

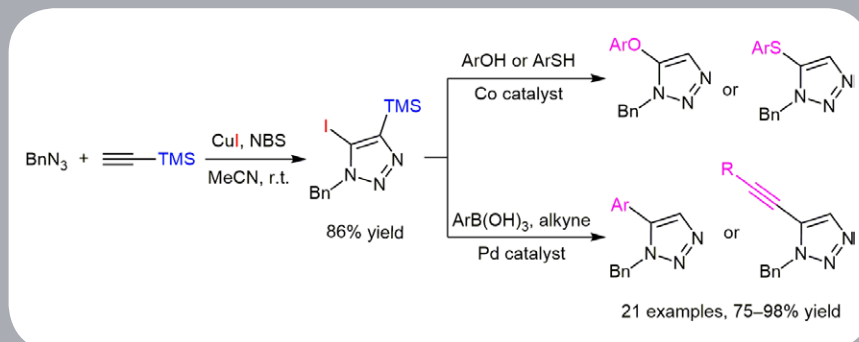
# Synform

People, Trends and Views in Chemical Synthesis

2015/06

## 4-Trimethylsilyl-5-iodo-1,2,3-triazole: A Key Precursor for the Divergent Syntheses of 1,5-Disubstituted 1,2,3-Triazoles

Highlighted article by L. Li, T. Shang, X. Ma, H. Guo,  
A. Zhu, G. Zhang



### Contact

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## Dear Readers,

I hope everyone likes the new look of SYNFORM, which is now published in the same layout as SYNLETT and SYNTHESIS. I believe this new layout is really amazing and browsing through the pages of our journals has become more appealing than ever. Furthermore, the color coding makes it very easy to spot the different types of articles published in SYNFORM. You will therefore note that this new issue is kick-started by the green code of a Young Career Focus dedicated to Joe B. Gilroy (Canada) who answers the traditional set of five questions asked by SYNFORM. The red code for articles covering the most exciting papers published in the recent literature appears in the upper right corner of two of the next three articles. The first story zooms in on a new method for introducing a  $\text{CF}_2$  fragment in ketones, developed by A. Dilman (Russian Federation). The second article reports on a new versatile strategy for functionalizing 'click' 1,2,3-triazoles, recently published in SYNLETT (and therefore color-coded in light-blue) by L. Li and L. Zhang (P. R. of China). Finally, G. Hreczycho (Poland) has the important duty of closing this issue with a highly selective hydrothiolation of organosilicon compounds.

Enjoy your reading!



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### Contact

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

## Young Career Focus: Professor Joe B. Gilroy (Western University, Canada)

**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 Young Career Focus presents Professor Joe B. Gilroy (Western University, London, Ontario, Canada).

### Biographical Sketch



Prof. J. B. Gilroy

**Joe Gilroy** was raised in Port Alberni, British Columbia, a small town located on the beautiful west coast of Canada, where he attended Alberni District Secondary School. He obtained his B.Sc. (2003) and Ph.D. (2008) degrees from the University of Victoria (Canada) where he conducted research under the tutelage of Professor Robin Hicks as part of a variety of projects involving stable radicals and their metal complexes, ligand design, and molecule-based magnetism. In 2008, he joined the group of Professor Ian Manners at the University of Bristol (UK). His work in the Manners group spanned a number of areas including the synthesis and self-assembly of metal-containing polymers, mechanistic organometallic chemistry, and the chemistry of  $\pi$ -conjugated polymers. Since 2012, Joe has been an Assistant Professor at Western University (formerly known as the University of Western Ontario) in London, Ontario, Canada. For details surrounding his independent research, please see: <http://publish.uwo.ca/~jgilroy5/>.

research projects combine fundamental organic, inorganic, and polymer synthesis with advanced characterization tools and nanofabrication techniques in an effort to address globally relevant research problems.

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

**Prof. J. B. Gilroy** As far back as I can remember, I always wanted to 'make' things. My interests advanced from working with wood and metal as a young teenager to chemical synthesis as a high school student. However, it wasn't until I was introduced to a Schlenk line by Dr. Dave Berry at the University of Victoria that I was truly hooked. The notion that careful manipulation of simple chemicals under an inert atmosphere could lead to a vast range of useful materials with tunable properties was truly astonishing to me. I have been involved in synthesis in its various forms ever since.

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

**Prof. J. B. Gilroy** In my opinion, organic synthesis has changed significantly over the past few decades, perhaps not coincidentally due to the growing pressure that researchers face to conduct applied rather than fundamental research. I am hopeful that global funding agencies and researchers alike will continue to value (and fund) fundamental organic synthesis projects, as the advances they produce are integral to so many of the 'big picture' problems. Personally, I can't wait to read about the next big discoveries that lead to new anti-cancer drugs, new synthetic materials that allow for energy to be produced efficiently and without pollution, and catalysts and methodologies that allow for conversion of bioavailable feedstock that do not interfere with the food chain into commodity materials with few (or no) byproducts. Organic synthesis will play a key role in reaching each of these milestones, as well as so many others.

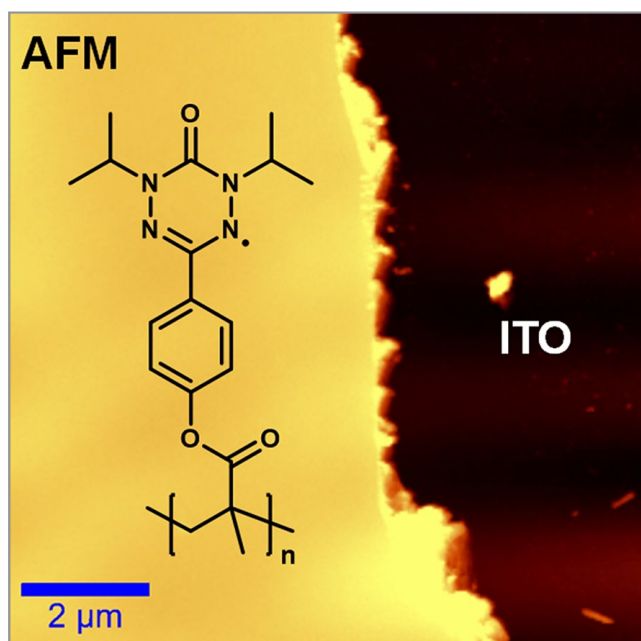
### INTERVIEW

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

**Prof. J. B. Gilroy** My research program is highly collaborative and interdisciplinary. Broadly, we target synthetic functional molecular and polymeric materials with potential applications ranging from alternative energy production and heterogeneous catalysis to fluorescence cell imaging. All of our

**SYNFORM** Your research group is active in the areas of polymers and materials science. Could you tell us more about your research and its aims?

