SYNSTORIES

■ Ion-Paired Chiral Ligands for Asymmetric Palladium Catalysis

■ Fluoroform-Derived CuCF₃ for Low-Cost, Simple, Efficient, and Safe Trifluoromethylation of Arylboronic Acids in Air

■ Enantioselective Conjugate Addition of Alkylboranes Catalyzed by a Copper–N-Heterocyclic Carbene Complex

■ Young Career Focus: Dr. Maja Köhn (European Molecular Biology Laboratory in Heidelberg, Germany)
Dear readers,

as you will notice this issue of SYNFORM is thicker than the issues we have been publishing in the last few years: four articles instead of three. In fact, I am pleased to announce that this is an anticipation of what is going to happen to the 2013 version of SYNFORM, which returns to the original four-articles-per-issue format. Essentially, this means that the “emergency” situation resulting from my move to Scotland in 2009 is now overcome and we can go back to the good old SYNFORM habits. This is mostly due to the addition of a new SYNFORM team member, who officially joins us in 2013: Mrs. Alison Sage, the new Editorial Assistant. Welcome Alison!

So, definitely more quantity in 2013! But hopefully you will recognize that quality is improving too. And this “four-article pilot issue” is here to make that clear! We start with a new strategy for achieving the trifluoromethylation of boronic acids using a very convenient and simple starting material: fluoroform, as demonstrated by Dr. V. Grushin (Spain). We continue with an exciting new concept in asymmetric catalysis, as exemplified by Professor T. Ooi (Japan) and his ion-paired chiral ligands. Following on from that, we have the opportunity to learn more about the enantioselective Michael-type addition of alkylboranes developed by Professor M. Sawamura and Professor H. Ohmiya (Japan). Dulcis in fundo, the Young Career Focus on Dr. M. Köhn (Germany).

Enjoy your reading!

Matteo Zanda
Editor of SYNFORM
**Fluoroform-Derived CuCF$_3$ for Low-Cost, Simple, Efficient, and Safe Trifluoromethylation of Arylboronic Acids in Air**


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Aromatic molecules bearing a trifluoromethyl group on the ring constitute one of the most important classes of selectively fluorinated compounds that often exhibit biological activity, enhanced thermal stability, and useful processing properties.  

Trifluoromethylated aromatic building blocks and intermediates that are needed to produce agrochemicals, drugs and special materials are manufactured by a two-step process based on the Swarts reaction (Equation 1). There are two major problems associated with this technology. First, the process is environmentally unsustainable: per one equivalent of the desired trifluoromethylated aromatic compound produced, three equivalents each of the hazardous and corrosive Cl$_2$ and HF are consumed and six equivalents of HCl (chlorine waste) are co-generated, as dictated by the process stoichiometry. In real life, however, the situation is often even worse because the yields are not always quantitative. Second, the functional group tolerance of the process is low because of the involvement of highly reactive Cl$_2$, HF, and HCl. Even simple alkyl, alkoxy, and acyl groups do not survive the reaction conditions, as they easily get chlorinated in the first step.

An attractive alternative to the Swarts reaction based process to produce benzotrifluorides is the cross-coupling of an aromatic partner and a trifluoromethyl source, as shown in Equation 2. Since the pioneering work of McLoughlin and Thrower, who discovered the first example of such coupling in the mid-1960s, there has been an enormous amount of activity in the area of aromatic trifluoromethylation, especially in the last two to three decades.

Over the past three years, the area has become particularly hot and some interesting findings have been reported, such as the first examples of catalytic trifluoromethylation of aryl halides and Cu-promoted trifluoromethylation of arylboronic acids. Nonetheless, not a single large-scale industrial process has emerged from the tremendous research efforts toward the development of new trifluoromethylation methods. The main reason for that is the prohibitively high cost of the CF$_3$ sources employed in the developed trifluoromethylation reactions, such as CF$_3$SiR$_3$, CF$_3$I, and even more expensive Umemoto and Togni electrophilic reagents.

