic sulfenate (Scheme 1) as a viable methodology in the asymmetric synthesis of sulfoxide in high optical purity. “This should be complementary to current methodologies based on an electrophilic sulfur center (Andersen method and its variants) and oxidation of sulfide,” he said. “In particular, sulfoxides with heterocycles that are sensitive to oxidation and organo-magnesium reagents could be synthesized.”



Scheme 1



The reaction optimization was performed solely by Dr. Lili Zong. “Initially, I used pentanidium **1b** (Scheme 1) for development, but the desired sulfoxide was formed with only a moderate level of enantioselectivity. It was frustrating and discouraging because extensive variation of reaction parameters could not increase the ee value,” said Lili. “Based on recent work by the groups of Professors Huber and Bolm, I was motivated to synthesize the halogenated analogue of **1b** and, to my delight, much better results in terms of yield and ee value were obtained with **1d** and **1e**.” The additional halogen-bonding non-covalent interaction was preliminarily postulated, and the synergistic effect within the halogenated pentanidium provided an enhanced asymmetric induction in the reaction processes.

Dr. Choon Wee Kee performed the computational work. “After listening to Lili when she reported her work during our group meeting and together with my experience with halogen bonds from my time with Professor Wong at the National University of Singapore, I was immediately convinced that halogen bonds could be important in the transition states (TS). This motivated me to study the reaction computationally,” said Dr. Choon Wee Kee.

From the calculations, a halogen bond between the iodine of the catalyst and the leaving bromide in the TS is indeed evident (Figure 2). The halogen bond was estimated to provide

6.6 kcal/mol of stabilization. In addition, multiple non-classical hydrogen bonds are also found to provide stabilizing non-covalent interactions in the TS.

“Halogen bonds are often regarded as similar to hydrogen bonds in terms of directionality and interaction energies and have found widespread applications in supramolecular chemistry and medicinal chemistry,” said Professor C.-H. Tan. “However, in contrast to the ubiquitous application of hydrogen bonds in organocatalysis, the use of halogen bonds is relatively less common; thus, this work provides a rare example in which there is theoretical evidence that a halogen bond is involved in the TS of an enantioselective reaction.”

“In conclusion, we have found a novel methodology to synthesize valuable sulfoxides of high optical purity and demonstrated the feasibility of halogen bonding in asymmetric organocatalysis via theoretical calculations,” said Professor Tan. “It is satisfying to know that sulfenate, an active intermediate, can be stabilized using halogen bonding and be directed towards a productive reaction,” added Dr. Choon Wee Kee. ■

Matteo Zanda

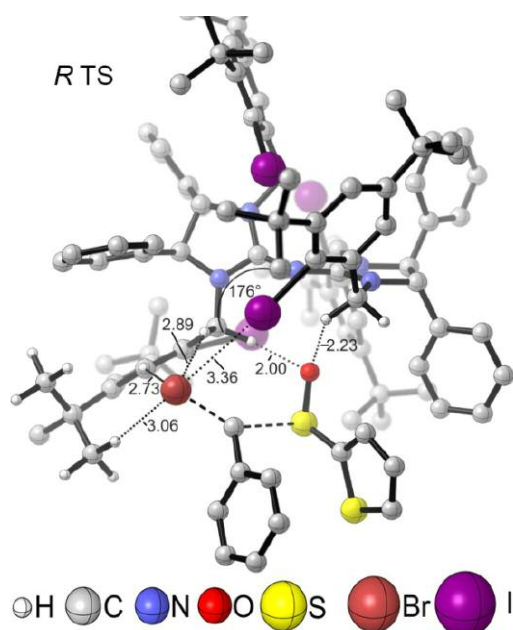


Figure 2

### About the authors



From left to right: Dr. C. W. Kee, Prof. C.-H. Tan, Dr. L. Zong

**Lili Zong** obtained her Bachelor's degree from Harbin Institute of Technology (P. R. of China) in 2006 and then her Master's degree in organic chemistry from Nanjing University (P. R. of China) in 2009. She received her PhD from National University of Singapore (Singapore) in 2014 and will join Professor Choon-Hong Tan's group as a research follow.