**Prof. J. B. Gilroy** I am very lucky to have a hard-working and talented research team engaged in a variety of projects centered around the synthesis of functional molecular, polymeric, and nanostructured materials. Our current projects include: the synthesis and characterization of stable verdazyl radical polymers for use as hydrophobic hole-transport materials (Figure 1),<sup>1</sup> the production of highly metallized phosphonium polymers as precursors to novel heterogeneous catalysts,<sup>2</sup> the synthesis and evaluation of  $\pi$ -conjugated metallopolymers for use in polymer-based electronics,<sup>3</sup> and the development of redox-active formazanate ligands for use in main-group and transition-metal coordination chemistry.<sup>4,5</sup>

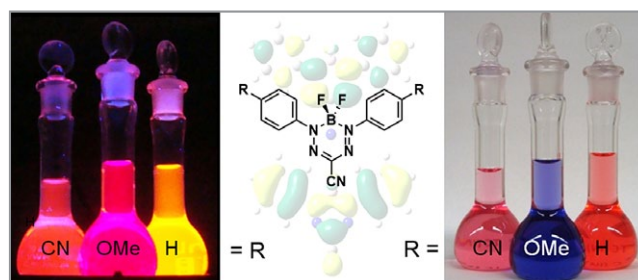


**Figure 1** AFM image of a thin film of a 6-oxoverdazyl-based stable radical polymer on indium tin oxide (ITO)

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

**Prof. J. B. Gilroy** This is difficult, as I feel like we're just getting started. So far, I am most proud of our work towards the development of boron difluoride formazanate dyes as alternatives to BODIPYs and related compounds. These complexes can be synthesized in two straightforward and high-yielding

steps from commercial starting materials for just a few dollars per gram.<sup>4,5</sup> The spectroscopic and electrochemical properties of the complexes are very sensitive to the nature of the substituents appended to the formazanate backbone (Figure 2), which can be easily modified. We have demonstrated the efficient electrochemiluminescence<sup>6</sup> of these complexes and we are currently exploring their application as donor materials in solar cells and as fluorescence imaging agents. We are excited about the potential of this novel family of compounds and look forward to their future development in our group as well as others.<sup>7</sup>



**Figure 2** Boron difluoride formazanate complexes with tunable properties under long-wavelength UV irradiation (left) and ambient conditions (right)

*Mattias Fanchini*

## REFERENCES

- (1) J. T. Price, J. A. Paquette, C. S. Harrison, R. Bauld, G. Fanchini, J. B. Gilroy *Polym. Chem.* **2014**, *5*, 5223.
- (2) A. Rabiee Kenaree, B. M. Berven, P. J. Ragogna, J. B. Gilroy *Chem. Commun.* **2014**, *50*, 10714.
- (3) J. A. Paquette, E. R. Sauv e, J. B. Gilroy *Macromol. Rapid Commun.* **2015**, *36*, 621.
- (4) S. M. Barbon, P. A. Reinkeluers, J. T. Price, V. N. Staroverov, J. B. Gilroy *Chem. Eur. J.* **2014**, *20*, 11340.
- (5) S. M. Barbon, J. T. Price, P. A. Reinkeluers, J. B. Gilroy *Inorg. Chem.* **2014**, *53*, 10585.
- (6) M. Hesari, S. M. Barbon, V. N. Staroverov, Z. Ding, J. B. Gilroy *Chem. Commun.* **2015**, *51*, 3766.
- (7) M.-C. Chang, E. Otten *Chem. Commun.* **2014**, *50*, 7431.

