

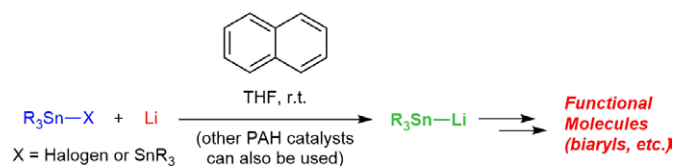
# Synform

People, Trends and Views in Chemical Synthesis

2016/03

## Stannyl-Lithium: A Facile and Efficient Synthesis Facilitating Further Applications

Highlighted article by D.-Y. Wang, C. Wang, M. Uchiyama



also applicable for other group-14 elements: e.g.  $R_3GeLi$

### Contact

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

## Dear Readers,

This very rich new issue of SYNFORM is opened by an important new methodology developed by M. Uchiyama (Japan) for preparing, in a very efficient and user-friendly way, stannyl lithium reagents, a class of organometallic compounds which have traditionally posed significant challenges to organic chemists, in spite of their usefulness in synthesis. Notably the method can also be used to prepare the corresponding germanium derivatives. The second article covers a new and very clever strategy for achieving the synthesis of  $\beta$ -hydroxy- $\alpha$ -substituted ketones via stereocontrolled addition of Grignard reagents to  $\alpha$ -epoxy *N*-sulfonyl hydrazones, a method devised by D. M. Coltart (USA). The next contribution explores the efficient method recently published by S. Fletcher (UK) for performing a highly stereoselective arylation of racemic allylic compounds using a chiral rhodium complex and aryl-boronic acids. The issue is closed by an article exploring the work of K. Hull (USA) on the atom-economical and selective rhodium-catalyzed anti-Markovnikov hydro-amination of homoallylic amines that leads to 1,4- diamines.

Enjoy your reading!



### In this issue

- Literature Coverage  
**Stannyl-Lithium: A Facile and Efficient Synthesis Facilitating Further Applications** ..... A38
- Literature Coverage  
**Diastereoselective Addition of Grignard Reagents to  $\alpha$ -Epoxy *N*-Sulfonyl Hydrazones** ..... A40
- Literature Coverage  
**Rhodium-Catalyzed Asymmetric Allylic Arylation of Racemic Halides with Arylboronic Acids** ..... A42
- Literature Coverage  
**Anti-Markovnikov Hydroamination of Homoallylic Amines** ..... A44
- Coming soon..... A47

### Contact

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

## Stannyl-Lithium: A Facile and Efficient Synthesis Facilitating Further Applications

*J. Am. Chem. Soc.* **2015**, *137*, 10488–10491

Stannyl-lithium compounds are extremely versatile and useful reagents for the construction of carbon–carbon bonds; however, the available methods for preparing these compounds are affected by a number of important drawbacks such as low yields and competing side reactions, production of toxic by-products, inconvenient and difficult-to-handle reaction conditions, and the need to use large excesses of Sn sources.

Recently, the group of Professor Masanobu Uchiyama at The University of Tokyo (Japan) reported a breakthrough method for accessing these reagents, consisting in a highly efficient, practical, polycyclic aromatic hydrocarbon (PAH)-catalyzed synthesis of stannyl-lithium (Sn-Li), in which the tin resource (stannyl chloride or distannyl) is rapidly and quantitatively transformed into the Sn-Li reagent at room temperature. Professor Uchiyama explained: “The resulting Sn-Li reagent can be stored at ambient temperature for months, and shows higher reactivity toward various substrates, with quantitative atom-efficiency, than existing Sn-Li reagents.”

Most chemical reagents carry some risk of toxicity and many synthetic chemists avoid using very poisonous compounds such as organotin, even if efficient preparatory methods exist. In fact, when such toxic reagents are treated in a professional way, the risks are much reduced (see Figure 1). Professor Uchiyama said: “What would cause more problems is the ‘derivate’ toxicity arising from the other side, that is, the toxic by-product and residue of reactant due to excess use.” He continued: “By using the PAH-catalyzed protocol, Sn-Li can be generated quantitatively without formation of any of the toxic by-product that always occurred in traditional methodology, hence providing a ‘safe and clean’ way for usage of such toxic compounds.”