**Choon Wee Kee** was born in 1984 in Singapore. He received his BSc (1<sup>st</sup> class honours in chemistry) from the National University of Singapore in 2009 and performed research under the guidance of Dr. Zhao Jin as an undergraduate and also a research assistant. He was the valedictorian for the chemistry class of 2009. He performed both experimental and computational research as a graduate student under the supervision of Professors Choon-Hong Tan and Ming Wah Wong. He received his PhD in 2014.

**Choon-Hong Tan** graduated with a PhD from the University of Cambridge (UK) in 1999 under the supervision of Professor Andrew Holmes. Following that, he carried out postdoctoral training at Harvard University (USA). Subsequently, he worked as a Research Associate at Harvard Medical School (USA) before joining the National University of Singapore as Assistant Professor. He moved to Nanyang Technological University (Singapore) in 2012.

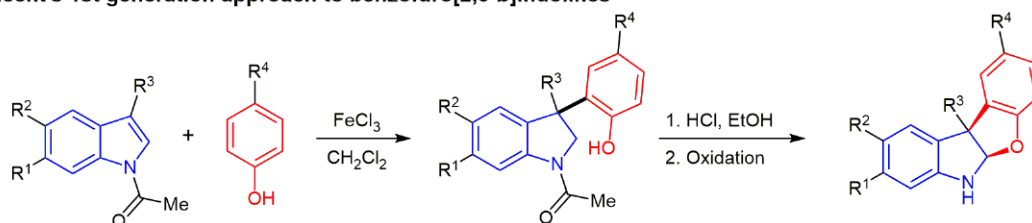
## Coupling of Indoles and Phenols under Oxidative Conditions for the Synthesis of Benzofuro[3,2-*b*]indolines

*Angew. Chem. Int. Ed.* **2014**, *53*, 11881–11885

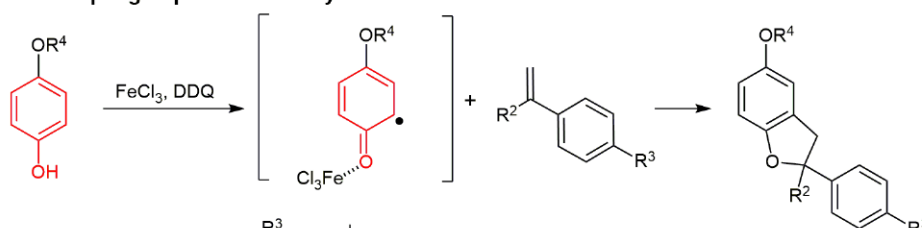
■ The group of Dr. Guillaume Vincent at the Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO) of Université Paris-Sud and CNRS (France) has been interested over the last four years in the development of new synthetic methods towards benzofuroindoline-containing frameworks which can be found in about a dozen natural products. "Their biosynthesis implies the oxidative coupling of indoles and phenols," explained Dr. Vincent. "In most cases this biogenetic annulation leads to the formation of a C–C bond between the C3- and *ortho*-positions of the indole and of the phenol, respectively, as well as a C–O bond between the C2-position of the indole and the oxygen of the phenol." Diazonamide A is the most famous compound of this family of benzofuro[2,3-*b*]indoline-containing natural products, displaying highly

promising anticancer activities. "Interestingly, to date, only one natural product, called phalarine, displays the regioisomeric benzofuro[3,2-*b*]indoline skeleton," said Dr. Vincent. The synthesis of benzofuro[3,2-*b*]indolines has been studied extensively. "One of the main achievements in this field is the biomimetic total synthesis of diazonamide A by Harran and co-workers (*Angew. Chem. Int. Ed.* **2003**, *42*, 4961)," acknowledged Dr. Vincent, "which relied on the hypervalent iodine mediated oxidation of a phenol and the intramolecular trapping of the resulting phenoxenium intermediate by a nucleophilic indole." He continued: "Other methods which take advantage of the nucleophilicity of the C3-position of indoles have also been reported. However, we felt that complementary and general methods to access these heterocycles