## Difluorohomologation of Ketones

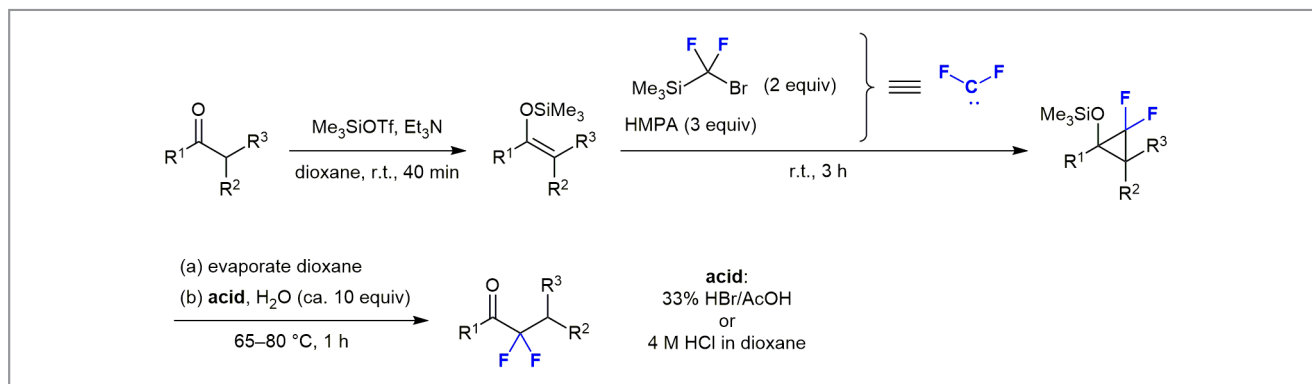
*Org. Lett.* **2015**, *17*, 760–763

Despite significant developments in the synthesis of organofluorine compounds, efficient methods for accessing *gem*-difluorinated products are still limited. Indeed, the existing approaches involve either harsh deoxofluorination reagents or multiple functional group manipulations.  $\alpha,\alpha$ -Difluorinated ketones are attractive substrates for medicinal chemistry and drug discovery applications, since they efficiently form adducts (hemiketals), with water and other nucleophiles, that may resemble tetrahedral intermediates involved in the hydrolysis of peptides. Recently, a general protocol for the conversion of readily available ketones into their difluorohomologues (Scheme 1) was described by Alexander Dilman, Mikhail Kosobokov, Vitalij Levin and Marina Struchkova from Zelinsky Institute of Organic Chemistry (Moscow, Russian Federation). Professor Dilman said: “The method involves a sequence of three steps, which are performed in a single reaction flask! It starts with the generation of silyl enol ether by using trimethylsilyltriflate and triethylamine – a clean, virtually quantitative, and rapid process. Second, to the resulting mixture were successively added (bromodifluoromethyl) trimethylsilane ( $\text{Me}_3\text{SiCF}_2\text{Br}$ ) and hexamethylphosphoramide (HMPA). In this step, Lewis basic HMPA attacks at silicon of  $\text{Me}_3\text{SiCF}_2\text{Br}$  and generates difluorocarbene, which readily (at room temperature!) reacts with the electron-rich enol–ether double bond to furnish difluorocyclopropanes.” While difluorocyclopropanes are typically stable and isolable, these cyclopropanes, bearing a silyloxy group, turned out to be quite unpleasant to handle, revealed Professor Dilman. Indeed, while some of them (those derived from cyclic ketones) can

be purified by chromatography and can even be distilled under vacuum, others (those derived from acetophenones) do not survive simple aqueous work-up. The latter observation suggested an opportunity for cyclopropane ring opening. But, in fact, a great amount of work was invested to optimize this particular stage.

“We were puzzled by the observation that under anhydrous conditions, protonation of silyloxycyclopropanes did not occur even under the action of strong acids such as trifluoroacetic or methanesulfonic acid,” said Professor Dilman. This led to the idea that water is needed to hydrolyze the silyl ether into a free hydroxyl group. Finally, after a series of optimization experiments, it was established that the reaction proceeded most effectively when a small amount of water was added. “It is likely that a cyclopropanol, not silyloxycyclopropane, is the real species that undergoes ring opening,” said Professor Dilman. “The hydroxyl group can engage in hydrogen bonding, thereby polarizing a C–C bond in the cyclopropane. Another feature of this step is that a solution of hydrogen bromide in acetic acid was the optimal acidic species to effect cyclopropanol protonation by heating to 80 °C,” explained Professor Dilman. “Preliminary evaporation of dioxane was necessary, since otherwise dioxane itself reacts with hydrogen bromide, affording by-products which complicate product purification.”

The majority of ketones worked well with this protocol, affording difluorohomologated ketones in good yields. However, for some substrates, heating with  $\text{HBr}/\text{AcOH}$  proved to be quite harsh (e.g., decomposition of ferrocene, or partial de-



**Scheme 1** Difluorohomologation process

methylation of methoxy groups). In these cases, a less drastic treatment was used – hydrogen chloride in dioxane with heating at 65 °C (Figure 1).

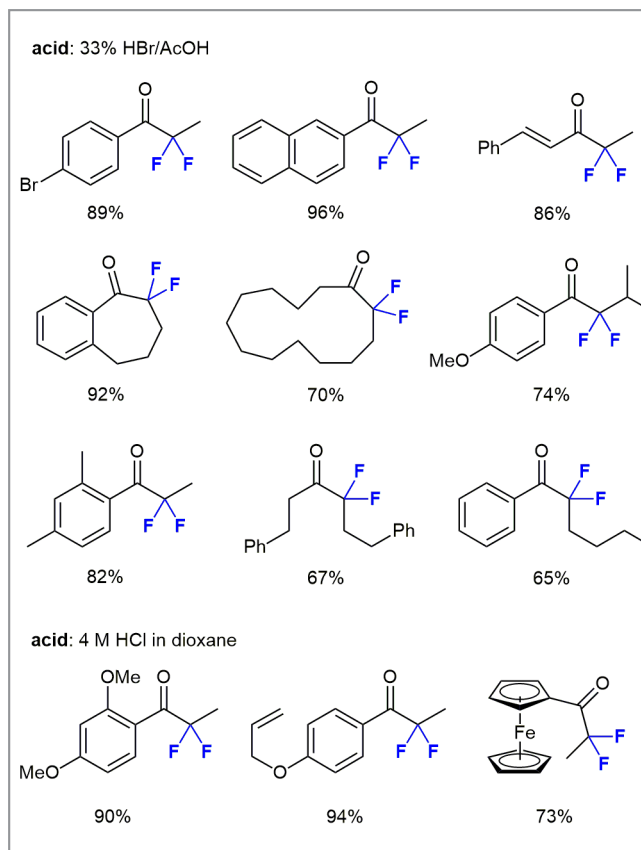


Figure 1 Substrate scope

With sterically hindered substrates (Figure 2), a different one-pot procedure was developed, involving generation of silyl enol ethers by means of conventional deprotonation of ketones with lithium diisopropylamide followed by quenching with  $\text{Me}_3\text{SiCl}$ . Subsequent difluorocarbene addition and cyclopropane ring opening were carried out under typical conditions.

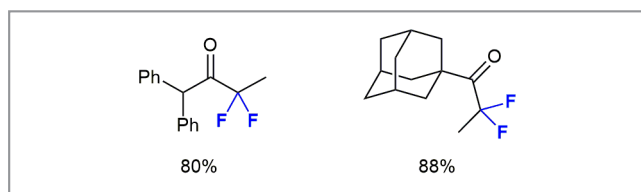


Figure 2 Difluorohomologation of hindered substrates

Professor Dilman concluded: “Taken together, these procedures allow for a straightforward transformation of a wide variety of ketones into their difluorohomologated counterparts. The key reagent,  $\text{Me}_3\text{SiCF}_2\text{Br}$ , is now available commercially from several companies, even on kilogram scale, or can be prepared according to literature procedures.”

