

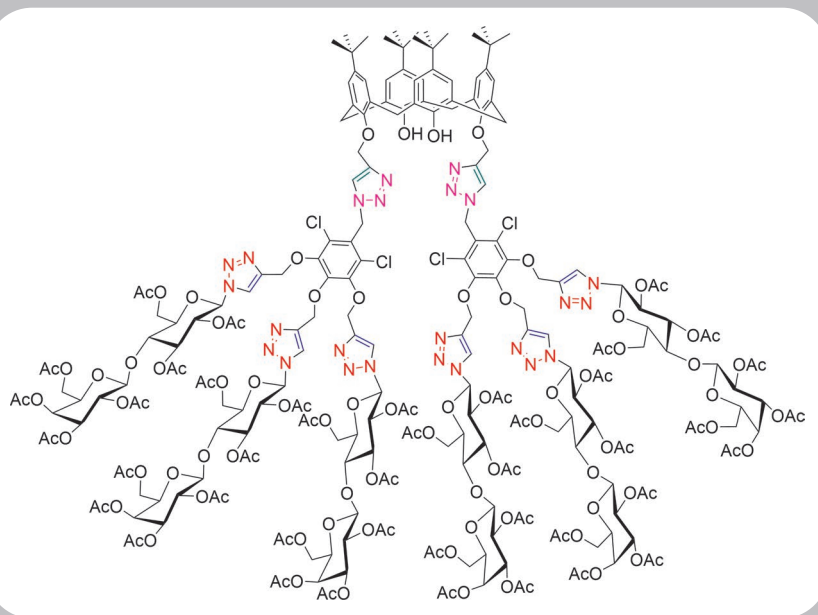
Synform

People, Trends and Views in Chemical Synthesis

2023/09

Synthesis of Calix[4]arene Appended Lactosylated G_1 and Galactosylated G_2 Generation Glycodendrimers Using a 'CuAAC' Click Approach

Highlighted article by S. Kumar, M. S. Yadav, S. K. Singh, S. Rajkhawa, V. K. Tiwari



Contact

Your opinion about Synform is welcome,
please correspond if you like:
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Dear Readers,

As you probably already know by now, our Open Access journal *SynOpen* has received its first Impact Factor (2022) and it is a hugely positive one: 2.5. Meanwhile, a lot has been happening in terms of editorial teams. *SynOpen* has a new Editor-in-Chief (Thierry Ollevier, Canada, who was recently interviewed by SYNFORM), supported by four enthusiastic Executive Board members (Tian-Sheng Mei, Raji Reddy, Dorota Gryko, Emma Gallo) and by a dream team of Editors who form the Associate Board. Meanwhile, *Organic Materials* – another vibrant Thieme Chemistry journal – has also seen new Editors joining the team. To celebrate the exciting developments in *SynOpen* and *Organic Materials*, in this September issue and in the forthcoming October issue we are publishing six interviews with scientists who have recently joined the Thieme Chemistry family. This month, we start with Ognjen Miljanic (USA) from *Organic Materials* and both Tharamlingam Punniyamurthy (India) and Taek Seung Lee (South Korea) from *SynOpen*.

The issue is opened by a Literature Coverage article on the recently developed photochemical diversification of strong C(sp³)–H bonds which has been achieved by L. Gong (P. R. China) using allyl bromide and sodium fluoride. To continue with *SynOpen*, a second Literature Coverage article features the remarkable ‘CuAAC’ click-type synthesis and isolation of complex calix[4]arene-functionalized glycodendrimers recently reported by V. K. Tiwari (India). This very rich issue is completed by another interview, a Young Career Focus article with the 2023 Thieme Chemistry Journal Awardee M. Nappi (Spain).

Enjoy your reading!



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

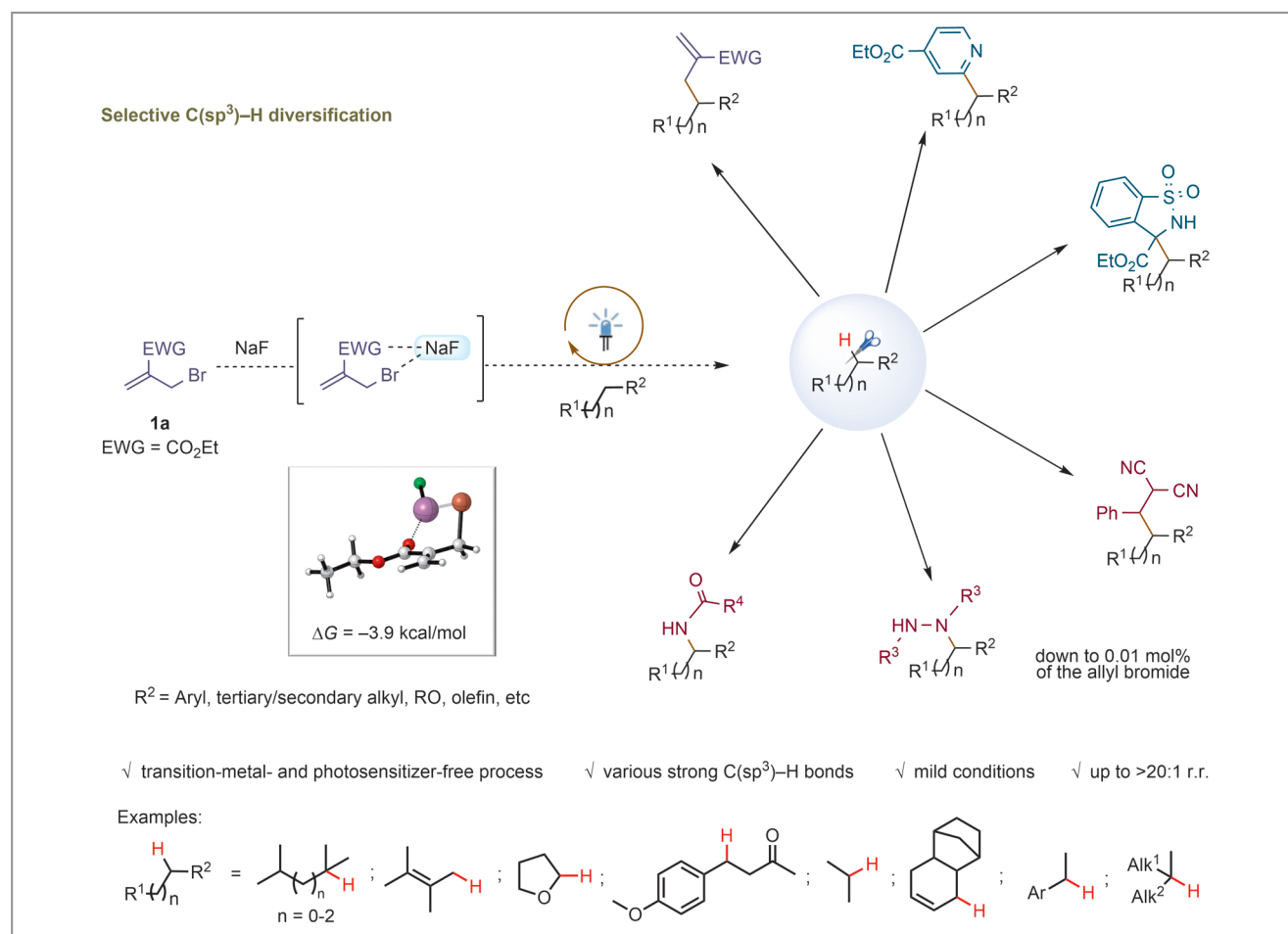
Photochemical Diversification of Strong C(sp³)-H Bonds Enabled by Allyl Bromide and Sodium Fluoride