Dr. Vladimir Grushin, group leader of the Institute of Chemical Research of Catalonia in Tarragona (Spain), has a long-standing interest in the area of organometallic fluorine chemistry, including fluorination and trifluoromethylation reactions using transition metals. “Recently, we set a tough goal to develop a CF$_3$-transferring reagent using the most readily available, cheap, and atom-economical source of the trifluoromethyl group, trifluoroethane,” he said. A side product of Teflon manufacturing, trifluoromethane (CHF$_3$, fluoroform, HFC-23) is generated in the amount of roughly 20,000–25,000 tons per year. Although fluoroform is nontoxic and does not deplete the ozone layer, it is a gas with a formidable global warming potential, 11,700 times that of CO$_2$ when...
A steady 5% annual increase in the concentration of HFC-23 in the atmosphere, where its lifetime is 264 years, poses a serious ecological danger. "There are two ways to address this threat," explained Grushin. "One is to incinerate the huge quantities of the side-produced fluoroform. This is difficult and expensive because CHF₃ is a flame retardant. A much more attractive option is to use CHF₃ as a feedstock for manufacturing fluorinated compounds. This would allow us to kill two birds with one stone by making valuable chemicals and materials from a compound that, otherwise, needs to be destroyed in a costly process. This is not easy, however, because CHF₃ is a poorly reactive molecule." Consequently, the development of new, industrially feasible routes to useful organofluorine compounds from fluoroform waste streams is one of the most important tasks and great challenges of modern research. Only very limited progress has been made toward the use of CHF₃ in synthesis thus far.⁵,⁶

"We have recently discovered a new transformation of fluoroform, leading directly to trifluoromethylcopper in one step (Scheme 2). The reaction of CuCl with t-BuOK in a 1:2 molar ratio gives [K(DMF)][Cu(Ot-Bu)₂], a novel dialkoxy-cuprate that we have characterized," Grushin continued. "This cuprate, isolated or generated in situ, reacts smoothly with fluoroform at room temperature and atmospheric pressure to produce CuCF₃ in >90% yield. This freshly prepared CuCF₃ is then stabilized with Et₃N⋅3HF. Importantly, only low-cost materials are used in the entire procedure, which we hope makes the fluoroform-derived CuCF₃ reagent industrially attractive."

Grushin said: "Since our discovery of the fluoroform cupration reaction (Scheme 2), we have been actively developing applications of the CuCF₃ reagent in synthesis. A number of successful trifluoromethylation reactions of various electrophiles with our CuCF₃ have been published in a preliminarily communication (Scheme 3)."

"In a more recent study, we explored the reactivity of fluoroform-derived CuCF₃ toward arylboronic acids," said Grushin. Since the original reports of Cu-promoted trifluoromethylation of arylboronic acids by Chu and Qing⁴ and Buchwald’s group,⁵ half a dozen or so publications on this subject have appeared in the literature. Some of these methods certainly provide synthetic opportunities for medicinal and agrochemical research. Applications of these methods on a larger scale are hard to imagine, however, because of the prohibitively high cost of the CF₃ sources employed, mainly CF₃SiMe₃. Moreover, all these methods require other costly materials in stoichiometric quantities, such as 1,10-phenanthroline or other ligands. Unless the priciest electrophilic CF₃ sources are used, the reaction needs an oxidant, an expensive silver salt in stoichiometric quantities, or pure oxygen that is certainly more economical but unsafe to use on a large scale.

"When launching our arylboronic acid project, we knew that our fluoroform-derived CuCF₃ was by far the cheapest tri-
fluoromethylating reagent ever developed. However, the low cost of the CF$_3$ source would matter only if we could find conditions to use it in an equally cost-efficient, high-yielding, and safe trifluoromethylation process,” continued Grushin. “Of course, there was no guarantee at all that our CuCF$_3$ would trifluoromethylate arylboronic acids efficiently in air, the cheapest and most readily available oxidant, and in the absence of costly ligands and promoters or additives. The method eventually developed, however, has surpassed our expectations.”