Professor David O’Hagan from the School of Chemistry, University of St. Andrews (UK), an organofluorine chemistry expert, commented: “This is a nice straightforward and general method for the synthesis of  $\alpha,\alpha$ -difluoro ketones. The authors demonstrate that the chemistry can be carried out on a wide range of ketones, and such products have proven useful, for example as rationally designed inhibitors for hydrolytic enzymes. There is no doubt that the  $\text{CF}_2$  group is enjoying a high profile at present, largely due to the availability of a next generation of reagents that can generate difluorocarbene. This chemistry from Dilman’s lab is another nice example demonstrating the utility and versatility of difluorocarbene in organic synthesis.”

*Mattias Fenske*

### About the authors



Dr. M. Kosobokov

**Mikhail Kosobokov** was born in Orel (Russia) in 1988. After finishing his MSc degree in organic chemistry from Lomonosov State University (Moscow, Russia) in 2011, he joined Professor A. Dilman’s group. Mikhail defended his PhD thesis in 2014, developing chemistry of the fluorinated silicon reagents. He is currently working as postdoctoral associate with Professor Norio Shibata (Nagoya, Japan).



Dr. V. Levin

**Vitalij Levin** was born in 1983 in Moscow (Russia). He studied chemistry at the Moscow Chemical Lyceum (1998–2000), and then at the Higher Chemical College (2000–2005). In 2003, he joined the group of Professor A. Dilman working on synthetic applications of organosilicon reagents. He obtained his PhD degree in 2007, and continued research work in the

>>

same group. His interests include organic synthesis, music, and choir singing.



*Dr. M. Struchkova*

**Marina Struchkova** graduated from Moscow State University (Russia) in 1968, and obtained her PhD degree in 1977 at the Moscow University of Chemical Technology. Then, she joined the NMR laboratory of the Zelinsky Institute of Organic Chemistry (Russia). Her major interests involve NMR spectroscopy.



*Prof. A. Dilman*

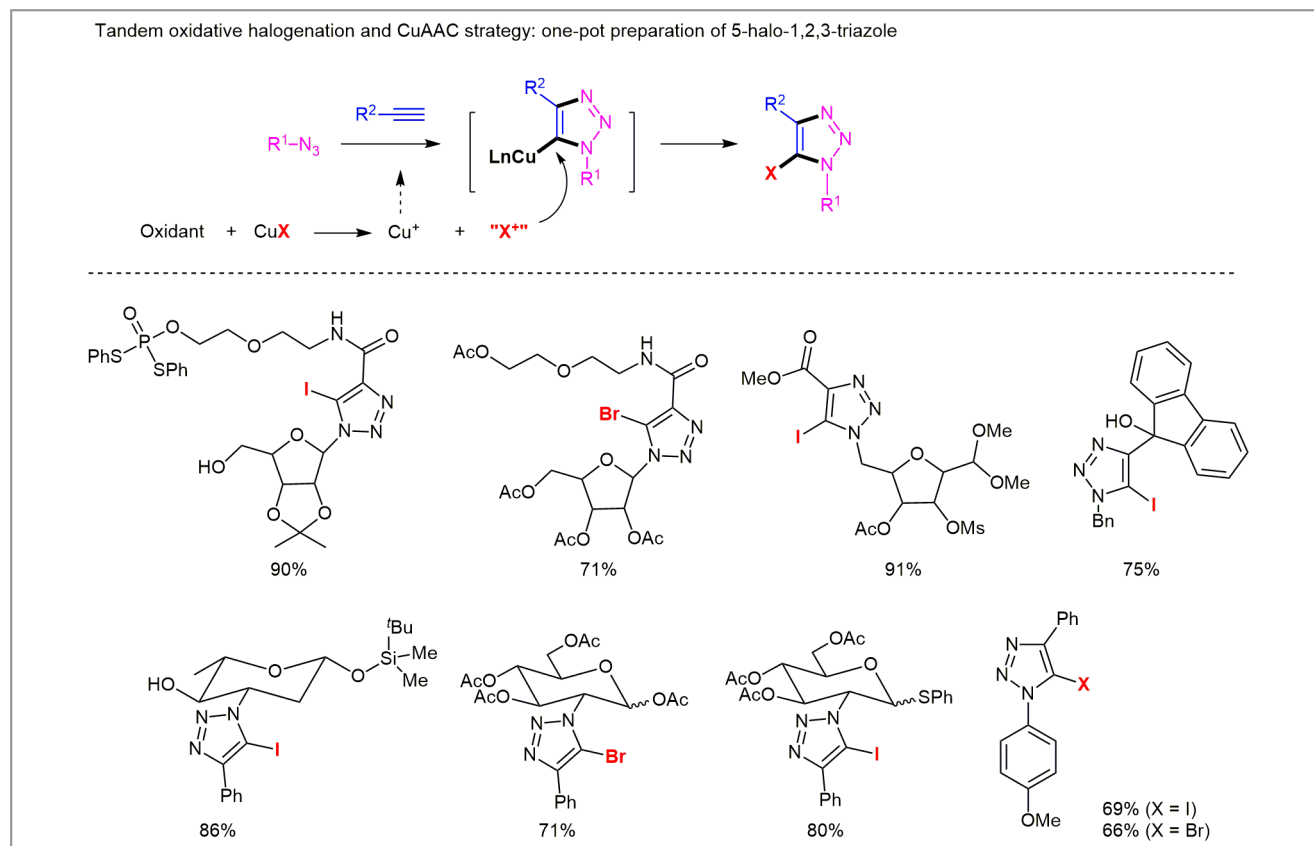
**Alexander Dilman** was born in 1976 in Moscow (Russia). From 1991–1993 he studied at the Moscow Chemical Lyceum (a high school specialized on chemistry). In 1993, he entered the Higher Chemical College, and then, in 1999, continued education in the Graduate School of Zelinsky Institute of Organic Chemistry (with Professor S. L. Ioffe). After obtaining his PhD degree in 2001, he spent one year as a postdoctoral researcher in the group of Professor H. B. Kagan at the Université Paris Sud (France). In 2003, he returned to the Zelinsky Institute and started independent work. In 2008, he completed his habilitation studies (Dr. Sci. in Russia), and in 2011 became a head of laboratory. His interests include the chemistry of fluorine and silicon.