Nat. Synth. **2023**, in press; DOI: 10.1038/s44160-023-00291-w

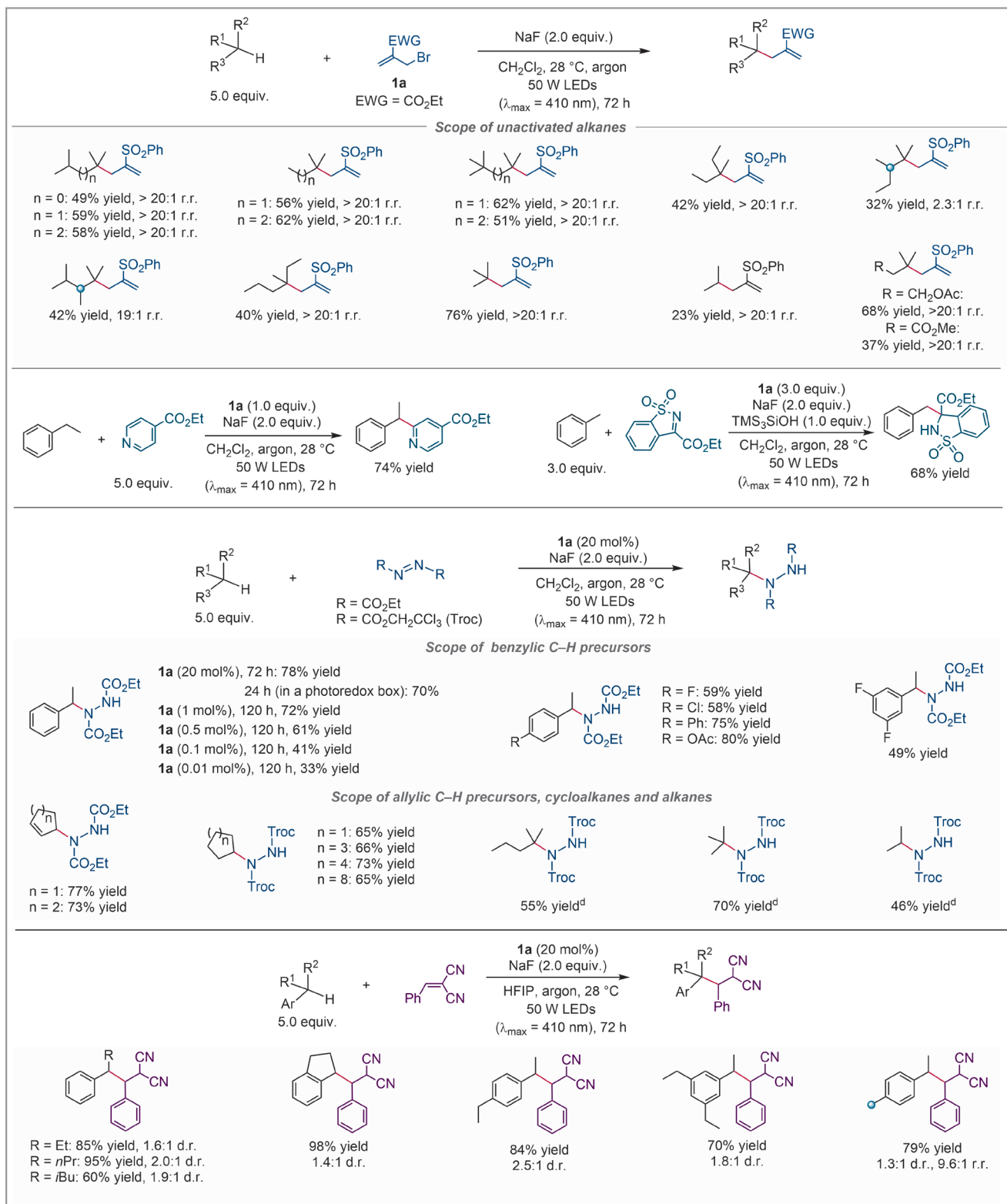
The direct functionalization of C(sp³)-H bonds has become a hot research topic and has been recognized as one of the most convenient approaches to increase the value of cheap raw chemical materials in synthetic chemistry due to its atom- and step-economy. "The high bond-dissociation energies (96–105 kcal/mol), low polarity and similar chemical environments for alkane C(sp³)-H bonds mean that the available methods often rely on harsh reaction conditions with strong redox systems, or expensive and sophisticated catalysts, which limits the industrial applications. Therefore, the exploration of convenient

methods to realize the cost-effective and mild C-H bond functionalization of alkanes is highly desired," said Professor Lei Gong from Xiamen University (P. R. of China), who has been investigating this topic.

In a study recently published in *Nature Synthesis*, a team led by Professor Gong developed a new strategy for the diversification of strong C(sp³)-H bonds enabled by allyl bromide and sodium fluoride under visible-light irradiation (Scheme 1). "In this work, we have successfully developed a C(sp³)-H functionalization strategy through the interaction of sodium



Scheme 1 Overview of this work



Scheme 2 Scope of selected substrates

fluoride and an allyl bromide. Binary NaF–allyl bromide adducts generated *in situ* appear to play essential roles in the reaction as light-active species, initiators for radical-mediated C–H cleavage and potential functionalization reagents. This new strategy does not rely on expensive and complex metal catalysts and organic catalysts,” explained Professor Gong. He continued: “This would provide a new opportunity for the C–H diversification of hydrocarbon feedstocks and the late-stage modification of bioactive molecules.”