Dr. Petr Novák was pleased to find that the CuCF$_3$ reagent reacted readily with phenylboronic acid at room temperature in air to give benzotrifluoride in nearly 100% yield. “There is not much room for improvement when one gets a nearly quantitative yield of the desired product from a reaction that runs smoothly at room temperature in air,” said Dr. Novák. “Nonetheless, I tested a variety of additives and ligands in the reaction to find that none of them had any noticeable beneficial effect on the process.” That, according to Dr. Novák, was a particularly encouraging observation, since the goal of the project was to come up with a method as economical and simple as possible. Dr. Novák and his laboratory colleague Dr. Anton Lishchynskyi then proceeded to explore the scope of the method and optimized conditions for two dozen varieties of ArB(OH)$_2$ substrates. The results of their studies are summarized in Scheme 4, showing that the method exhibits excellent selectivity and unprecedentedly high functional group tolerance for a diverse array of substrates bearing electron-donating, -withdrawing, or -neutral substituents at the o-, m-, and p-positions. “We were particularly delighted to achieve previously impossible trifluoromethylation of formyl-substituted arylboronic acids in good yield,” said Dr. Novák.

**Scheme 4**
In all previous publications on the subject it has been reported that in parallel to trifluoromethylation, arylboronic acids undergo facile protodeborylation, a highly undesirable side process. In order to minimize or avoid this side reaction, dry O₂ in the presence of molecular sieves could be used, or more expensive and less atom-economical boronate esters employed as the substrates in place of arylboronic acids. “Fortunately, our method, while employing arylboronic acids and non-dried air as the oxidant, does not suffer significantly from the protodeborylation. In a handful of cases, however, the reaction had to be run at 0 °C to suppress the side formation of the corresponding arene,” said Dr. Lishchynskyi.

Grushin concluded: “To summarize our work, we have developed the first method for trifluoromethylation of readily available arylboronic acids with our low-cost fluoroform-derived CuCF₃ reagent. The process is exceedingly simple, occurring cleanly at room temperature in air to furnish trifluoromethylated aromatic compounds in high yield and exhibiting unprecedentedly high functional group tolerance. There is no need to use any additional ligands, costly oxidants, drying agents, or pure O₂ to trifluoromethylate arylboronic acids by our method, which is not only synthetically useful and inexpensive, but also advantageously simple and safe to run.”

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Conventional chiral ligands, including those recognized as privileged ligands, are generally covalently constructed, single chiral molecules embedded with coordinative functional groups. However, the iterative synthesis of such effective chiral ligands can be complicated, and this can hinder the identification of the best chiral catalyst for any particular asymmetric transformation. Recently, Professor Takashi Ooi of the Department of Applied Chemistry at the Graduate School of Engineering of Nagoya University (Japan) and his research group consisting of Dr. Koosuke Ohmatsu, graduate students Mitsunori Ito and Tomoatsu Kunieda have developed a new strategy for the design of a chiral ligand for asymmetric transition-metal catalysis. This novel approach to catalyst design is based on the use of a catalyst assembled as an ‘ion-paired Lego’, where an anionic chiral molecule is combined with an achiral cation incorporating a chemical function that can act as a ligand, such as a phosphine. Professor Ooi said, “Our strategy is to divide the chiral ligand into two simple molecules; these two components attract each other with electrostatic interaction.” Since the electrostatic interaction is non-directional, the assembled architecture might be too flexible to make such ligands suitable for asymmetric metal catalysis. Professor Ooi explained, “In this work, however, an ion pair composed of an achiral ammonium-phosphine and a chiral binaphtholate ion has proven to act as an effective chiral ligand for palladium-catalyzed asymmetric allylic alkylation of structurally diverse α-nitro carboxylates. The success relies heavily on the elaborated structure of the ammonium-phosphine hybrid ligand, whose coordinative phosphine functionality and ammonium ion moiety are spatially arranged within an appropriate proximity.” In principle, a wide variety of the achiral ammonium ions with coordinative functionalities can be easily designed and synthesized, and their possible combinations with readily available chiral acids are unlimited. Professor Ooi concluded, “Because of this, the concept of the ion-paired chiral ligand provides unprecedented possibilities regarding the design, preparation, and optimization of structurally diverse chiral ligands, which should be greatly appreciated in developing a broad range of metal-catalyzed, stereoselective chemical transformations.”
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 time 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 a Lecturer in 1998. He moved to Kyoto University (Japan) as an Associate Professor (2001), and became a Full Professor at 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), and the IBM Japan Science Prize (2011). His current research interests are focused on the design of chiral organic ion pairs, particularly chiral quaternary onium salts, and their applications as molecular catalysts for the development of new and useful synthetic methodologies.
The development of increasingly efficient and sophisticated catalytic systems for controlling the stereoselectivity of organic reactions continues to attract enormous interest in synthetic organic chemistry. Organoboron compounds find widespread utility in modern organic synthesis because of their broad availability and excellent functional group compatibility. They are especially useful for carbon–carbon bond formations. Transition-metal-catalyzed enantioselective conjugate additions of organoboron compounds are at the forefront of the field. Unfortunately, usable organoboron reagents are limited to aryl, alkenyl, and allyl derivatives, using Rh, Pd or Ni as a metal, and the methodology had not been expanded to cover the use of alkylboron compounds until very recently.