## 4-Trimethylsilyl-5-iodo-1,2,3-triazole: A Key Precursor for the Divergent Syntheses of 1,5-Disubstituted 1,2,3-Triazoles

*Synlett* 2015, 26, 695–699

The investigation of synthetic methods involving 5-substituted 1,2,3-triazoles began several years ago when Professor Lingjun Li was a PhD candidate under the supervision of Professor Lihe Zhang at Peking University (Beijing, P. R. of China). At that time, they applied 4-amide-1,2,3-triazole as the bioisostere of purine nucleobase for the design and synthesis of cyclic ADP-ribose (cADPR, known as a cellular signaling molecule) analogues (*J. Med. Chem.* 2004, 47, 5674). Professor Li said: “However, we could not find an existing method to efficiently incorporate an iodine atom to the 5-position of 4-amide-1,2,3-triazole nucleobase at that time. Thus, we decided to explore new methods.” Based on the study of a 1,2,3-triazolyl copper intermediate in the literature, they

developed a new tandem oxidative iodination and copper-catalyzed alkyne azide cycloaddition (CuAAC) strategy, by which the 5-iodo-4-amide-1,2,3-triazole nucleobase could be constructed directly from two building blocks without touching the other functional groups (*J. Org. Chem.* 2008, 73, 3630). Then, the Li group extended this strategy to ‘tandem oxidative bromination and CuAAC’ (*Synlett* 2011, 874). “The above protocols provided mild, efficient and one-pot synthetic routes to 5-halo-1,4-disubstituted 1,2,3-triazoles from readily prepared terminal alkynes, azides and halide, for a wide scope of substrates, especially various sugar moieties (Scheme 1),” said Professor Li.



Scheme 1

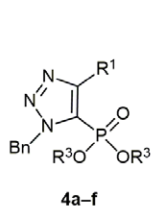
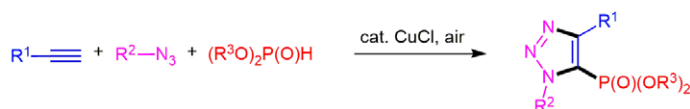


“To our delight, our methods were soon applied for the synthesis of carbonic anhydrase inhibitor libraries, focusing on the diverse modification of the 1,2,3-triazole pharmacophore (*J. Med. Chem.* **2011**, *54*, 6905),” said Professor Li. “Besides, the one-pot preparative protocol for 5-iodo-triazole-containing cADPR analogues was considered to open new prospects for further interesting modifications of this molecule (*Chem. Rev.* **2009**, *109*, 4207).” This success prompted the Li group to continue pursuing more concise synthetic methodologies that would allow for the straightforward incorporation of various functional groups into the 5-position of the 1,2,3-triazole moiety from alkyne and azide building blocks as starting materials. “As an example, we recently reported another oxidative tandem protocol to prepare 1,2,3-triazolyl-5-phosphonates from terminal alkynes, azides and H-phosphates (*Chem. Eur. J.* **2013**, *19*, 14403, Scheme 2),” explained Professor Li.

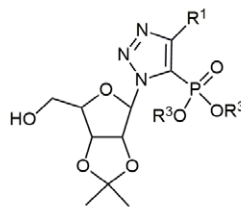
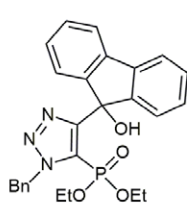
“Compared with the extensive research on the synthesis of 1,4-disubstituted 1,2,3-triazoles, effective methods for the preparation of 1,5-disubstituted 1,2,3-triazoles were fairly limited,” said Professor Li. “Therefore, we hope to explore some

practical synthetic protocols for 1,5-disubstituted 1,2,3-triazoles, especially biologically relevant derivatives that are difficult to prepare through other known methods. In the current paper (*Synlett* **2015**, *26*, 695), we developed a novel divergent synthetic protocol for 1,5-disubstituted 1,2,3-triazoles (Scheme 3).” 4-Trimethylsilyl-5-iodo-1,2,3-triazoles (TMSIT), that are prepared successfully from an inexpensive TMS-alkyne and an azide, as the versatile precursors, along with copper(I) iodide, can be conveniently transformed into 5-phenoxy-, 5-arythio-, 5-alkynyl-, and 5-aryl-1,2,3-triazoles. The directing effects of the TMS group allow iodine atoms to be incorporated into the 5-position of the 1,2,3-triazole regioselectively using a tandem oxidative iodination and CuAAC strategy. “TMS groups can then be deprotected smoothly, under conditions compatible with classic Cu/Pd-catalyzed cross-coupling reactions, and thus can give 1,5-disubstituted 1,2,3-triazoles in one pot from TMSIT,” said Professor Li. “Moreover, 1-benzyl TMSIT, which is a light-brown crystalline solid (mp 96–98 °C) and stable enough to be stored in air for several months, can be prepared on gram scale.

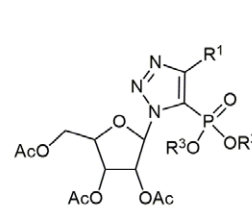
#### One-pot assembly of 1,2,3-triazolyl-5-phosphonates from azides, alkynes, and H-phosphates