The key to success for the transformation was the homolytic cleavage of C–Br bonds and the consequent formation of bromine radicals through the weak interaction between sodium fluoride and ethyl 2-(bromomethyl)acrylate induced by visible light. The generated bromine radicals can effectively activate C(sp³)–H bonds of alkanes by hydrogen atom transfer to produce alkyl radicals, which undergo radical cross-coupling with allyl radicals to provide allylated products. “The C(sp³)–H functionalization can also be achieved by adding

competitive reagents,” said Professor Gong. In a further development of the research project, the alkyl radical produced could be effectively captured by adding heteroaromatics and sulfimide. “At the same time, we were surprised to find that the hydrazination and alkylation of C(sp³)–H bonds can be successfully realized even with a catalytic amount of allyl bromide as initiator,” said Professor Gong. Diverse C(sp³)–H functionalizations of alkanes, cycloalkanes and other relatively unreactive substances were enabled by this catalytic system, which furnished various allylated, heteroarylated, alkylated, hydrazinated and aminated products in good yields, with high chemoselectivity and site selectivity (Scheme 2).

“Experimental and DFT studies support the interaction between sodium fluoride and allyl bromide. The sodium fluoride plays an essential role in stabilizing radicals and regulating their electrical properties. DFT calculations show that the low energy barrier for the activation and transfer of hydrogen bromide by N-centered radicals is the key to the

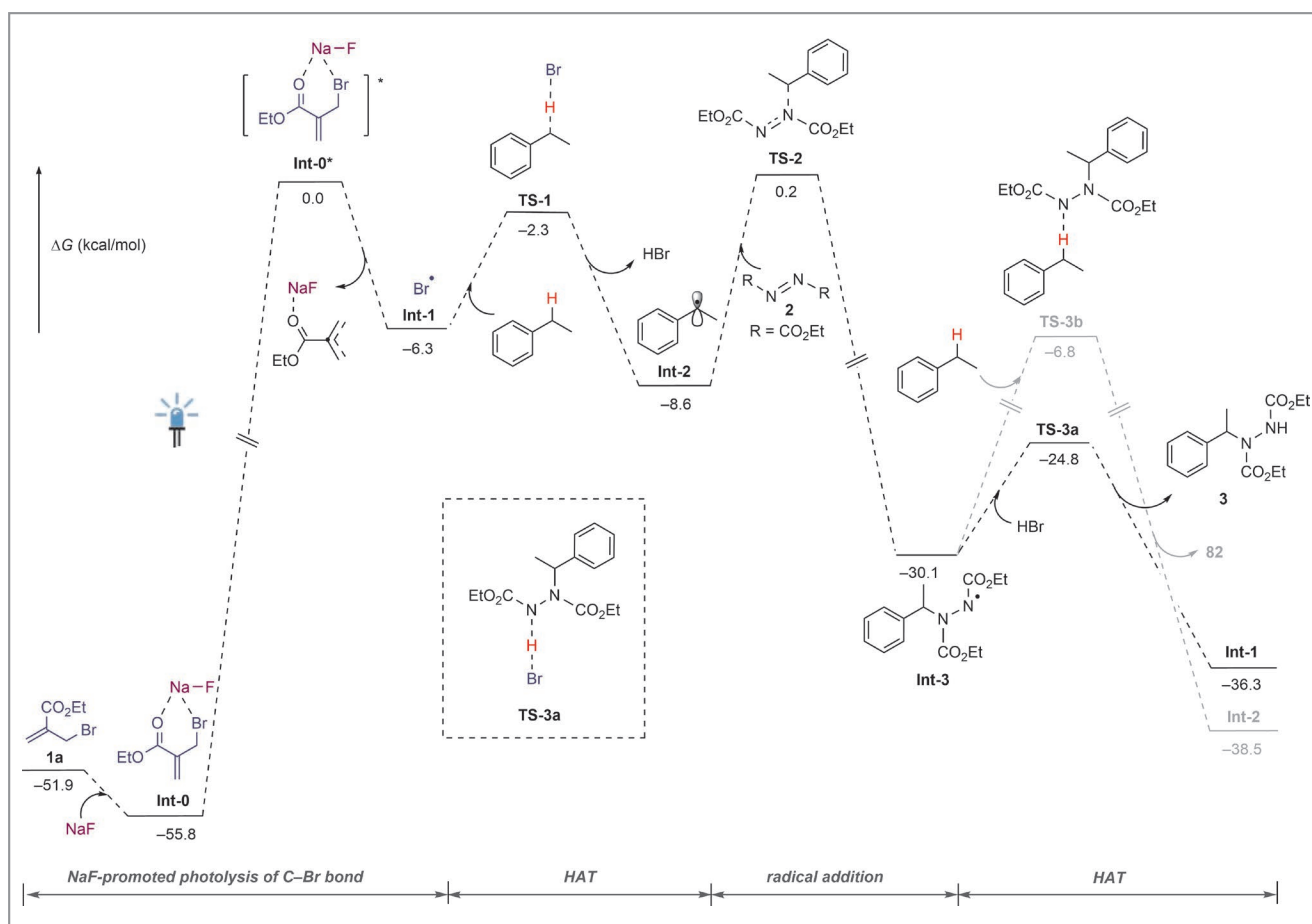


Figure 1 The barrier of the hydrazination reaction

reaction through the use of catalytic amounts of allyl bromide (Figure 1),” said Professor Gong.

Professor Gong concluded: “In summary, this study provides a new strategy for the conversion of inert C(sp³)-H bond without photocatalysts and transition metals. It also reveals

the regulatory role of main-group elements in the photochemical process, and provides a new green modification method for pharmaceutical chemists.”

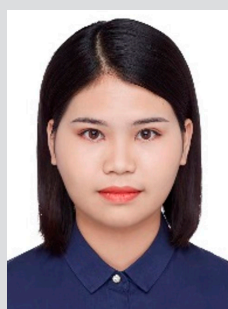
Mattias Fanola

About the authors



Z. Ye

Ziqi Ye was born in Fujian, P. R. of China, in 1996. He received his B.Sc. degree from Fuzhou University, P. R. of China (2018) and then became a postgraduate student under the guidance of Professor Lei Gong at Xiamen University. His current research interest is the development of new photochemical methods for selective C–H functionalization.



Y. Chen

Yuehua Chen was born and grew up in Danzhou, Hainan Province (P. R. of China). She received her B.S. degree from China Agricultural University (P. R. of China) in 2020 and then joined Prof. Lei Gong’s group at Xiamen University (P. R. of China) to further her studies in organic chemistry. Her research interests include photoredox catalysis, asymmetric catalysis, and synthesis of bioactive molecules.