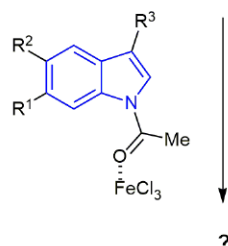
### Vincent's 1st generation approach to benzofuro[2,3-*b*]indolines



### Lei's oxidative coupling of phenols and styrenes



### The new approach

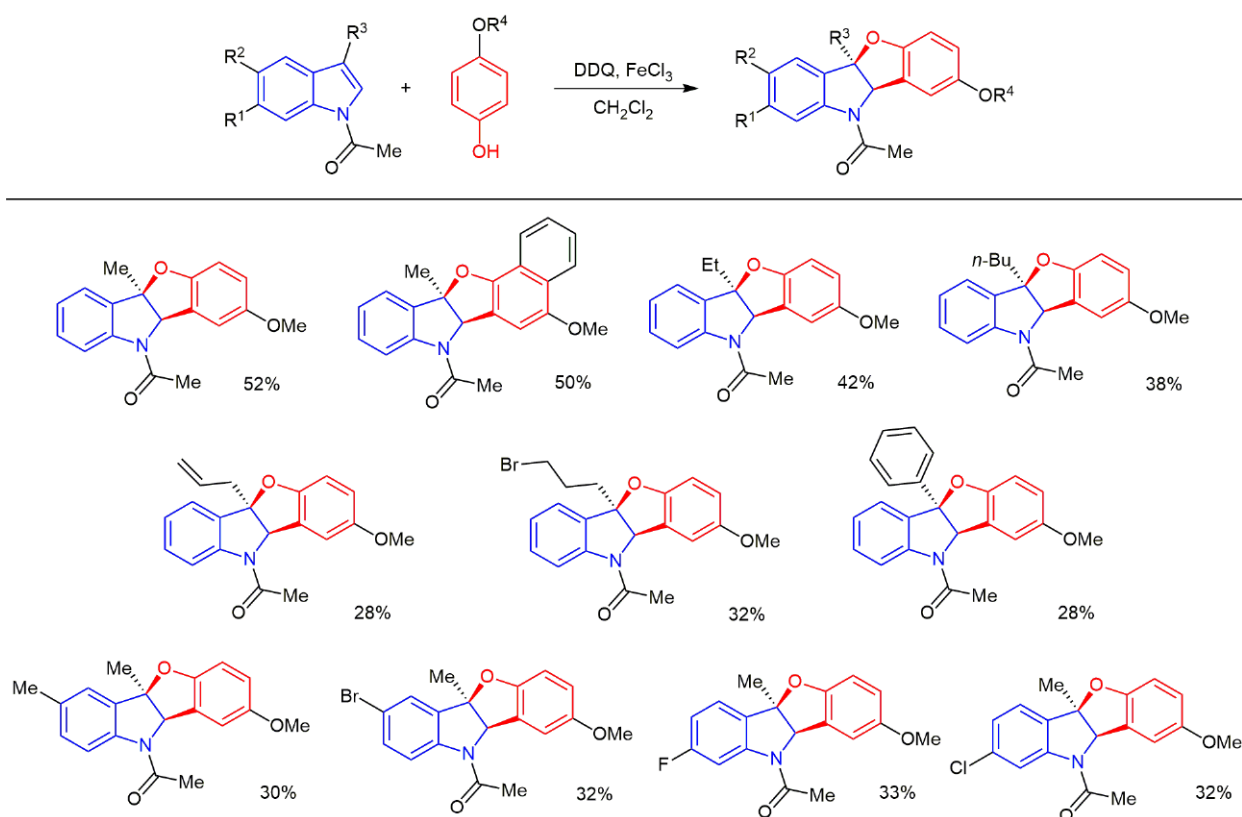


Scheme 1

were needed.” In 2012, Dr. Vincent’s team reported a two-stage strategy towards benzofuro[3,2-*b*]indolines related to diazonamide A (Scheme 1), involving a hydroarylation reaction of *N*-acetyl indoles by phenols mediated by FeCl<sub>3</sub>, followed by an oxidation (*Angew. Chem. Int. Ed.* **2012**, *51*, 12546; *Chem. Eur. J.* **2014**, *20*, 7492). “The first stage features an umpolung of the indole, since in the hydroarylation step the heterocyclic nucleus became electrophilic at its C3-position, which is very unusual,” said Dr. Vincent.

Professor Vincent continued: “Eager to improve our process, we wished to develop a one-step oxidative coupling between *N*-acetyl indoles and phenols. At this time, we came across a report from Lei and co-workers (*Angew. Chem. Int. Ed.* **2013**, *52*, 7151) that described the [3+2] oxidative coupling of phenols and styrenes or alkylalkenes mediated by DDQ and catalyzed by FeCl<sub>3</sub>.” Addition of a carbon-centered quinone radical, activated by FeCl<sub>3</sub>, to the styrene was invoked (Scheme 1). Indeed, Dr. Vincent and co-workers were interested to see if a similar carbon-centered quinone radical could add to *N*-acetyl indoles activated by FeCl<sub>3</sub>. After

some experimentation, PhD student Terry Tomakinian was delighted to find that the treatment of *N*-acetyl indoles and phenols with stoichiometric amounts of DDQ and FeCl<sub>3</sub> allowed the synthesis of tetracyclic heterocycles (Scheme 2). “At first, we thought that we had made the desired benzofuro[3,2-*b*]indolines, since <sup>1</sup>H NMR spectra and mass spectrometry analyses seemed consistent,” explained Dr. Vincent. “However, when looking more closely at the <sup>13</sup>C NMR spectra, we noticed some inconsistencies.” The expected chemical shifts of about 55 ppm (C–C–C) and 110 ppm (N–C–O) for the carbons at the junction of the indole and the phenol were missing. Instead, chemical shifts of about 90 ppm (C–C–O) and 70 ppm (C–C–N) were observed, which are consistent with the regioisomeric