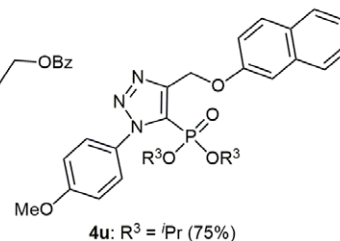
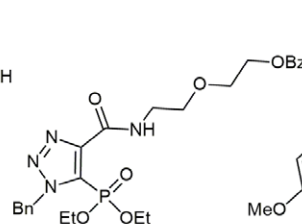
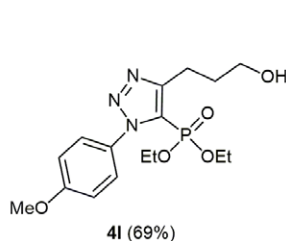
- 4a: R<sup>1</sup> = Ph, R<sup>3</sup> = Et (78%)  
 4b: R<sup>1</sup> = 4-MeC<sub>6</sub>H<sub>4</sub>, R<sup>3</sup> = Et (82%)  
 4c: R<sup>1</sup> = 4-FC<sub>6</sub>H<sub>4</sub>, R<sup>3</sup> = Et (83%)  
 4d: R<sup>1</sup> = 2-pyridinyl, R<sup>3</sup> = Et (73%)  
 4e: R<sup>1</sup> = Ph, R<sup>3</sup> = <sup>i</sup>Pr (80%)  
 4f: R<sup>1</sup> = Ph, R<sup>3</sup> = Bn (62%)



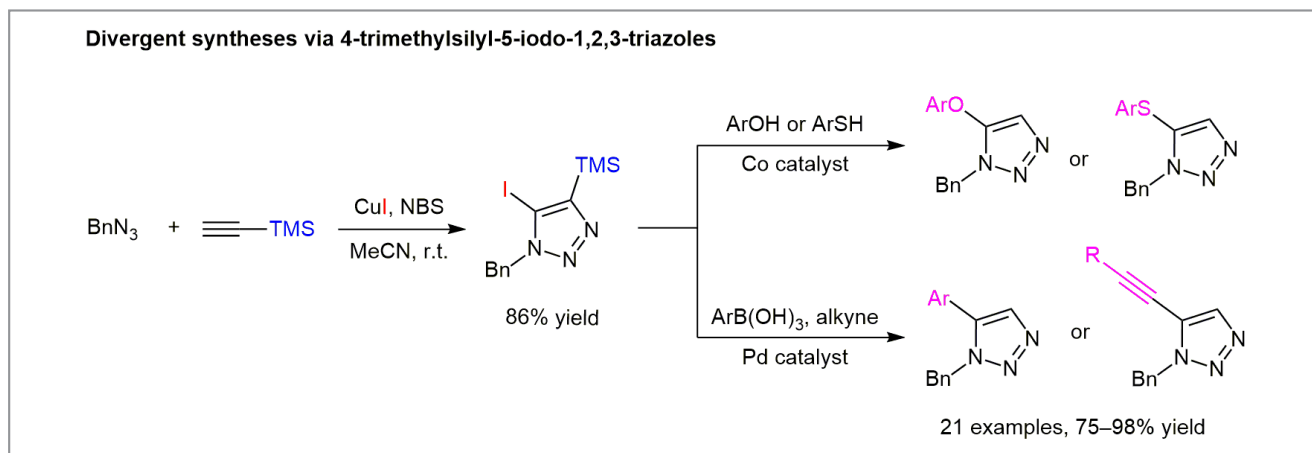
- 4p: R<sup>1</sup> = Ph, R<sup>3</sup> = Et (76%)  
 4q: R<sup>1</sup> = Ph, R<sup>3</sup> = <sup>i</sup>Pr (69%)



- 4r: R<sup>1</sup> = Ph, R<sup>3</sup> = Et (73%)  
 4s: R<sup>1</sup> = Ph, R<sup>3</sup> = <sup>i</sup>Pr (75%)



Scheme 2



Scheme 3

Together with the concise synthesis routes and the stability of the key precursors, this work provides an attractive alternative for the preparation of structurally diverse 1,5-disubstituted 1,2,3-triazoles.”

Professor Li concluded: “The exploration of more convenient methodologies for the preparation of 5-functionalized 1,2,3-triazoles, and further application of these synthetic methods in the design of bioactive molecules are currently ongoing in our lab.”

*Li Junjun*

### About the authors



Prof. L. Li

**Lingjun Li** was born in Henan (P. R. of China) in 1979. He defended his PhD in 2007 under the supervision of Professor Lihe Zhang (Peking University, P. R. of China), working on the design and synthesis of nucleotide cellular signaling molecules. Subsequently, he worked as a teacher at Henan Normal University (P. R. of China). He carried out postdoctoral training at The Scripps Research Institute (USA) in Professor Floyd E. Romesberg’s research group, working on the chemical biology of unnatural base pairs. Now, he is an Associate Professor in the Department of Chemistry at Henan Normal University. His research interests include synthetic methodology and chemical biology.



T.-P. Shang

**Tong-Peng Shang** was born in Henan (P. R. of China) in 1989. He received his BSc in applied chemistry from Huanghuai University (P. R. of China) in 2013 and is currently performing research under the guidance of Professor Li Lingjun in Henan Normal University as a postgraduate student. His research interest concerns triazole chemistry.

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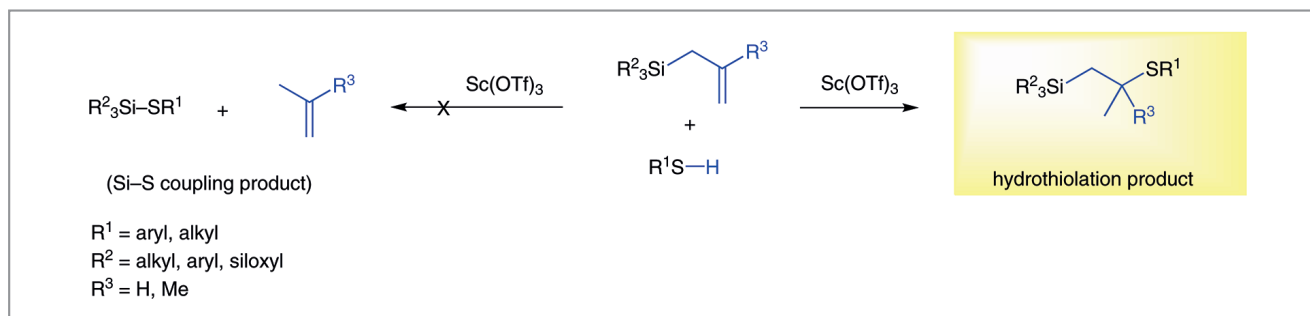
*Prof. G. Zhang*

**Guisheng Zhang** was born in Henan (P. R. of China) in 1965 and obtained his Bachelor's degree in organic chemistry in 1986 from Jilin University (P. R. of China). After receiving his Master's degree at Jilin University in 1989, he immediately joined the Faculty of Henan Normal University. He was promoted to Full Professor of Chemistry in 1999. In 2002, he completed his PhD under the supervision

of Professor Li-He Zhang in Peking University. He then joined Professor Peng George Wang at Ohio State University (USA) as a postdoctoral associate. At the beginning of 2006, he returned to China as an Eminent Professor at Henan Normal University, and he was appointed as the Dean of School of Chemistry and Chemical Engineering in 2012. His research interests are in the fields of synthetic methodology and medicinal synthesis.