Y. Yu

Ying Yu was born in Fujian, P. R. of China, in 1996. She received her B.Sc. degree from Shanxi University (P. R. of China, 2018) and then became a postgraduate student under the guidance of Professor Lei Gong at Xiamen University. Her current research interest is the functionalization of inert C(sp³)-H by photochemistry.



S. Song

Silin Song was born and grew up in Hefei, Anhui Province (P. R. of China). He received his B.S. degree from Anhui University (P. R. of China) in 2020 and then joined Prof. Lei Gong’s group at Xiamen University (P. R. of China) to further his studies in organic chemistry. His research interests include photoredox catalysis and asymmetric catalysis.



Prof. Y.-M. Lin

Yu-Mei Lin received her Ph.D. degree from Xiamen University (P. R. of China) in 2010, directed by Prof. Haiping Xia. Then, she worked with Prof. Stefanie Dehnen at Philipps-Universität Marburg (Germany) as a Alexander Humboldt fellow. She joined Xiamen University as an Associate Professor in 2013. Her current research interests involve the synthesis, reactivity and properties of metalla-aromatics, and the design of new catalysts based on organometallic scaffolds.



Prof. L. Gong

Lei Gong received his BSc (2002) and PhD degrees (2008) from Xiamen University (P. R. of China) under the guidance of Professor Haiping Xia. Thereafter he moved to Philipps-Universität Marburg, Germany, where he worked as a postdoctoral fellow with Professor Eric Meggers. In 2011, he was appointed as an associate professor at the College of Chemistry and Chemical Engineering at Xiamen University. Since 2019, he has been a full

professor at Xiamen University. He received the Thieme Chemistry Journals Award in 2021. His current research interests are the development of economic and environmentally friendly photochemical synthesis, as well as selective C–H functionalization.

Synthesis of Calix[4]arene Appended Lactosylated G₁ and Galactosylated G₂ Generation Glycodendrimers Using a ‘CuAAC’ Click Approach

SynOpen 2023, 7, 145-153

Bioconjugate chemistry is an expanding area of research at the interface between chemistry and biology that is attracting enormous and still-increasing interest. The group of Professor Vinod K. Tiwari at Banaras Hindu University (India) has been interested in the use of carbohydrates in bioconjugate chemistry, and their latest research achievements have been published recently in *SynOpen*. “Just after the Sharpless Click Chemistry concept^{1a} was proposed in 2001 and the discovery of Cu(I)-catalyzed azide–alkyne cycloaddition reactions (CuAAC ‘Click Chemistry’) in 2002 by two independent investigators, Professor M. Meldal^{1b} and Professor K. B. Sharpless,^{1c} this regioselective 1,4-disubstituted 1,2,3-triazole forming reaction has seen exponentially growing applications in almost all branches of science and technology,” said Professor Tiwari, adding: “An opposite triazole regioisomer can be obtained exclusively by reacting azide with alkyne in the presence of Ru-catalysis.^{1d} Further, Professor C. Bertozzi brilliantly explored the Wittig Strain-Promoted Azide–Alkyne Cycloaddition (SPAAC) concept^{1e} and its application under bioorthogonal conditions in living systems (Bertozzi Bioorthogonal Chemistry).”^{1f} Professor Tiwari went on to explain: “The field of ‘Click Chemistry and Bioorthogonal Chemistry’ has recently been recognized with the 2022 Nobel Prize in Chemistry, awarded to Professor Bertozzi, Professor Meldal and Professor Sharpless. Nowadays, CuAAC is acknowledged as one of the most reliable synthetic tools with widespread applications in chemistry, biology, medicine, and materials science. Its scope is also of great interest in glycoscience, with diverse applications including glycodendrimer synthesis.”²

Considering the widespread applications of click chemistry, the biocompatible nature and manifold importance of glycodendrimers and the group’s previous experience in click chemistry for glycodendrimer synthesis,³ Professor Tiwari and co-workers decided to explore a regioselective and modular CuAAC ‘Click Chemistry’ tool and recently reported a convenient synthesis of a class of calix[4]arene-cored lactosylated G₁ and galactosylated G₂ glycodendrimers from commercially available sugars, by utilizing a convergent route.⁴ “Calixarenes, which have a unique three-dimensional architecture, possess notable features such as an ease of functionalization at both

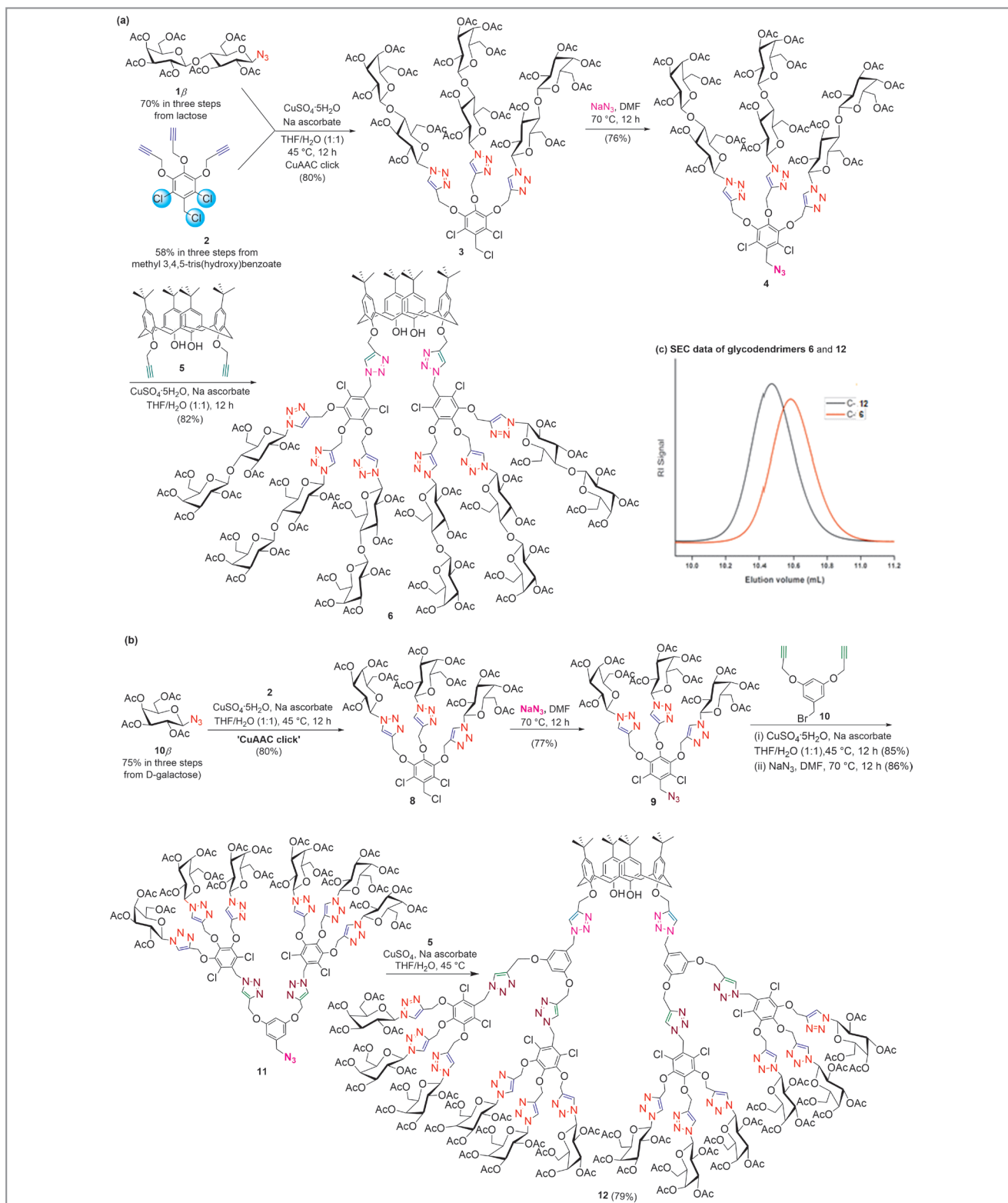
upper and lower rim, and can swiftly serve as suitable supramolecular scaffolds for use in synthesis, catalysis, sensing, molecular recognition and drug development,” said Professor Tiwari.⁵