benzofuro[3,2-*b*]indolines. Professor Vincent continued: “Eventually, Terry Tomakinian was able to obtain crystals of some of our compounds, and Dr. Régis Guillot was able to resolve their structures by X-ray crystallography and confirmed that we had indeed obtained benzofuro[3,2-*b*]indolines related to phalarine.” The Paris-based researchers also thought that their compounds were contami-



Scheme 2

nated with a small amount of impurities until they realized that two rotamers of benzofuro[3,2-*b*]indolines were present in the CDCl<sub>3</sub> solution in a ratio of about 4:1 because of the slow rotation around the N–(CO) bond of the *N*-acetyl. The ratio was almost 1:1 in DMSO at room temperature. Upon heating the DMSO-*d*<sub>6</sub> solution, disappearance of the rotamers was noticed. “The yields may seem modest but the complexity of the transformation should be taken into account!” said Dr. Vincent.

“To conclude, we have developed an unprecedented oxidative coupling between the indole and phenol nuclei that allows the synthesis of benzofuro[3,2-*b*]indolines,” said Dr. Vincent.

“The reaction proceeds by the oxidation of the phenol into a radical intermediate. We believe that the FeCl<sub>3</sub> promoter is crucial for the success of the reaction since it activates both the quinone radical and the *N*-acetyl indole. We also believe that the association of FeCl<sub>3</sub> and the carbonyl of the *N*-acetyl indole results in the decrease of electronic density on the indole nucleus. We are still pursuing the design of new methods towards benzofuroindolines (*Org. Lett.* **2014**, *16*, 5752) as well as the investigation of new reactive modes of indoles.” ■

Matteo Zanda

### About the authors



T. Tomakinian

**Terry Tomakinian** was born in Marignane (France) in 1988. After completion of his Bachelor's degree in organic chemistry from Université Aix-Marseille III (France) in 2009, he moved to ENSC Rennes (France) to obtain an engineering degree and an MSc degree in 2012. He carried out an internship at Oxford University (UK) supervised by Professor Stephen G. Davies in 2012. He is currently completing his PhD at Université Paris-

Sud with Dr. Guillaume Vincent on the development of new methodologies towards the synthesis of benzofuroindolines.