# Highly Selective Hydrothiolation of Unsaturated Organosilicon Compounds Catalyzed by Scandium(III) Triflate

*Chem. Eur. J.* **2015**, *21*, 4940–4943



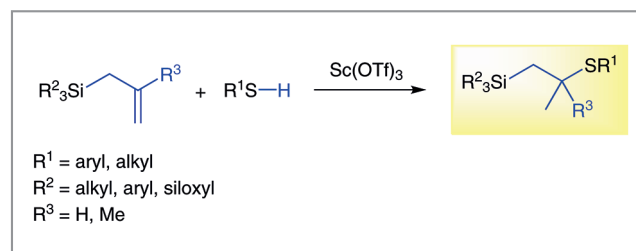
Scheme 1

Many research groups around the world have been looking for efficient synthetic methods which would allow introduction of the thioether functionality into unsaturated systems. The hydrothiolation reaction, known also as the thiol–ene or thiol–yne coupling, has attracted significant attention because of its simplicity and practical use in various fields of chemistry and materials science. Moreover, the reaction conditions are very mild in the majority of reports.

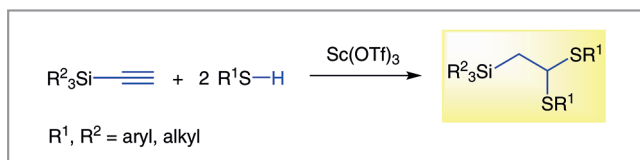
For many years, the main area of concern at the Department of Organometallic Chemistry, Adam Mickiewicz University in Poznań has been broadly defined as organosilicon chemistry. Recently, the research work of Dr. Grzegorz Hreczycho's group has also been directed towards novel applications of unsaturated organosilicon compounds in reactions catalyzed by Lewis acids. As Dr. Hreczycho put it: "After the successful O-silylation of silanols and silanediols by alkenylsilanes, we decided to extend our work on the O–H bond to other groups with similar properties, like S–H." Surprisingly, the formation of an Si–S bond was not observed. Instead of Si–S coupling, the selective hydrothiolation of allylsilanes was observed (Scheme 1). Professor Marciniec, one of the authors of this work, commented: "A lot of scientists would have moved on, but our group always faces the problems. We therefore decided to exploit this unpredicted activity to achieve novel applications of the hydrothiolation of organosilicon compounds."

"To the best of our knowledge, all earlier research on the addition of thiols to allylsilanes has been based on free-radical reactions. In these, the substrates are activated by temperature, UV radiation or free-radical generators and as far as we

know, no catalytic method of allylsilane hydrothiolation has yet been reported," said Dr. Hreczycho. "The graduate student Krzysztof Kuciński – who is working towards his doctorate under the supervision of Dr. Piotr Pawluć – started with tests of various catalysts and solvents. Scandium(III), bismuth(III), indium(III) and samarium(III) triflates were considered as catalyst for this process," he continued. "Among the above-mentioned triflates, only scandium(III) triflate and indium(III) triflate were found to be active catalysts, although scandium(III) triflate demonstrated the highest activity and selectivity in the hydrothiolation reaction. Toluene and fluorobenzene proved to be the most suitable solvents for this process." Subsequently, the nature of substituents attached to silicon and sulfur was examined and proved to be insignificant for the reaction. The use of allylsilanes in hydrothiolation catalyzed by scandium(III) triflate led to the products consistent with Markovnikov's rule (Scheme 2). This result was confirmed by  $^1H$  NMR spectroscopy.



Scheme 2



Scheme 3

“The radical type of hydrothiolation leads to the anti-Markovnikov regioisomer. Our discovery not only reports an unprecedented use of Lewis acids in allylsilane hydrothiolation, but it is also the first reaction to allow access to Markovnikov regioisomers in this kind of process,” said Dr. Hreczycho, adding: “Therefore, each product obtained by us in these reactions was classified as a novel thioether-functionalized silane. The curiosity and enthusiasm of Krzysztof Kuciński, who performed the experiments, made us go further and investigate ethynylsilanes as well.” These compounds showed relatively high reactivity in the hydrothiolation catalyzed by scandium(III) triflate; however, the reaction was slower (Scheme 3). Indium(III) triflate proved to be inactive in this process. As a result, the Poznań based researchers obtained various products of double-addition.

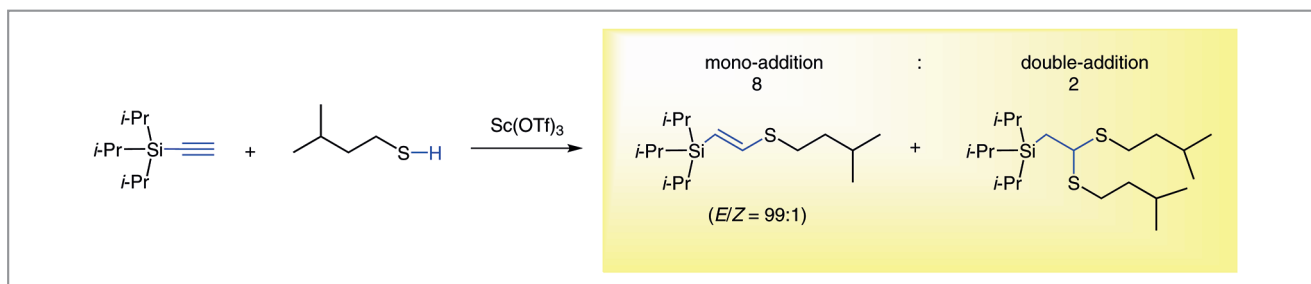
Dr. Piotr Pawluć suggested the possibility of obtaining a mono-addition product by the use of equimolar amounts of substrates. Indeed, when the reaction of ethynyltriisopropylsilane with 3-methylbutanethiol in a 1:1 ratio was performed, the mono-addition product was predominantly obtained

in the anti-Markovnikov fashion ( $E/Z = 99:1$ ). However, the mono-addition product was still contaminated by double-addition product (Scheme 4).