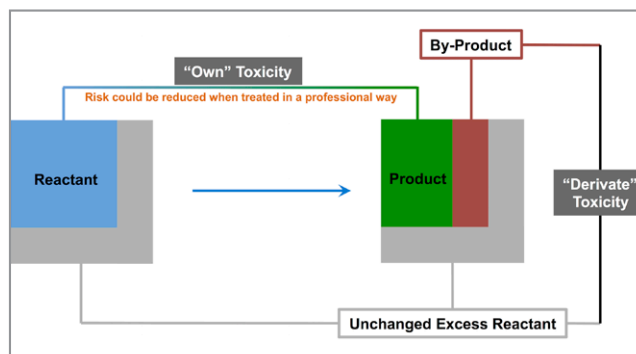
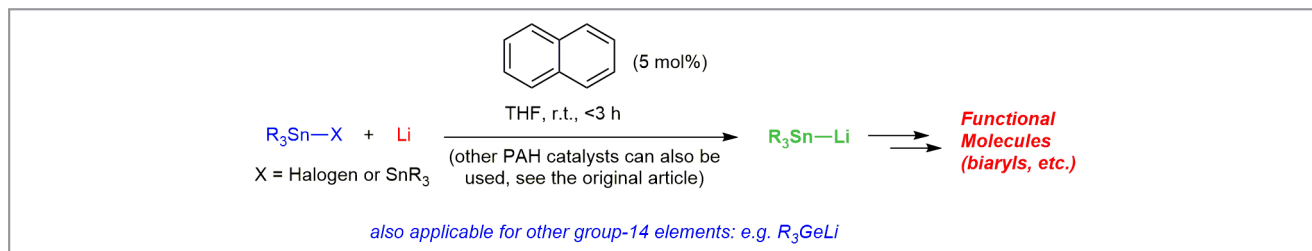


Figure 1

Another important problem in the synthesis of Sn-Li is the stability of the product. Until now, Sn-Li reagents prepared by known methods have usually shown very low stability; hence, they needed to be used directly after preparation. The by-products (especially  $R_3SnSnR_3$ ) have been proved to accelerate the decomposition of Sn-Li. “In sharp contrast, Sn-Li made by our method showed excellent stability,” said Professor Uchiyama. “After storage at room temperature for weeks, no decomposition was detected. The reasons for this may be attributed to: 1) no ‘Sn’-containing by-products were formed in this preparative system; and 2) Li/PAH could well restrain the decomposition.” Such advantages provide a possibility for Sn-Li to be produced as large-scale, commercially available reagents, such as organolithium or Grignard reagents, which would be convenient for utilization of such compounds.

Although Sn-Li and other  $^{14}E$ -Li (group 14 elements) reagents have been known for over half a century, their synthe-



Scheme 1

sis methods always suffer from low yields and other disadvantages, and hence the chemistry of  $^{14}\text{E-Li}$  has long been limited. Professor Uchiyama said: "This PAH-catalyzed protocol shows many practically applicable advantages, thus provides an easily accessible starting point for the  $^{14}\text{E-Li}$  reagents." He continued: "As shown in the paper, several interesting reactions, such as the stannylmetalation of alkynes, the stannylation of aryl halides, and so on, have been greatly improved by means

of this synthetic protocol and thus new synthetic possibilities are now available."

Professor Uchiyama concluded: "Overall, we hope that these advantages will encourage synthetic chemists to take up this methodology to open new windows for  $^{14}\text{E-Li}$  chemistry."

*Mattias Fenske*

### About the authors



From left to right: Dr. C. Wang, Prof. M. Uchiyama, D.-Y. Wang

**Dong-Yu Wang** was born in Liaoning Province (P. R. of China) in 1986. He received his BS degree from Shenyang Pharmaceutical University (P. R. of China) in 2010 and then became a graduate student under the supervision of Professor Youjun Xu in the same university. During his Master's course, he also studied at the Shanghai Institute of Materia Medica, Chinese Academy of Sciences (P. R. of China), as an exchange student in Professor Ao Zhang's lab. Since October 2013 he has been a PhD student at the Graduate School of Pharmaceutical Sciences, The University of Tokyo (Japan), under the supervision of Professor Uchiyama. His main research interest is the development of synthetic methodology.

**Chao Wang** obtained his BS degree in 2002 from Peking University (P. R. of China). He did doctoral research under the supervision of Professor Zhenfeng Xi in the same university and obtained his PhD in 2007. During 2007–2008, he carried out postdoctoral research at Purdue University (USA) with Professor Ei-ichi Negishi. In 2009, he joined Professor Uchiyama's lab as a research group leader. His research involves synthetic organic chemistry, organometallic chemistry, and theoretical and computational chemistry.

**Masanobu Uchiyama** obtained his MS (1995) and PhD (1998) degrees from The University of Tokyo (Japan). He worked as an assistant professor at Tohoku University (Japan, 1995–2001) and The University of Tokyo (2001–2003), and was promoted to lecturer (2003–2006). He became Associate Chief Scientist (PI) at RIKEN in April 2006. Since April 2010, he has been a full professor at the Graduate School of Pharmaceutical Sciences, The University of Tokyo, and also held the position of Research Team Leader (PI) and Chief Scientist (PI, since 2013) in RIKEN. His research interests cover a variety of areas, including organic synthesis, organometallics, theoretical chemistry, materials, medicines and spectroscopy.