The β-D lactose azide **1** (Scheme 1) was obtained from the respective sugar in three high-yielding steps under standard protocols reported in the literature. The tris-*O*-propargylated analogue **2**, on regioselective click reaction with sugar azide **1**, afforded the dendritic architecture **3** in 80% yield.

“Furthermore, azidation of the dendritic architecture **3** through nucleophilic substitution with NaN₃ in DMF at 70 °C afforded the required glycosyl triazole-based dendron **4**,” added Professor Tiwari. Then dendron **4** was subjected to click conjugation with calix[4]arene-cored **5** in the presence of CuSO₄·5H₂O and sodium ascorbate in THF/water to afford the desired G₁-generation lactose-coated glycodendrimer **6** in 82% yield. “A similarly optimized approach was utilized to develop the galactosylated G₂-generation glycodendrimer **12** in good yield from D-Gal-βN₃ followed by CuAAC click, azidation, then click, azidation and again click with calix[4]arene-core **5**,”⁴ explained Professor Tiwari.

The synthesized G₁-generation glycodendrimer **6** and galactosylated G₂-generation glycodendrimer **12** could be isolated in pure form by flash chromatography and were fully characterized spectroscopically. “The easy and high-yielding steps involved in synthesis, purification, and supramolecular assembly of the calix[4]arene core, and the biocompatible nature of the developed glycodendrimers, are the most notable features of the method,” concluded Professor Tiwari. “These glycodendrimers have potentially promising applications in drug delivery as well as chemotherapeutic potential, particularly anti-bacterial and anti-biofilm activities. The group is currently working in this direction.”

Anasthis Tawale



REFERENCES

- (1) (a) H. C. Kolb, M. G. Finn, K. B. Sharpless *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021. (b) C. W. Tornøe, C. Christensen, M. Meldal *J. Org. Chem.* **2002**, *67*, 3057–3064. (c) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless *Angew. Chem.* **2002**, *114*, 2708–2711. (d) G. Wittig, A. Krebs *Chem. Ber.* **1961**, *94*, 3260–3275. (e) L. Zhang, X. Chen, P. Xue, H. H. Y. Sun, I. D. Williams, K. B. Sharpless, V. V. Fokin, G. Jia *J. Am. Chem. Soc.* **2005**, *127*, 15998–15999. (f) N. J. Agard, J. A. Prescher, C. R. Bertozzi *J. Am. Chem. Soc.* **2004**, *126*, 15046–15047.
- (2) (a) V. K. Tiwari, B. B. Mishra, K. B. Mishra, N. Mishra, A. S. Singh, X. Chen *Chem. Rev.* **2016**, *116*, 3086–3240. (b) A. K. Agrahari, P. Bose, M. K. Jaiswal, S. Rajkhowa, A. S. Singh, S. Hotha, N. Mishra, V. K. Tiwari *Chem. Rev.* **2021**, *121*, 7638–7956. (c) V. K. Tiwari *Chem. Rec.* **2021**, *21*, 3029–3048.
- (3) (a) D. Kushwaha, V. K. Tiwari *J. Org. Chem.* **2013**, *78*, 8184–8190. (b) A. K. Agrahari, A. S. Singh, A. K. Singh, N. Mishra, M. Singh, P. Prakash, V. K. Tiwari *New J. Chem.* **2019**, *43*, 12475–12482. (c) A. K. Agrahari, A. S. Singh, R. Mukherjee, V. K. Tiwari *RSC Adv.* **2020**, *10*, 31553–31562. (d) A. K. Agrahari, A. K. Singh, A. S. Singh, M. Singh, P. Maji, S. Yadav, S. Rajkhowa, P. Prakash, V. K. Tiwari *New J. Chem.* **2020**, *44*, 19300–19313. (e) A. K. Agrahari, M. K. Jaiswal, M. S. Yadav, V. K. Tiwari *Carbohydrate Res.* **2021**, *508*, 108403. (f) A. K. Agrahari, S. Kumar, M. D. Pandey, S. Rajkhowa, M. K. Jaiswal, V. K. Tiwari *ChemistrySelect* **2022**, *7*, e202202273.
- (4) S. Kumar, M. S. Yadav, S. K. Singh, S. Rajkhowa, V. K. Tiwari *SynOpen* **2023**, *7*, 145–153.
- (5) (a) S. B. Nimse, T. Kim *Chem. Soc. Rev.* **2013**, *42*, 366–386. (b) A. Dondoni, A. Marra *Chem. Rev.* **2010**, *110*, 4949–4977. (c) A. Dondoni, A. Marra *J. Org. Chem.* **2006**, *71*, 7546–7557. (d) A. Yousaf, S. A. Hamid, N. M. Bunnori, A. A. Ishola *Drug Des. Devel. Ther.* **2015**, *9*, 2831–2838.

