

Young Career Focus: Dr. Lukasz T. Pilarski (Uppsala University, Sweden)

Background and Purpose. SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents Dr. Lukasz T. Pilarski (Uppsala University, Sweden).

Biographical Sketch



Dr. L. T. Pilarski

Lukasz Pilarski grew up in Poland, the UK and Canada. He studied chemistry at the University of Bristol (UK), graduating with an MSc degree in 2004 after a research project in the group of Professor Booker-Milburn. He completed his PhD under the guidance of Professor Robin Bedford in 2009, specializing in the design and applications of palladacyclic complexes. For the year prior to his viva voce exam, he was a 'pre-doc' in the group of Professor David Cole-Hamilton at the University of St Andrews (UK). There he worked on an industrially sponsored project oriented around the mechanistic investigation of challenging Ru-catalyzed hydrogenations. In 2009, Lukasz moved to Stockholm University in Sweden and joined Professor Kálmán Szabó's group as a Carl Trygger postdoctoral fellow. During this time his work focused on Pd-catalyzed oxidative functionalizations of allylic C–H bonds. In 2011, Lukasz received a generous Young Researcher grant from the Swedish Research Council (Vetenskapsrådet), which allowed him to establish his own group at Uppsala University (Sweden). In 2016, Lukasz received the Thieme Chemistry Journals Award and became Associate Senior Lecturer (Biträdande Lektor).

INTERVIEW

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

Dr. L. T. Pilarski My group is interested in the discovery and development of new synthetic methods based on catalytic C–H functionalization, the reactivity of (hetero)aryne intermediates and that of organo-main-group compounds. Each of these can offer great flexibility in synthesis; we seek to combine them in interesting new ways that benefit organic synthesis.

SYNFORM *When did you get interested in synthesis?*

Dr. L. T. Pilarski I gravitated towards synthesis though a combination of influences. I was lucky to have excellent lecturers during my undergraduate degree at the University of Bristol, several of whom managed to impress upon me the synergy that exists between logic and creativity in synthesis. Moreover, my Masters project (supervised by Professor Booker-Milburn), PhD research (supervised by Professor Robin Bedford) and postdoc work (supervised Professor Kálmán Szabó at Stockholm University) were flexible and curiosity-driven, which I greatly enjoyed.

Despite its central role in science,¹ I think that synthesis shares many similarities with engineering. Synthetic chemists are, ultimately, in the construction business. I like the idea of making molecules that might previously not have existed anywhere in the Universe except a person's imagination.

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

Dr. L. T. Pilarski Organic synthesis was responsible in the twentieth century for some of humanity's greatest achievements, many of which contributed to improving life expectancy and quality far beyond what could previously have

been anticipated. Twenty-first century science will be more complex and sophisticated, but I think organic synthesis will remain at the heart of things; our health and influence on the environment, for example, will always depend on the ability to understand and manipulate molecules.

I think it is important to emphasize the enormously positive influence of curiosity-driven research. History shows that the most important scientific advances, including in synthesis, have come to us that way. For this reason I am heartened every time the Nobel Prize in Chemistry is awarded for fundamental and curiosity-driven work related to synthesis, as it was just a few months ago (to Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard Feringa for their work on the synthesis of molecular machines).

SYNFORM *Your research group is active in the area of catalytic C–H functionalization and the reactivity of (hetero)aryne intermediates. Could you tell us more about your research and its aims?*

Dr. L. T. Pilarski Organic synthesis is fraught with compromises: atom- and step-economies, functional group tolerance, purification costs – and many other complications. We are interested in uniting three powerful approaches to address these challenges: catalytic C–H activation, (hetero)aryne chemistry and organo-main-group reactivity. The selective substitution of a C–H bond is one of the most direct ways of building up molecular complexity in organic molecules. It can not only expedite a synthetic route but also make previously impossible transformations available, or even easy. (Hetero)arynes are unusually versatile intermediates for producing functionalized aromatics; they can form two bonds selectively at the same time to an almost bizarrely broad range of elements/functional groups, and often under mild conditions. Organo-main-group compounds can also be very versatile. We believe some of their properties can be harnessed to afford unusual modes of selectivity in C–H activation and (hetero)aryne chemistry. One of our goals is to bring together these three areas of synthesis, for example by using them to create flexible molecular building blocks in which multiple functional groups can be converted selectively.