Prof. C. Kouklovsky

**Cyrille Kouklovsky** was born in Paris (France) and educated at Université Paris-Sud. He defended his PhD in 1989 under the supervision of Professor Yves Langlois (CNRS, Gif-Sur-Yvette, France), working on the cationic asymmetric Diels–Alder reaction. He then took up a postdoctoral position in Professor Steven V. Ley's research group (University of Cambridge, UK), working on the total synthesis of rapamycin. In 1995, he was appointed

as a “Chargé de Recherche” CNRS at Université Paris-Sud, working on asymmetric dipolar cycloaddition reactions and their synthetic applications. He was promoted to Professor of Chemistry in 2003. His research interests are in the fields of synthetic methodology, asymmetric synthesis and peptide synthesis.



Dr. G. Vincent

**Guillaume Vincent** was born in 1978 in Lyon (France). He graduated in 2002 from the Ecole Supérieure de Chimie Physique et Electronique de Lyon (CPE Lyon). During this period he spent one year at the Dupont Pharmaceuticals Company in Wilmington (USA) working with Dr. Patrick Y. S. Lam on the copper-catalyzed cross-coupling between boronic acids and NH-containing substrates. In 2002, he also obtained his MSc

degree from Université Lyon I in the group of Professor Marco A. Ciufolini. He completed his PhD in 2005 under the supervision of Professor Ciufolini where he achieved the synthesis of the macrocycle of soraphen A. He then joined Professor Robert M. Williams at Colorado State University (USA) as a postdoctoral associate where he completed the total synthesis of cribrostatin IV. At the beginning of 2007 he returned to France in the group of Professors Max Malacria and Louis Fensterbank at the Université Pierre et Marie Curie - Paris 6 to study anionic-radical tandem reactions. Finally, at the end of 2007 he was appointed “Chargé de Recherche” by the CNRS at the Institut de Chimie Moléculaire et des Matériaux d'Orsay at Université Paris Sud working on nitroso-Diels–Alder cycloadditions and total syntheses of natural products. In 2011, he launched an independent research program towards the synthetic applications and understanding of unusual reactivities of the indole nucleus.

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■ **Asymmetric  $\alpha$ -Photoalkylation of  $\beta$ -Ketocarboxyls by Primary Amine Catalysis: Facile Access to Acyclic All-Carbon Quaternary Stereocenters**

*(Focus on an article from the current literature)*

■ **Gold(I)-Catalyzed Polycyclization of Linear Dienenynes to Seven-Membered Ring-Containing Polycycles via Tandem Cyclopropanation/Cope Rearrangement/C-H Activation**

*(Focus on an article from the current literature)*

■ **Rhodium-Catalyzed Enantioselective Hydrogenation of Tetrasubstituted  $\alpha$ -Acetoxy  $\beta$ -Enamido Esters**

*(Focus on an article from the current literature)*

**FURTHER HIGHLIGHTS** + + + +

**SYNTHESIS**

**Review on: Transition-Metal-Catalyzed Direct C-H Bond Functionalization under External Oxidant Free Conditions**

*(by X. Cui et al.)*

**SYNLETT**

**Account on: Diels-Alder Reactions with the  $>C=P-$  Functionality of Annelated Azaphospholes**

*(by R. K. Bansal et al.)*

**SYNFACTS**

**Synfact of the Month in category "Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions": [Asymmetric Alkylation via Photoredox Pathway Using a Chiral Iridium Complex](#)**

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