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Dr. S. S. Singh

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Dr. S. Rajkhowa

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contributed 20 peer-reviewed publications, has been awarded the 'CONIAPS Young Scientist Award' and has delivered 21 invited lectures. Her current research is focused on surface chemistry, ionic liquids and carbohydrate chemistry.



Dr. V. K. Tiwari

Vinod K. Tiwari is a Professor of Organic Chemistry at Banaras Hindu University (India). He earned his MSc in 1998 from BHU, his PhD from the Council of Scientific & Industrial Research - Central Drug Research Institute (CSIR-CDRI) in 2004 and had post-doctoral experience at the University of Florida (USA), UC-Davis (USA) and Universität Konstanz (Germany). Dr. Tiwari has completed 10 projects, supervised 16 PhD students, contributed

167 peer-reviewed publications (citations: 7315, h-index: 41), 8 patents, 24 book chapters, 4 books, and delivered 250 invited lectures. Dr. Tiwari is awarded with several honors from various academic societies and holds the Secretary Position, ACCT(I) and is a council member of CRSI. His current research is focused on synthetic carbohydrate chemistry and carbohydrates in drug development.

Editorial Board Focus: Prof. Dr. Ognjen S. Miljanic (University of Houston, USA)

Background and Purpose. From time to time, SYNFORM portraits Thieme Chemistry Editorial Board or Editorial Advisory Board members who answer several questions regarding their research interests and revealing their impressions and views on the developments in organic chemistry as a general research field. This Editorial Board Focus presents Prof. Dr. Ognjen S. Miljanic (University of Houston, USA) who joined the Editorial Board of Organic Materials with effect of January 2023.

Biographical Sketch



Prof. Dr. O.S. Miljanic

Ognjen S. Miljanic was born in Belgrade, then Yugoslavia, in 1978. He attended the University of Belgrade, from which he graduated in 2000 with a Diploma in Chemistry. In the same year, he moved to California (USA) to pursue his PhD at UC Berkeley with Prof. Peter Vollhardt. After graduating from Berkeley in 2005, he moved to UCLA (USA) for postdoctoral work with Prof. Fraser Stoddart. Since 2008, he has been a faculty member at the University of Houston (USA), where he is currently a Professor of Chemistry. Ognjen's research interests are in the field of porous molecular crystals, dynamic combinatorial chemistry, and macrocyclic chemistry. He has published over 90 papers and a textbook on Introduction to Energy and Sustainability (Wiley, 2021), and has given more than 120 invited lectures at universities and conferences in 28 countries. For his work, he has been honored with a National Science Foundation CAREER award, a Cottrell Scholar award, and an Alexander von Humboldt fellowship for advanced researchers, among other distinctions. He lives in Houston with his three children.

common ideas. As the journal is quite new, there is a lot of excitement as we jointly bring in new authors and their excellent contributions. In addition, it is just personally rewarding to be a member of the Thieme Chemistry family. My first paper was published in SYNLETT some 20 years ago – it is still among the most highly cited ones!

SYNFORM *You are a leading researcher in the field of organic materials science. Could you tell us more about the importance of that field and your current research activities?*

Prof. Dr. O.S. Miljanic I started my training as an organic chemist, before becoming more and more interested in the materials side of things. Building organic materials allows the use of the immense versatility of organic chemistry – with its continuously expanding arsenal of reactions and an almost limitless diversity of structures – to tackle virtually any technological problem of modern society. Our group has been particularly interested in building porous organic materials, which are based on small molecules that self-assemble into structures with numerous microscopic voids. We use these materials to capture greenhouse gases such as carbon dioxide, hydrofluorocarbons, and various fluorinated anesthetics.

SYNFORM *Could you tell us something about yourself outside the lab, such as your hobbies or extra-work interests?*

Prof. Dr. O.S. Miljanic I think that my hobbies are quite diverse, much like my research interests. I enjoy cooking (and eating!), playing water polo, dancing Argentine tango, and traveling the world. As my kids are getting older, I get to share some of these hobbies with them, which is truly a blessing!

Ognjen S. Miljanic

INTERVIEW

SYNFORM *Please comment on your role as a member of the Editorial Board of Organic Materials.*

Prof. Dr. O.S. Miljanic Being an Associate Editor of Organic Materials is a wonderful opportunity to influence the community and have these like-minded researchers coalesce around

Young Career Focus: Dr. Manuel Nappi (University of Santiago de Compostela, Spain)

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. Manuel Nappi (USC Manuela Barreiro Distinguished Researcher, CIQUS – University of Santiago de Compostela, Spain).

Biographical Sketch



Dr. M. Nappi

Manuel Nappi did his BSc and MPhil degrees at the University of Turin, Italy. In 2014, he obtained his PhD in organic chemistry at ICIQ (Institute of Chemical Research of Catalonia, Tarragona, Spain) under the supervision of Prof. Paolo Melchiorre. In 2012, he held a six-month research stay in the group of Nobel laureate David MacMillan at Princeton University (NJ, USA) working on photo-redox catalysis. His thesis focused on the development of novel aminocatalytic and photochemical reactions. At the end of 2014, he joined the group of Prof. Matthew Gaunt as postdoctoral research associate at the University of Cambridge, UK. From 2016 to 2018 he was awarded the Marie Skłodowska-Curie fellowship from the European Commission. At Cambridge, Manuel had the great opportunity to work on different fields of chemistry such as palladium catalysis, C–H activation, DNA and RNA chemistry, epigenetics and protein functionalisation. In 2021, Manuel joined CIQUS in Santiago de Compostela (Spain) as USC Manuela Barreiro Distinguished Researcher to develop his independent research programme. Manuel is one of the recipients of a 2023 Thieme Chemistry Journals Award and was selected as 2019 outstanding reviewer for the RSC journal *Chemical Science*. His research interests lie within the fields of organic chemistry, photochemistry and biochemistry, and these same fields are the focus of his research group's activities.

INTERVIEW

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

Dr. M. Nappi The design of sustainable reactions is one of the most important and challenging objectives that chemists are pursuing in industry as well as academic research. Our group is dedicated to the invention of new sustainable chemical transformations at the interface of synthetic chemistry, biochemistry, and materials science. Currently, we are working on the development of organic reactions promoted by visible light. Sunlight is a unique natural resource, which is a non-polluting, abundant, and endlessly renewable source of clean energy. Therefore, transformations that can be promoted by visible light are highly desirable, since they can occur under mild reaction conditions using inexpensive and harmless artificial lamps or direct sunlight. Our aim is to use visible light to activate and valorise simple organic feedstocks in synthetic chemistry. However, the mild reaction conditions make our novel methodologies particularly attractive to other disciplines such as medicinal chemistry, chemical biology and polymer chemistry.