Professors Hirohisa Ohmiya and Masaya Sawamura, together with graduate student Mika Yoshida, from Hokkaido University (Japan) recently reported the first catalytic enantioselective conjugate addition of alkylboron compounds. “The reaction between alkylboron compounds (alkyl-9-BBN) and imidazol-2-yl α,β-unsaturated ketones proceeded with high enantioselectivities under the influence of a copper(I) catalyst system, prepared in situ from CuCl, consisting of a new chiral imidazolium salt as a precursor for the N-heterocyclic carbene ligand, and PhOK,” said Professor Ohmiya (Scheme 1).

According to the Japanese scientists, this transformation has significantly expanded the scope of transition-metal-catalyzed enantioselective conjugate additions of organoboron reagents to α,β-unsaturated carbonyl compounds. Furthermore, the availability of alkylboranes (alkyl-9-BBN) through in situ alkene hydroboration is an attractive feature from a synthetic viewpoint. “In recent days, scientists in various fields recognize replacing rare and precious metals with abundant metals to be important. In this regard, copper is relatively abundant in the Earth’s crust and thus cheap and environmentally benign,” explained Professor Sawamura.

Development of this new reaction is based on the copper-catalyzed, γ-selective allylic substitution of alkylboron compounds (alkyl-9-BBN), which was discovered in 2010 (J. Am. Chem. Soc. 2010, 132, 2895; J. Am. Chem. Soc. 2012, 134, 8982). “A key aspect of these reactions is the catalytic formation of alkylcopper species through B/Cu transmetallation from alkylboranes. Our copper catalyst system enables the formation and subsequent transformations of alkylcopper(I) species without the problem of β-hydride elimination which precludes the use of most transition metals for alkyl group transfer,” explained Professor Ohmiya (Scheme 2).

![Scheme 1](Image) Copper-catalyzed enantioselective conjugate addition of alkylboranes
"In the course of our study for expanding this alkylboration–copper chemistry, Miss Yoshida found that alkylboranes undergo conjugate addition in the presence of a catalytic amount of a copper(I)–N-heterocyclic carbene (NHC) complex (Org. Lett. 2011, 13, 482). The use of imidazol-2-yl α,β-unsaturated ketones as enone substrates was key for an efficient reaction. On the basis of this principle established for the achiral system, she aimed at developing a catalytic enantioselective alkylboron conjugate addition. The work was much more difficult than we had expected and demanded tremendous efforts, but Miss Yoshida, through two important findings, led this project to a beautiful success!" said Professor Ohmiya. “First, she designed and synthesized a new ring-unsaturated C2-symmetric chiral NHC ligand having a 3,5-di-tert-butyl-4-methoxyphenyl (DTBM) substituent at the two stereogenic carbon centers of the N-alkyl side arms, and found it to be an efficient chiral ligand. Second, she identified PhOκ to be an excellent base. Of particular interest is the effect of PhOκ. We ascribe it to a proper Lewis acidity of an in situ generated phenoxyborane for activating the enone toward organocopper addition," said Professor Ohmiya. Enantiodiscrimination models that explain such an effect of the phenoxyborane are shown in Figure 1.

“While the development of more efficient catalytic systems is desirable, this chemistry is conceptually new in that it represents efficient catalytic enantioselective alkyl group transfer from alkylboron compounds. Furthermore, our work demonstrates that copper is a useful metal for catalytic molecular transformations of this kind. Chemistry based on alkyl-copper(I) species will enjoy further expansion to solve various problems in organic synthesis,” concluded Professor Sawamura.