## Diastereoselective Addition of Grignard Reagents to $\alpha$ -Epoxy *N*-Sulfonyl Hydrazones

*Nat. Chem.* **2015**, *7*, 1024–1027

The development of a broadly applicable approach to the asymmetric  $\alpha$ -alkylation of ketones is a long-standing and – until recently – unresolved problem in the field of organic synthesis. In the December 2015 issue of *Nat. Chem.* Professor Don M. Coltart and co-workers from the University of Houston (Texas, USA) reported the development of the broadest method ever reported for the  $\alpha$ -functionalization of ketones or their derivatives. The article describes the highly (up to >25:1) *syn*-selective formation of  $\beta$ -hydroxy *N*-sulfonyl hydrazones having  $\alpha$ -tertiary or  $\alpha$ -quaternary centers by the simple combination of Grignard reagents – the most readily available and common of all organometallic reagents – and  $\alpha$ -epoxy *N*-sulfonyl hydrazones.

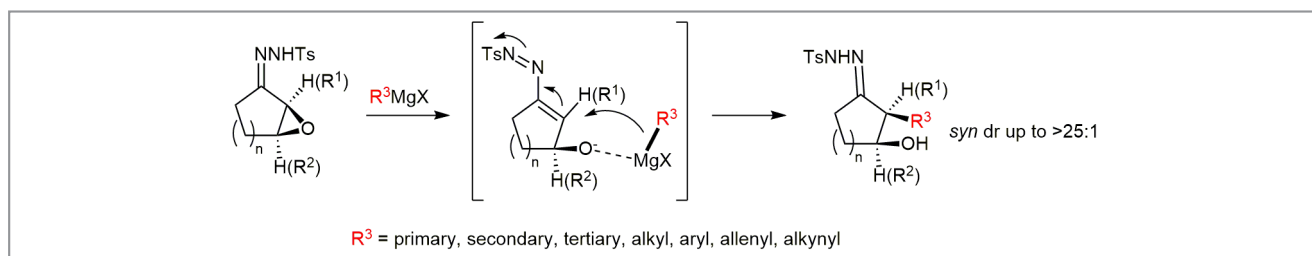
The Texas-based researchers recognized a possibility that was under the synthetic community's nose for nearly 50 years – the interception of the Eschenmoser–Tanabe fragmentation (first reported in 1967) intermediate with a Grignard reagent (introduced in the late 1800s). Professor Coltart said: "As simple as this solution is, the most remarkable feature is its generality: it is able to incorporate an unprecedentedly wide range of carbon-based substituents, including 1°, 2° and 3° alkyl, alkenyl, allenyl, aryl, and alkynyl. Indeed, almost every combination of carbon nucleophile and epoxyhydrazone examined provided the desired compound with superb selectivity." He continued: "Subsequent hydrolysis of the  $\beta$ -hydroxy *N*-sulfonyl hydrazone products produces the corresponding  $\beta$ -hydroxy ketones. In addition to hydrolysis, the  $\beta$ -hydroxy *N*-sulfonyl hydrazone products are poised to undergo numerous different known synthetic transformations via well-established chemistry, giving rise to a wide array of useful structures."

The synthesis of substituted  $\beta$ -hydroxy ketones is as fundamental to organic chemistry, natural product synthesis,

biochemistry, and chemical biology as the aldol reaction. "This motif is common to molecules essential to metabolism, biosynthesis, certain medicines, and a variety of tool compounds for biological studies," confirmed Professor Coltart, adding: "The myriad diverse – and sometimes cumbersome – methods developed over the past several decades to access targets that contain one or more embodiments of this array are a testament to the importance of the motif itself. This method provides a direct, reliable, and broad method to access these high-value molecules."

Professor Coltart explained: "In developing our synthetic method we have had the enormous benefit of being able to stand on the shoulders of some of the greats in the area of organic synthesis, and we owe a great debt to those individuals." The group has recently been working to extend their method to other hydrazones and related species, in the context of aziridine and other applicable moieties, and with various coupling partners in addition to Grignard reagents. "We have also been exploiting the multipolar nature of the intermediate 3-alkoxy-2-azopenes (and related species) for novel annulation processes," said Professor Coltart. "From these initial studies, it appears that these hitherto unexplored arrangements of functional groups may prove quite fruitful as a synthetic platform, leading to a variety of interesting and synthetically useful structures." He concluded: "I believe this work has provided a fresh perspective on some well-known reactions: what's old is new again!"

Professor Gregory B. Dudley, from Florida State University (USA), an expert in the chemistry of sulfonyl hydrazones and related compounds, commented: "Coltart and co-workers described an exciting and innovative strategy for producing  $\beta$ -hydroxy ketones from epoxy hydrazones. Their results are remarkable for the excellent selectivity and scope in forming



quaternary centers, and also for the unprecedented new utility of epoxy hydrazones. Epoxy hydrazones are long known as intermediates in the Eschenmoser–Tanabe fragmentation, but they are typically generated and reacted *in situ*,” he continued. “Here, they are isolated and then harnessed for completely different purposes; namely, for use as electrophiles in

new Grignard addition pathways. The result is a stereocontrolled synthesis of quaternary carbon stereocenters under straightforward and conceptually novel conditions,” concluded Professor Dudley.