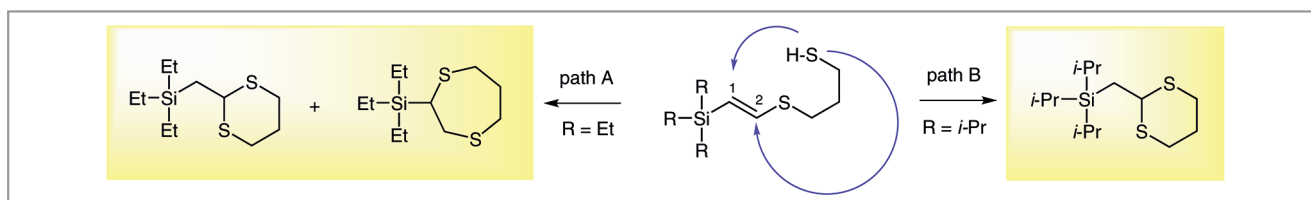
A very interesting example was the reaction between ethynyltriethyl- and ethynyltriisopropylsilane with propane-1,3-dithiol. When ethynyltriethylsilane was used, two types of products were observed: 1,2- and 2,2-double-addition products. Hydrothiolation of ethynyltriisopropylsilane by 1,3-propanedithiol led exclusively to  $\beta$ -dithioacetal (Scheme 5). “The steric hindrance of bulky isopropyl groups prevents the formation of 1,2-double-addition product,” suggested Mr. Kuciński.

“In summary, we have reported the highly selective hydrothiolation of unsaturated organosilicon compounds catalyzed by scandium(III) triflate. The use of allylsilanes led to products that are consistent with Markovnikov’s rule. The application of ethynylsilanes led to the formation of double-addition products – mostly  $\beta$ -dithioacetals. As an expansion of our method, in future we will explore its applicability to multi-unsaturated organosilicon compounds,” concluded Dr. Hreczycho.

*Mattias Farnok*

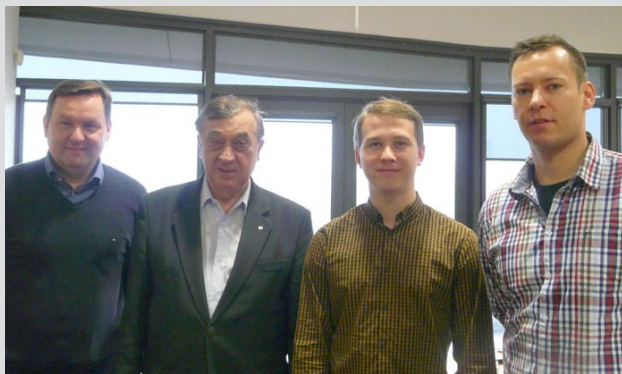


Scheme 4



Scheme 5

## About the authors



From left: Dr. P. Pawluć, Prof. B. Marciniak, K. Kuciński, Dr. G. Hreczycho

**Krzysztof Kuciński** was born in 1989 in Inowrocław (Poland). He obtained his two BSc degrees in Spatial Economy (2011) and in Chemistry (2012), followed by his MSc degree in Chemistry (2014) at Adam Mickiewicz University in Poznań (Poland). From September to December 2012 he joined Dr. Giuliano Giambastiani's group (ICCOM-CNR Florence, Italy) as part of the Erasmus Placement Programme. In 2014 he started doctoral studies under the supervision of Dr. Piotr Pawluć. His main interests involve Lewis acids catalysis.

**Piotr Pawluć** received his D.Sc. (2004) and habilitation (2012) in Chemistry from the Adam Mickiewicz University in Poznań. He was a postdoctoral fellow with Professor Andre Mortreux at the Lille University (France). His research interests involve developing catalytic methodologies for the preparation of organosilicon building blocks and their application to organic synthesis.

More than 50 research publications, patents, and book chapters document his activity in the fields of organometallic chemistry, homogeneous catalysis and organic synthesis.

**Bogdan Marciniak** is Professor at the Faculty of Chemistry and Director of the Center for Advanced Technologies of Adam Mickiewicz University, and a member of the Polish Academy of Sciences and European Academy of Arts, Sciences and Humanities. He was Doctor honoris causa of the Łódź University of Technology (Poland) in 2013, was Dean of the Faculty of Chemistry (1985–1988) and Rector of the Adam Mickiewicz University (1988/1990), and Founder and Director of Poznań Science and Technology Park. His research is focused on the synthesis of organosilicon (also boron and germanium) compounds on the basis of new reactions and new catalysts of known reactions. He has published over 400 scientific papers, including 15 books (9 in English), 200 patents and over 17 technologies implemented in industry. He has been given the Prime Minister Award (2001), J. Śniadecki Medal (2003) of the Polish Chemical Association and the Award of the Foundation for Polish Science in technical sciences (2009) and the "Honorary Pearl" in science awarded by "Polish Market" (2009).

**Grzegorz Hreczycho** was born in Zielona Góra (Poland) in 1977. He obtained his D.Sc. in 2007 from the Adam Mickiewicz University under the supervision of Professor Bogdan Marciniak. His research interests cover novel applications of unsaturated silicon and germanium compounds in addition and cross-coupling reactions catalyzed by transition-metal complexes and Lewis acid catalysts.

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