SYNFORM *When did you get interested in synthesis?*

Dr. M. Nappi When I was 12, I began to be fascinated by the matter that shapes and surrounds us, and I asked myself what were the principles that allow such a wonderful organization of things and living beings. In particular, I was curious about the composition of matter. Watching a famous Italian scientific TV program 'Superquark', I then realised that all matter is made by very small particles called 'atoms'. I was so excited about that discovery that I immediately wanted to know more, and I asked my parents to buy me a book about chemistry. Reading the book and then studying chemistry in high school, I became interested in how Nature brings these

atoms together and I discovered the fundamental role of organic chemical reactions. During my degree I then learned that humans, inspired by Nature, can also synthesize new molecules using certain reactions. At this point it was clear to me that I wanted to become a synthetic organic chemist, to have the opportunity to create new molecules and expand the set of organic reactions available.

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

Dr. M. Nappi Organic synthesis is the art of assembling organic molecules through chemical reactions. Traditionally, synthetic chemists focused on the synthesis of natural products, providing the basis for pharmaceutical companies to access biologically relevant scaffolds and develop medicines. 50 years ago, the discovery of metal-catalysed cross-coupling reactions and asymmetric catalysis revolutionized the scientific world. Previously inaccessible chemical space was easily available, triggering the progress of basic and applied research in many disciplines, as well as technological advances in drug discovery, medicinal chemistry, materials science, etc. In recent decades, synthetic chemists have focused on the development of more sustainable reactions. Despite great advances, many methods still rely on the use of non-abundant metals and have poor atom economy. Given the increasing pressure of climate change and resource depletion, I believe the next generation of synthetic chemists should focus on developing

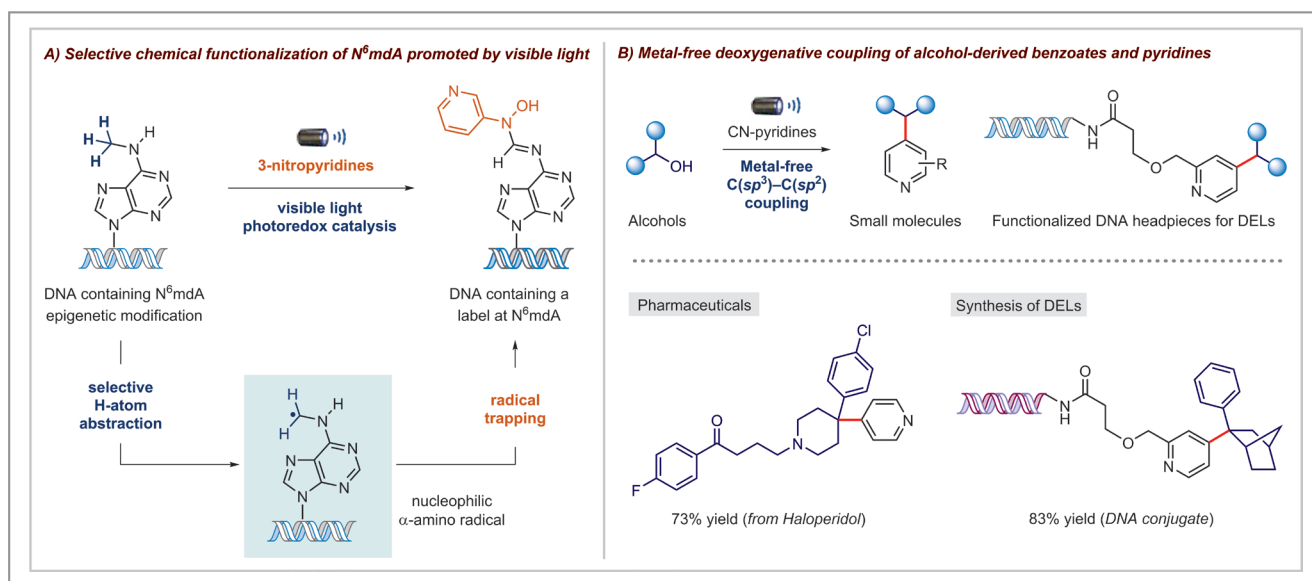
reactions without the use of precious metals and critical raw materials, limiting chemical waste and non-renewable energy input to mitigate carbon emissions.

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

Dr. M. Nappi Arguably, one of the most rewarding achievements for a synthetic chemist is the development of a new method that helps address a challenge in other disciplines. During my career I had the great opportunity to attain this twice.

In the course of my postdoctoral studies in the group of Prof. Matthew Gaunt, in collaboration with the group of Prof. Shankar Balasubramanian, we developed a visible-light-mediated selective modification of N⁶-methyl deoxyadenosine (N⁶mdA) and N⁶-methyl adenosine (m⁶A), epigenetic modifications of emerging importance (Scheme 1A).¹ This approach represents the first chemical methodology to selectively functionalise N⁶mdA in DNA, giving the basis for the development of a novel detection method to study its potential epigenetic activity in mammals and humans (patent licensed).

Recently, as part of my independent research programme, we reported a general metal-free platform for the deoxygenative coupling of alcohol-derived benzoates and pyridines promoted by visible light (Scheme 1B).² Feedstock and complex alcohols can be readily converted into the desired products in high yields, even in the case of top-selling pharmaceuticals



Scheme 1 New synthetic methods that help address challenges in other disciplines

such as haloperidol and ezetimibe. Notably, our chemistry can be utilized to functionalize DNA headpieces under dilute aqueous conditions, allowing, for the first time, the use of alcohols as building blocks for the synthesis of DNA-encoded libraries (DELs). Given the paucity of on-DNA reactions available from abundant building blocks and the widespread application of DELs in pharma, we believe that the flexibility and simplicity of our newly developed method will make this procedure of interest to practitioners of medical chemistry.

SYNFORM *What is the most exciting aspect of your job, the one you like the most?*

Dr. M. Nappi The design of a new reaction is always an incredible adventure. Trying to think of something that does not exist yet is probably the hardest task of my job, but also the most exciting and rewarding when it materializes in a tangible result. The creative process always starts from the search for a problem to solve. Often it is an intrinsic synthetic problem, but occasionally it can be part of a general challenge, from another scientific discipline or with broader socio-economic impact. Once the synthetic target has been identified, an iterative cycle of reaction design and feasibility leads to the final proposal to be tested in the lab. The freedom of pursuing different ideas is another stimulating aspect of my job, often leading to exciting multidisciplinary collaborations.