![Scheme 2](image)

**Scheme 2** β-Hydride elimination from alkylmetal species

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**About the authors**

**Masaya Sawamura** was born in Kochi (Japan) in 1961. He received his Ph.D. degree from Kyoto University (Japan) in 1989 under the supervision of Professor Yoshihiko Ito (Department of Synthetic Chemistry, Faculty of Engineering). In 1989, he joined the faculty of the same department as an Assistant Professor. He spent one year as a researcher at Harvard University (USA, with Professor Stuart L. Schreiber, 1993–1994). In 1995, he moved to the Tokyo Institute of Technology and to the University of Tokyo (Japan) to join the group of Professor Eiichi Nakamura as an Assistant Professor. He was promoted to Lecturer in 1996 and to Associate Professor in 1997. Since 2001, he is a Full Professor at Hokkaido University. He received The Chemical Society of Japan Award for Young Scientists (1996) and The Chemical Society of Japan Award for Creative Work (2012).
Hirohisa Ohmiya was born in Osaka (Japan) in 1978. He received his Ph.D. degree from Kyoto 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 working with Professor Masaya Sawamura. He was promoted to Associate Professor in 2010. His current research focuses on the development of new transition-metal-catalyzed reactions and their application to organic synthesis.

Mika Yoshida was born in Hokkaido (Japan) in 1986. She received her B.Sc. in 2010 and her M.Sc. degree in 2012 from Hokkaido University under the supervision of Professor Masaya Sawamura. She is currently a researcher at Nippon Shinyaku Co., Ltd (Japan). She carried out all the experiments for the conjugate addition work.
Young Career Focus: Dr. Maja Köhn (European Molecular Biology Laboratory in Heidelberg, Germany)

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 SYNSTOREY with a Young Career Focus presents Dr. Maja Köhn, European Molecular Biology Laboratory in Heidelberg, Germany.

Maja Köhn was born in Kiel (Germany) in 1975. She studied chemistry at the Christian Albrechts University in Kiel. She prepared her diploma thesis on carbodiimide-centered carbohydrates in the group of Professor T. K. Lindhorst, graduating in 2001. After a three-month internship at the Centro de Investigaciones Químicas, CSIC (Spain), in the group of Dr. J. M. García Fernández, working on the synthesis of carbohydrate-centered glycoclusters, she conducted her PhD work with Professor H. Waldmann at the Max Planck Institute of Molecular Physiology (Germany). There she worked on the development of immobilization methods for small molecule and peptide microarrays and their applications. She received her PhD in organic chemistry from the Technical University Dortmund (Germany) in 2005. She then joined the lab of Professor G. L. Verdine at the Department of Chemistry and Chemical Biology at Harvard University (USA), where she synthesized short RNA-interacting polynucleotides as inhibitors for hepatitis C viral translation. Since November 2007 she is a group leader at the European Molecular Biology Laboratory in Heidelberg (Germany). Her group applies organic synthesis to develop and apply chemical tools, and also uses biochemistry, molecular and cell biology approaches, to study protein and phosphoinositide phosphatases.

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

Dr. Köhn | My group is interested in investigating disease-promoting phosphatases with the help of tailor-made chemical tools based on phosphoinositide and peptide synthetic organic chemistry as well as protein semisynthesis. We are also working with molecular and cell biology approaches (Figure). Phosphatases hydrolyze protein or second messenger bound phosphomonoesters and play a crucial role in cellular life. Biologically, the main focus is on phosphatases of regenerating liver (PRLs). Other phosphatases include PTP1B, PP1 and PP2C. Chemically, we are working on cell-penetration and stabilization concepts for peptides as bioactive molecules (inhibitors/activators) to modulate phosphatase activity. In addition, we recently developed the first solid-phase organic synthesis strategy for phosphoinositides. Currently, we are using this strategy to create a library of phosphoinositide analogues for structure–activity relationship studies with phosphoinositide phosphatases, aiming at the design of specific inhibitors for these phosphatases. The lab consists of 50% chemists and 50% biologists.

SYNFORM | When did you get interested in synthesis?

Dr. Köhn | My interest in organic chemistry started in high school, particularly regarding natural compounds like carbohydrates, nucleotides and peptides. I liked the relation to biology, and most of all I was fascinated by the fact that we can synthesize basically the same compounds as Nature can. During my university studies, I was most fascinated by the mechanisms behind chemical reactions and the logic with which we can explain the outcome of chemical reactions.