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

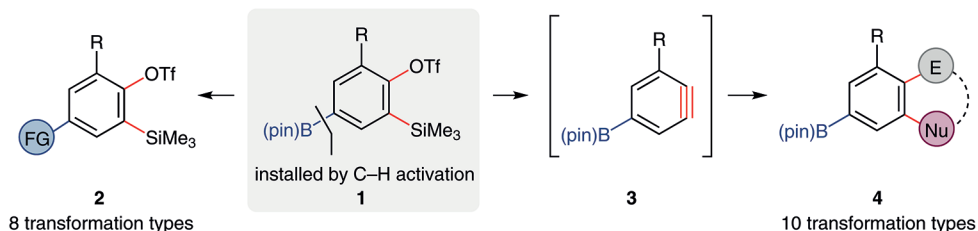
Dr. L. T. Pilarski I hope my group's most important achievements lie in the future. My group has published work which we are very proud of, for example protocols that offer previously unavailable functional group tolerance (Scheme 1).

We showed that it is possible to leverage the immense versatility of aryl boronates and that of fluoride-activated aryne precursors for their *mutual* derivatization. Through selective, catalytic C–H borylation,² we were able to generate precursors **1**, in which the reactivity of B(pin) or the aryne triple bond may be accessed selectively (Scheme 1a). Thus, it is possible to generate a wide range of more complex aryne precursors (**3**) or use aryne reactivity to generate new, previously inaccessible aryl boronates (**4**). The latter, for example, allows the facile introduction of heteroatoms to the aryl boronate backbone, for which there were very few methods prior to this work (and even those were limited). We were also pleasantly surprised to discover that under appropriately chosen conditions, fluoride sources may be used to activate the boronate or the aryne component of precursors **1** and their derivatives.^{3,4}

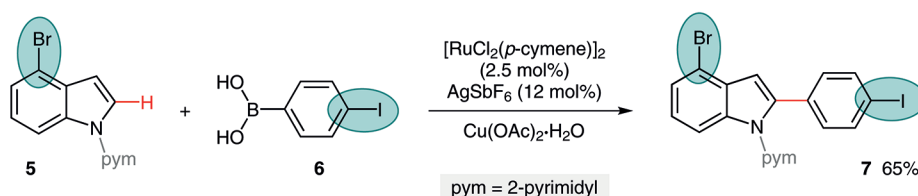
Our Ru-catalyzed C–H functionalizations of heteroarenes are also tolerant in unusual ways. For example, our indole and pyrrole C–H arylation conditions preserve aryl bromides and even aryl iodides, which would typically be cleaved or consumed but which can serve as handles for further manipulation (Scheme 1b).⁵ We also reported a Ru-catalyzed C–H silylation of heteroarenes that requires no protecting groups for alkyl or aryl amine substituents, and demonstrates for the first time that undirected C–H silylation is possible under Ru catalysis (Scheme 1c).⁶ Additionally, we found that electron-rich Ru centers are able to cleave the indole C4–H bond, which was previously the exclusive province of strongly electrophilic metals. We hope to build on these discoveries, of course.

Matthew Fenske

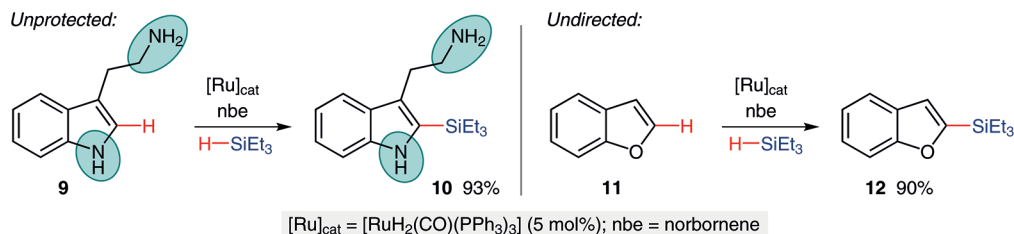
a. Our work on boryl aryne precursors:



b. An example of our functional-group-tolerant Ru-catalyzed heteroarene C–H arylation:



c. Our Ru-catalyzed C–H silylation of heteroarenes needs no protecting or directing groups:



Scheme 1 Our work on functional-group-tolerant (hetero)arene transformations enabled by catalytic C–H activation, the strained triple bond of arynes and/or organo-main-group elements

REFERENCES

- (1) R. Noyori *Nat. Chem.* **2009**, *1*, 5.
- (2) I. A. I. Mkhaliid, J. H. Barnard, T. B. Marder, J. M. Murphy, J. F. Hartwig *Chem. Rev.* **2010**, *110*, 890.
- (3) E. Demory, K. Devaraj, A. Orthaber, P. J. Gates, L. T. Pilarski *Angew. Chem. Int. Ed.* **2015**, *54*, 11765.
- (4) J. Larsson, E. Demory, K. Devaraj, C. Sollert, L. T. Pilarski *Synlett* **2016**, *27*, 969.
- (5) C. Sollert, K. Devaraj, A. Orthaber, P. J. Gates, L. T. Pilarski *Chem. Eur. J.* **2015**, *21*, 5380.
- (6) K. Devaraj, C. Sollert, C. Juds, P. J. Gates, L. T. Pilarski *Chem. Commun.* **2016**, *52*, 5868.