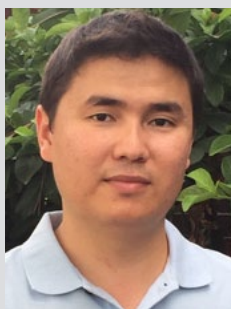
*Matthew Farokh*

### About the authors



*Prof. D. M. Coltart*

**Don Coltart** obtained his Master’s degree from the University of Manitoba (Canada), under the supervision of Professor James L. Charlton, and he then joined the research group of Professor Derrick L. J. Clive at the University of Alberta (Canada), where he obtained his Ph.D. His postdoctoral work was conducted at the Memorial Sloan-Kettering Cancer Center (USA) as an NSERC, AHFMR, and CRI Scholar, under the supervision of Professor Samuel J. Danishefsky. Don began his independent career at Duke University (USA) in 2004 and moved to the University of Houston (USA) in 2012. His research group studies the development of methods for asymmetric carbon–carbon bond formation, the application of those methods to the total synthesis of structurally complex biologically active natural products, and the study of those compounds in biological systems.



*M. M. Uteuliyev*

**Maulen M. Uteuliyev** was born and raised in Shymkent (Kazakhstan). He received his B.Sc. degree in chemistry from Pavlodar State University (Kazakhstan) in 2006. In 2009, Maulen spent a year working on Rh-catalyzed asymmetric hydroboration in the lab of Professor James Takacs at the University of Nebraska-Lincoln (USA). In 2010, he continued to pursue his M.Sc. degree under the direction of Professor Douglas Grotjahn at the San Diego State University (USA) where he focused on N-heterocyclic carbene catalysis. In 2012, he joined the group of Professor Don Coltart at the University of Houston (USA) as a Ph.D. stu-

dent. His current research in the Coltart laboratory focuses on  $\alpha$ -alkylation/functionalization of ketones via activated hydrazones and oximes.



*T. T. Nguyen*

**Thien Nguyen** was born and raised in Da Nang City (Vietnam). He received his B.Sc. degree in chemistry from Science University (Vietnam) in 2008 and M.Sc. degree in Advanced Spectroscopy in Chemistry from Helsinki University (Finland) in 2011. He joined Professor Coltart’s group in 2012 and studies the alkylation/functionalization of ketones via azoalkene species.

# Rhodium-Catalyzed Asymmetric Allylic Arylation of Racemic Halides with Arylboronic Acids

*Nat. Chem.* **2015**, *7*, 935–939

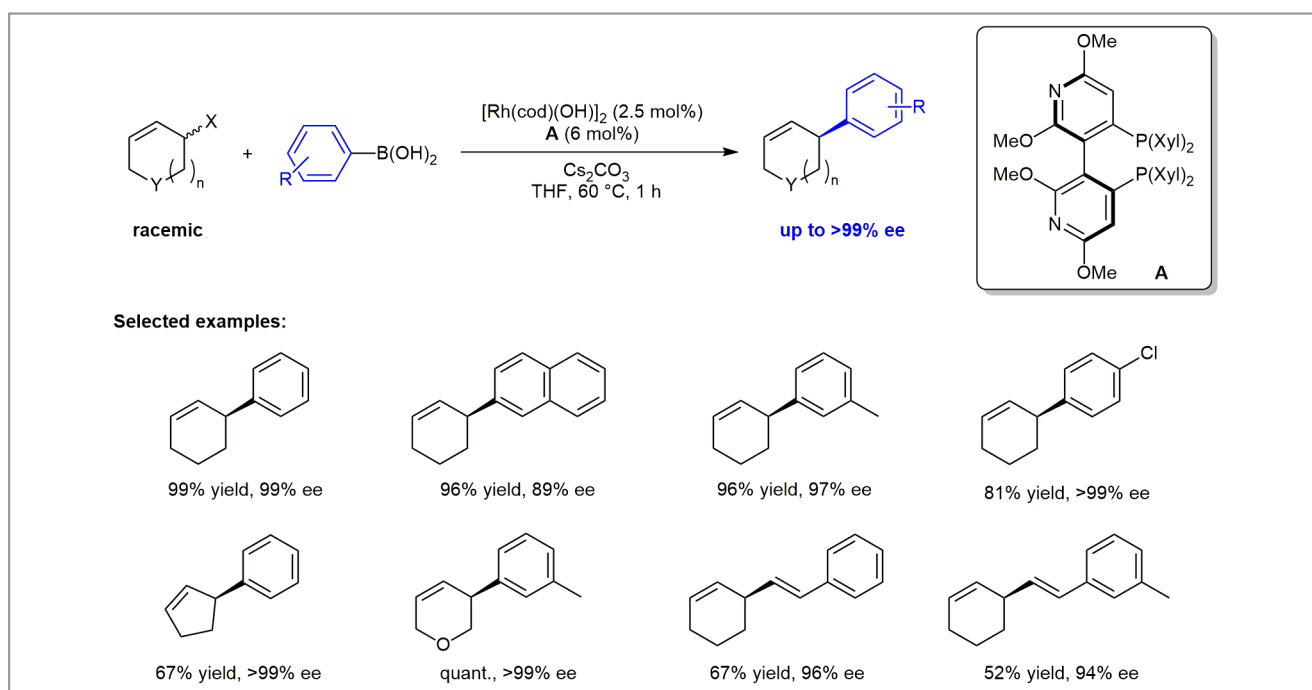
The achievement of stereocontrolled Csp<sup>2</sup>–Csp<sup>3</sup> cross-coupling reactions between allylic halides and arylboronic acids continues to represent a challenging problem in organic synthesis, despite the enormous potential of this transformation.