REFERENCES

- (1) M. Nappi, A. Hofer, S. Balasubramanian, M. J. Gaunt *J. Am. Chem. Soc.* **2020**, *142*, 21484–21492.
- (2) S. R. N. Kolusu, M. Nappi *Chem. Sci.* **2022**, *13*, 6982–6989.

Editorial Board Focus: Prof. Tharmalingam Punniyamurthy (Indian Institute of Technology Guwahati, India)

Background and Purpose. From time to time, SYNFORM portraits Thieme Chemistry Editorial Board or Editorial Advisory Board members who answer several questions regarding their research interests and revealing their impressions and views on the developments in organic chemistry as a general research field. This Editorial Board Focus presents Prof. Tharmalingam Punniyamurthy (Indian Institute of Technology Guwahati, India) who joined the Associate Board of *SynOpen* with effect of January 2023.

Biographical Sketch



Prof. T. Punniyamurthy

Tharmalingam Punniyamurthy completed graduate studies at the Bharathidasan University, Tiruchirappalli (India) and Ph.D. at the Indian Institute of Technology Kanpur (India) under the supervision of Prof. Javed Iqbal. Subsequently, he pursued postdoctoral research at the North Dakota State University, USA (Prof. M P Sibi), Kyushu University, Japan (Prof. T Katsuki), Montpellier University, France (Prof. A Vioux) and National School of Chemistry Montpellier, France (Prof. J E Moreau). In July 2001, he joined the Indian Institute of Technology Guwahati (India) and his research group focuses on the development of synthetic methods for sustainable organic synthesis. He served as Head, Department of Chemistry, Dean of Faculty Affairs and Chief Vigilance Officer at the Indian Institute of Technology Guwahati. He is recipient of CNRS, Fulbright, JSPS and UKIERI Research Fellowships and served as the Visiting Professor at The Scripps Research Institute, San Diego (USA), Kyushu University (Japan) and Oxford University (UK). He is a Fellow of the Indian Academy of Sciences, The National Academy of Sciences, India, the Indian National Science Academy and the Royal Society of Chemistry. He is the co-editor of the two-volume book *Transition-Metal-Catalysed C-H Functionalization of Heterocycles*, published by Wiley.

INTERVIEW

SYNFORM *You are a leading researcher in the field of organic synthesis. Could you tell us more about the importance of that field and your current research activities?*

Prof. T. Punniyamurthy Transition-metal-catalyzed C–H bond activation/functionalization has established itself as a breakthrough research area in catalysis as well as in organic synthesis. Over the years, it has been offering a concise pathway for the direct transformation of C–H bonds into C–C/C–heteroatom bonds, thereby streamlining the route of synthetic procedures and hence amplifying reaction yields by minimizing the formation of by-products. Moreover, the C–H activation strategy obviates the necessity of pre-functionalized starting materials and assures step- and atom-economy. Consequently, our research focuses on showcasing miscellaneous methods and their subsequent incorporation in fabricating heteroatom-embedded cyclic structural motifs. Lower catalyst loading and the use of readily available synthetic precursors for achieving site-selective functionalization has been our primary aim. For example, activation/functionalization of the intrinsically inert C4–H bond in indole-based moieties can lead to the formation of the structural scaffold of drug molecules as well as bio-active compounds, highlighting the importance of our recently developed methodologies. Currently, our efforts rely on C–H functionalization using strained ring systems as viable coupling partners to introduce molecular complexity to a simple substrate. In addition, functionalization of more inert sp^3 C–H bonds under milder reaction conditions using abundant 3d-transition metals is what we look forward to exploring in the near future. Further, employing a metalla-photoredox method as an alternative sustainable and greener aspect of accomplishing C–H bond functionalization would be an interesting topic to anticipate and expand our area of research.

SYNFORM *Please comment on your role as an Associate Editor of SynOpen.*

Prof. T. Punniyamurthy I am looking forward to taking on the responsibility of upholding the scope and aim of the journal, selecting the most original and important contributions.

SYNFORM *Could you tell us something about yourself outside the lab, such as your hobbies or extra-work interests?*

Prof. T. Punniyamurthy Outside of work, I enjoy listening to music, playing badminton and reading.

A handwritten signature in orange ink that reads "Mattes Fankle".

Editorial Board Focus: Prof. Taek Seung Lee (Chungnam National University, South Korea)

Background and Purpose. From time to time, SYNFORM portraits Thieme Chemistry Editorial Board or Editorial Advisory Board members who answer several questions regarding their research interests and revealing their impressions and views on the developments in organic chemistry as a general research field. This Editorial Board Focus presents Prof. Taek Seung Lee (Chungnam National University, South Korea) who joined the Associate Board of *SynOpen* with effect of January 2023.

Biographical Sketch



Prof. T. S. Lee

Taek Seung Lee received a PhD in fiber and polymer science in 1994. After post-doctoral research at the Korea Institute of Science and Technology (South Korea) and the University of Massachusetts Lowell (USA), he joined Chungnam National University as an assistant professor in 1997 and became a full professor in 2008. His research interest includes synthesis of functional organic materials and construction of hybrid nanomaterials, which have potential uses in photocatalysis, cathode materials for Li-ion batteries, OLED, and chemical/biological sensors.

INTERVIEW

SYNFORM *You are a leading researcher in the field of organic synthesis. Could you tell us more about the importance of that field and your current research activities?*

Prof. T. S. Lee Since three scientists were awarded the Nobel prize on “Electrically conductive plastic” in 2000, tons of organic materials have been developed for electronics and photonics. As a result, we can see various information through OLED-based smart phones and laptops. Electro- and photo-active organic materials are synthesized based on organic synthetic techniques, including many coupling reactions like Suzuki, Stille, Yamamoto, and Heck reactions.

SYNFORM *Please comment on your role as a member of the Associate Board of SynOpen.*

Prof. T. S. Lee My role is to assist with the rapid publication of high-graded papers.

SYNFORM *Could you tell us something about yourself outside the lab, such as your hobbies or extra-work interests?*

Prof. T. S. Lee My hobbies include running, golfing, boxing, watching TV, and reading.

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— Literature Coverage

Copper-Enabled Photo-Sulfonylation of Aryl Halides Using Alkylsulfonates

— Literature Coverage

Acceleration of Diels–Alder Reactions by Mechanical Distortion

— Literature Coverage

Design, Synthesis and Visible-Light-Induced Non-Radical Reactions of Dual-Functional Rh Catalysts

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(by A. Deepthi and co-workers)

Synlett Account: Lessons from the Total Synthesis of Highly Substituted Benzophenone Natural Products

(by L. Münzer, H.-G. Schmalz)

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