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

Dr. Köhn | Organic synthesis is applied in many different fields from materials science and drug discovery to basic biological research. I think that there are few disciplines that
have such widespread potential, and organic synthesis will continue to play an essential role in many fields. We still face several challenges such as non-degradable and toxic waste and expensive medications, and more efficient synthesis strategies and novel methodologies in organic synthesis are required to approach these challenges. I therefore believe that the prospect and the modern role of organic chemistry lies in its applications, and with that comes the necessity to develop organic synthesis further.

**Frontier of organic and biological chemistry: My research and its aims**

Protein and second messenger phosphorylation/dephosphorylation is fundamental to virtually all cellular signaling networks and thus to physiological function. In addition, phosphorylation and dephosphorylation are important processes in the biosynthesis of integral cellular components such as phosphoinositides and other phospholipids. Impairment of these processes contributes to the development of human diseases such as cancer and diabetes. Kinases catalyze phosphorylation by transferring the gamma-phosphate from ATP to the (protein) substrate, while phosphatases are responsible for phosphate hydrolysis from the (protein) substrate. Whereas kinases are established targets for drug discovery and quite well studied, the investigation of phosphatases and development of phosphatase inhibitors has lagged significantly behind due to the fact that they have traditionally been looked at as being unspecific housekeeping enzymes that counteract the important kinases. Therefore, the knowledge about phosphatase function, regulation and substrate interaction is still quite limited. To date, not a single phosphatase inhibitor is approved for clinical use. However, more and more evidence is now available that phosphatases and kinases are equally important in disease. Similar to phosphatases, it was thought to be impossible to design specific drugs that target kinases, but now various kinase inhibitors are applied in therapies. My overall aim is that my research will contribute to reach this challenging goal: that phosphatase inhibitors (or activators) will be used in a clinical setting.

Phosphatase inhibitors are not used in the clinic due to limited specificity and bioavailability. In addition, chemical modulators of phosphatase function and other tools to decipher phosphatase signaling are extremely limited or not available for the majority of phosphatases. Thus, we develop chemical...
tools to address phosphatases in basic research and also as drug targets. These tools are applied in my laboratory to investigate certain phosphatases, and in addition, the goal is that they will serve as a resource for the phosphatase research community. We apply synthetic organic chemistry to develop modulators of phosphatase function and to aid in structural and biochemical studies. We also study biological pathways and roles of particular phosphatases using molecular cell biology, imaging and genomic approaches, because the more you know about how, and why, a phosphatase promotes a disease, the better you will be able to design bioactive molecules against its activity.

We are focussing on natural compounds (phosphoinositides, peptides) as the basis for our work. These compounds are inherently difficult to use as bioactive molecules due to their poor bioavailability and stability, and peptides can also trigger an immune response. In addition, phosphoinositides are synthetically very challenging compounds. Although both compound classes have great potential as bioactive molecules, their application is very limited and, in the case of phosphoinositides, academic. We address these challenges in order to be able to make use of that great potential in the future.

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

**Dr. Köhn** | I believe that our solid-phase organic synthesis strategy for phosphoinositides is an important scientific accomplishment, because it makes the synthesis of these challenging compounds much faster and more flexible. I also think that the discovery of cancer metastasis-promoting phosphatase PRL-3 having phosphoinositide phosphatase activity will significantly help in understanding the molecular mechanisms of this oncogene. Finally, for the ubiquitous phosphatase PP1 we have developed a selective peptidic activator that works well in cells, and given the multiple roles of this protein in cancer, diabetes, Alzheimer’s and viral translation, I believe that we can make an important contribution in the future by developing this activator further.
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with CF₃SiMe₃ and Elemental Sulfur
(Focus on an article from the current literature)

■ Iron-Catalyzed, Highly Regioselective Synthesis of α-Aryl Carboxylic Acids from Styrene Derivatives and CO₂
(Focus on an article from the current literature)

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Synfacts on: Biomimetic Syntheses of the Flindersial
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(by R. Vallakati, J. A. May)

SYNFACTS

Synfact of the Month in category “Metal-Mediated Synthesis”:
Fe-Catalyzed sp³–sp² Cross-Coupling

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