In 2015, Professor Steve Fletcher and his group at the University of Oxford (UK) reported that non-stabilized alkyl nucleophiles generated through the hydrometalation of alkenes could be used in Cu-catalyzed asymmetric allylic alkylation (AAA) reactions with cyclic racemic allyl halides (*Nature* **2015**, *517*, 351). This reaction is complementary to the widely used Pd-catalyzed AAAs using stabilized nucleophiles in dynamic kinetic asymmetric transformations (DYKAT) initially developed by Trost et al. (*Chem. Rev.* **1996**, *96*, 395). Professor Fletcher explained: “DYKATs are attractive because they allow racemic, rather than prochiral, starting materials to be used in asymmetric catalysis. Currently, there are only very few types of reactions that can convert both enantiomers of a starting material into highly enantioenriched products

in more than 50% yield, and the use of non-stabilized nucleophiles enormously broadens the scope of these transformations.”

Mechanistic work suggested that the copper-catalyzed DYKATs occur because the starting materials are being racemized by the same Cu catalyst that selects one of the enantiomers of the starting material for a highly enantioselective AAA. In follow-up work, Professor Fletcher’s group managed to extend these methods to sp<sup>2</sup>-hybridized alkenylzirconium nucleophiles, but these proved much more challenging; only moderate enantioselectivities were observed and cryogenic reaction temperatures were required (*Chem. Commun.* **2015**, *51*, 5044).

Professor Fletcher said: “An elegant and efficient alternative method recently reported by our group involves arylboronic acids as the non-stabilized sp<sup>2</sup>-hybridized nucleophile and rhodium(I) catalysts in addition to racemic cyclic allyl chlorides.”



**Scheme 1** Dynamic kinetic allylic alkylation using boronic acids

Professor Fletcher explained: “The new DKYAT arylation uses mild conditions (1 h at 60 °C in THF) and allows addition of a broad range of arylboronic acids. The arylation tolerates racemic 5-, 6- and 7-membered-ring electrophiles as well as addition to oxygen-containing heterocycles and the use of electron-rich styrylboronic acids.” He continued: “Electron-deficient, electron-rich and sterically hindered arylboronic acids can undergo highly enantioselective addition by using a commercially available allyl bromide instead of the usual allyl chloride. Without any further optimization, the reaction was scaled up to prepare more than 600 mg of product while the catalyst loading was reduced to 1 mol% of Rh(I) with no loss of selectivity despite a slower reaction rate.”

Professor Fletcher believes that this latest reaction is particularly appealing as it is effectively a catalytic asymmetric Suzuki–Miyaura coupling that forms new Csp<sup>2</sup>–Csp<sup>3</sup> bonds. “Viewed in this way the method could significantly broaden the scope of normal ‘2D cross-coupling’ that is extensively used in academic and industrial labs to provide new 3D building blocks for synthesis,” he added.

Professor Fletcher said that preliminary studies on the reaction mechanism using 3,5-disubstituted cyclohexenyl chlorides show that the reaction proceeds via an overall inversion of configuration, where both enantiomers of a starting diastereomer get converted into a single enantiomer of product. He commented: “Both the new copper- and rhodium-catalyzed processes are highly robust and tolerate a wide range of functional groups. The asymmetric arylboronic acid additions may prove to be useful in the future because so many boronic acids are commercially available or easily prepared.”

Perhaps the most remarkable aspect of these reactions is that they all appear to operate through completely different reaction mechanisms. Professor Fletcher concluded: “As the mechanisms haven’t been previously identified, or completely characterized in the preliminary reports, further studies are necessary to fully understand these reactions. The work also suggests that a wide range of further DYKATs remain to be discovered and that these could impact the strategies that are currently used in asymmetric catalysis.”

*Mattes Fenske*

## About the authors



Prof. S. P. Fletcher

**Stephen P. Fletcher** was born in Halifax, Nova Scotia (Canada) and studied chemistry at Mount Allison University (Canada) and the University of Alberta (Canada). After postdoctoral work with Professors Ben Feringa (Groningen, The Netherlands) and Jonathan Clayden (Manchester, UK) he started a research group at the University of Oxford (UK) in 2009 as an EPSRC Career Acceleration Fellow. He is currently Associate Professor and a

Fellow and Tutor in Chemistry at Keble College (Oxford, UK). Steve’s research interests focus on transition-metal-mediated asymmetric catalysis, the origins of life, and dynamic stereochemistry.



Dr. M. Sidera

**Mireia Sidera** was born in Barcelona, Catalonia (Spain). She received her undergraduate degree from the University of Barcelona (Spain). In 2011, she obtained her PhD at the same university working with Professor Jaume Vilarrasa. In 2012, she joined Professor Fletcher’s group at the University of Oxford (UK) as a postdoctoral research associate. Her research interests include asymmetric catalysis and the synthesis of biologically active molecules.



## Anti-Markovnikov Hydroamination of Homoallylic Amines

*J. Am. Chem. Soc.* **2015**, *137*, 13748–13751

Hydroamination, or the addition of an amine across an unsaturated C–C bond, is an attractive disconnection for C–N bond formation. Not only is this reaction completely atom-economical, but this transformation readily couples two easily accessed functional groups. Hydroamination can form either the Markovnikov product or the anti-Markovnikov product, where the C–N bond is formed at either the internal or terminal position of the olefin, respectively. Metal catalysts are often used for promoting hydroamination reactions, which are generally hampered by high activation energy and unfavorable entropy. While the Markovnikov selective addition of an N–H bond across an alkene is relatively well known, direct anti-Markovnikov hydroamination has remained a significant challenge to synthetic chemists. This transformation is considered to be particularly challenging, as it requires the nucleophilic amine to attack the less electrophilic terminal carbon and results in the formation of the more sterically encumbered internal [M]–C bond. However, elegant approaches using nucleophilic hydrides and electrophilic amines have recently been developed, allowing for reversal of the regioselectivity at the expense of the atom- and step-economy.

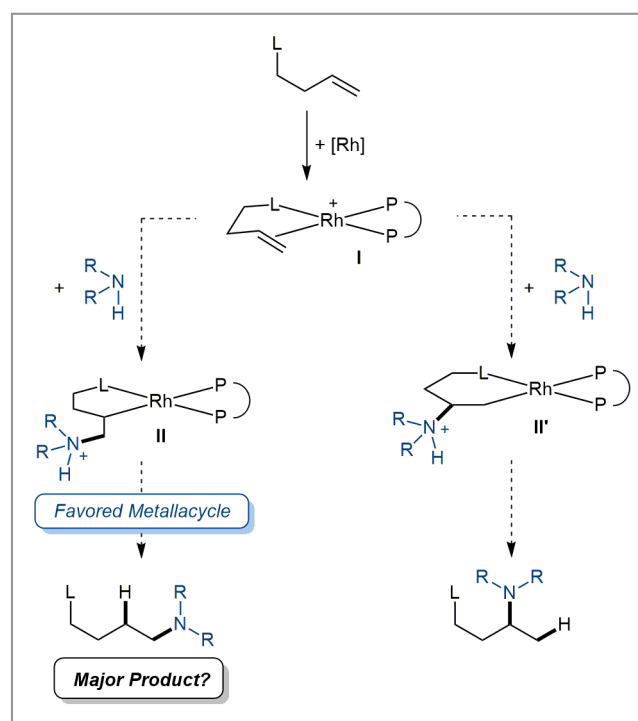
The group of Professor Kami Hull at the University of Illinois at Urbana–Champaign (USA) is interested in studying alternative strategies for controlling the selectivity of olefin functionalization reactions. Professor Hull said: “Previously, we reported that a cationic rhodium complex can catalyze the hydroamination of *N*-allylimines for the synthesis of 1,2-diamines. In this transformation, coordination by the Lewis basic imine promotes reactivity, assists in enforcing chemo- and diastereoselectivity, and slows the formation of undesired side products.” The key intermediate in this transformation is a proposed five-membered metallacycle intermediate that is formed between the rhodium catalyst and substrate. The group hypothesized that this intermediate localizes the metal center at the terminal position of the olefin and not at the internal position (which would form a far more strained four-membered metallacycle).

“With this in mind, we considered that substrates with a Lewis basic group and homoallylic olefin may also be able to undergo this transformation,” explained Professor Hull, who continued: “In this case, the Rh–C bond could be formed at either the terminal or internal position of the olefin to give rise to either a six- or five-membered metallacycle, respectively. As a five-membered metallacycle should be less strain-

ed than the six-membered alternative, we reasoned that the strain developing in the regioisomer-determining transition state may favor the formation of the anti-Markovnikov product.”

The group began their investigations with 1,1-diphenyl homoallyl amine on the assumption that this should promote bidentate substrate binding through the Thorpe–Ingold effect. To their gratification, this substrate formed the desired anti-Markovnikov product (and 1,4-diamine) when morpholine was employed as a nucleophile. “With some optimization, it was determined that 5 mol%  $[\text{Rh}(\text{cod})_2]\text{BF}_4$  and 5 mol% DPEphos in DME at 100 °C for 48 hours were the optimal conditions,” said Professor Hull. These conditions were shown to be general for a variety of relatively electron-rich secondary cyclic amines as well as *N,N*-dimethylamine, to afford the desired products in good to excellent yield and as a single regioisomer (>20:1).

Professor Hull commented: “Interestingly, the reaction conditions were less selective for anti-Markovnikov hydroamination when substrates with smaller groups adjacent to the amine directing group are employed. This suggested to

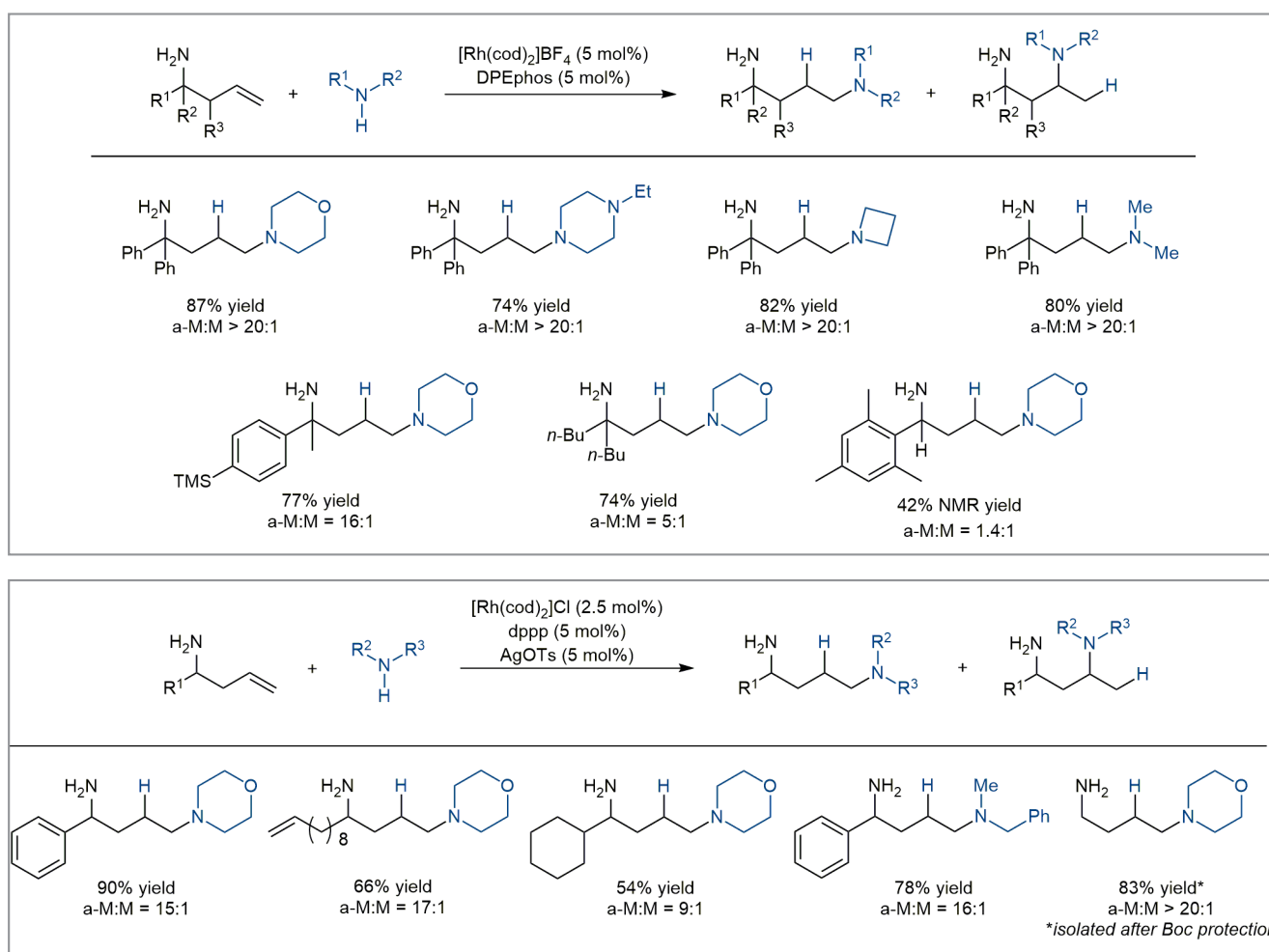


us that with DPEphos the strain difference between the five- and six-membered metallacycle was no longer sufficient to dictate the regioselectivity. Although frustrating at the time, fortunately we found that utilization of dppp restored the regioselectivity with less-hindered substrates, such that even homoallyl amine affords the desired anti-Markovnikov product.”

The Hull group is interested in investigating the mechanistic principles behind the catalysis they develop, towards a greater understanding of organometallic chemistry as a whole. Professor Hull and co-workers have previously demonstrated that proximal Lewis basic groups can direct the Rh-catalyzed anti-Markovnikov hydroamination of homo-

allylic amines. “Currently, we are investigating the mechanism of the transformation and seeking to better understand the profound ligand effect we observe, with the ultimate goal of developing a more general catalyst. We are also interested in determining if cobalt, rhodium’s smaller, cheaper, and more reactive sibling, can catalyze a similar reaction,” said Professor Hull. She concluded: “Finally, we are excited about the potential of this reaction being applied in the synthesis of biologically active compounds, as 1,4-diamines are a common functionality and prevalent in a variety of pharmaceuticals that treat neurological disorders.”

*Mattis Fenske*



## About the authors



Prof. K. L. Hull

**Kami L. Hull** received her B.A. degree in chemistry from Macalester College (USA) in 2003. She obtained her Ph.D. from the University of Michigan (USA) in 2009 under the mentorship of Professor Melanie S. Sanford. She went on to be an NIH postdoctoral fellow at Stanford University (USA) from 2009–2012 in the laboratory of Professor Barry M. Trost. Professor Hull joined the faculty at the University of Illinois at Urbana–Champaign (USA) in fall 2012.



S. C. Ensign

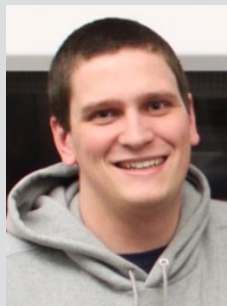
**Seth Ensign** received his B.S. in chemistry from James Madison University in Harrisonburg, VA (USA), where he worked in the research group of Professor Debra L. Mohler. He is currently a fourth-year Ph.D. student at the University of Illinois at Urbana–Champaign (USA) under the mentorship of Professor Kami L. Hull. His research focuses on developing new, regioselective rhodium-mediated hydroamination reactions.



E. P. Venable

**Evan P. Venable** received his B.S. degree in chemistry from Union College in Schenectady, NY (USA) in 2013. He began his graduate research at the University of Illinois at Urbana–Champaign (USA) with Professor Kami L. Hull in fall of the same year. His research focuses on the development of novel transition-metal-catalyzed methodologies, and the study of these reactions towards a greater understanding of their complexities.

His interests include the in-depth study of organometallic reaction mechanisms, obscure and interesting simple organic molecules, and reading science fiction.



K. D. Kortman

**Gregory D. Kortman** received his B.S. in chemistry at Grand Valley State University in Allendale, MI (USA) in 2012. Afterwards, he joined the group of Professor Kami L. Hull at the University of Illinois at Urbana–Champaign (USA). His research focuses on designing hydro- and difunctionalization reactions of carbon–carbon single, double, and triple bonds by transition-metal catalysis.



L. J. Weir

**Lee J. Weir** received his B.S. degree in specialized chemistry from the University of Illinois at Urbana–Champaign (USA) in 2015. While studying there he was a member of the Hull Research Group from 2013–2015.

## Coming soon

### SYNLETT Highlight

#### A Second-Generation Chemoenzymatic Total Synthesis of Platencin

### SYNTHESIS Highlight

#### Silver-Promoted Oxidative Ring Opening/Alkynylation of Cyclopropanols: Facile Synthesis of 4-Yn-1-ones

### Literature Coverage

#### Catalytic Formal [2+2+1] Synthesis of Pyrroles from Alkynes and Diazenes via Ti(II)/Ti(IV) Redox Catalysis

## Further highlights

### Synthesis Review: Syntheses of Cinacalcet: An Enantiopure Active Pharmaceutical Ingredient (API)

(by S. Vázquez)

### Synlett Cluster with 11 contributions on: Radical Chemistry

(edited by T. Rovis, R. A. Shenvi)

### Synfacts Synfact of the Month in category "Polymer-Supported Synthesis": Suzuki Coupling with an N-Heterocyclic Carbene-Palladium Catalyst

For current SYNFORM articles, please visit [www.thieme-chemistry.com](http://www.thieme-chemistry.com)  
SYNFORM issue 2016/04 is available from March 15, 2016  
at [www.thieme-connect.com/ejournals](http://www.thieme-connect.com/ejournals)

### 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: Michael Binzner,  
[michael.binzner@thieme.de](mailto:michael.binzner@thieme.de), phone: +49 711 8931 788  
Scientific Editor: Selena Boothroyd,  
[selena.boothroyd@thieme.de](mailto:selena.boothroyd@thieme.de)  
Assistant Scientific Editor: Kathrin Ulbrich,  
[kathrin.ulbrich@thieme.de](mailto:kathrin.ulbrich@thieme.de), phone: +49 711 8931 785  
Editorial Coordinator: Hana Kim-Türk,  
[hana.kim-tuerk@thieme.de](mailto:hana.kim-tuerk@thieme.de), phone: +49 711 8931 776  
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/Synlett/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 2016 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.

Via e-mail: [customerservice@thieme.com](mailto:customerservice@thieme.com)

Via website: [www.thieme-chemistry.com](http://www.thieme-chemistry.com)

Phone: +1 212 760 0888; Fax: +1 212 947 1112

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

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

Via e-mail: [customerservice@thieme.de](mailto:customerservice@thieme.de)

Via website: [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 [www.thiemeconnect.com/products/ejournals/journals](http://www.thiemeconnect.com/products/ejournals/journals) where it is also possible to register for a free trial account. 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

Manuscript submissions will be processed exclusively online via <http://mc.manuscriptcentral.com/synthesis> and <http://mc.manuscriptcentral.com/synlett>, respectively. 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).

### 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 to 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.