Late-Stage Trifluoromethylthiolation of Benzylic C–H Bonds

Highlighted article by W. Xu, W. Wang, T. Liu, J. Xie, C. Zhu
Dear Readers,

Welcome to the February 2020 issue of SYNFORM! What’s special with it? Well, 2020 is a leap year so this February must be a bit special, right? It certainly is special for that former student of mine – born on February 29th – who will properly celebrate her birthday this year. Leap years are special also because they are synonymous with Olympic Games, or at least they were, before the Winter Games were entirely split from the Summer Olympics, arguably to make them more profitable. In certain countries, leap years are even considered unlucky by some people, either tout-court or concerning some specific activities, with some couples apparently planning to avoid getting married in a leap year. Unlucky or not, a leap year is always a bit special and even more so is this February 2020 issue, which starts with a report on a paper published in Chem by X. Lei and H. Li (P. R. of China) on a photoinduced rearrangement that unravelled new aspects of the synthesis of terpenoids, also allowing for a conceptually new radical-mediated approach to some of them. The second article covers a very intriguing Science contribution authored by T. Carell (Germany) on prebiotic chemistry with potential implications for the synthesis of nucleoside anti-virals. The Young Career Focus this month features J. C. Slootweg (Van ’t Hoff Institute for Molecular Sciences, University of Amsterdam, The Netherlands) who tells us about his interests in circular and green chemistry, and beyond. The closing article – from Nat. Commun. – comes once again from the P. R. of China and specifically from the labs of J. Xie and C. Zhu with their late-stage introduction of a medicinally important SCF₃ group in benzylic positions via organophotoredox chemistry.

Well, on second thought, I may decide to keep that Italian anti-bad luck red horn in my pocket for the rest of the year, you never know…

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
Photoinduced Skeletal Rearrangements Reveal Radical-Mediated Synthesis of Terpenoids

Chem 2019, 5, 1671–1681

Isodon diterpenoids are a large family of bioactive polycyclic natural products isolated from plants of Isodon species. Bio-synthetically, these diterpenoids are derived from geranyl-geranyl-diphosphate (GGPP) by carbocationic cyclization rearrangements, which are catalyzed by a series of terpenoid cyclases. Several known bicyclo[3.2.1]octene containing isodon diterpenoid skeletons (ent-kaurane-type, jungermannenone-type, ent-beyerene-type, etc.) are generated via carbocationic rearrangements from a common intermediate ent-pimaranyl cation. An initial biosynthetic hypothesis speculated that jungermannenone-type diterpenoids could be generated from ent-kaurane diterpenoids via two intermediates through carbocatonic rearrangements (Scheme 1A). During a research program aimed at developing the synthesis of complex isodon diterpenoids, the research group led by Professor Xiaoguang Lei and Professor Houhua Li at Peking University (P. R. of China) discovered a late-stage photoinduced radical skeletal rearrangement of the bicyclo[3.2.1]octene ring system, which suggested that these photoinduced radical rearrangements are possibly involved in the biosynthetic pathway of ent-kauranes and jungermannenones.

Previously, the Lei group had accomplished the scalable total synthesis of isodon diterpenoids rac-jungermannenones B and C via a regioselective 1,6-dienyne reductive radical cyclization reaction. Professor Lei said: “We are interested in studying the biosynthetic pathways of natural products. Based on our previous work and inspired by the aforementioned biosynthetic hypotheses, we undertook the investigation of the biomimetic rearrangement of ent-kaurane diterpenoids to jungermannenone diterpenoids.” As a result, in this work the authors developed an enantioselective and protecting-group-free synthesis of the ent-kaurane-type diterpenoid (+)-ent-kauradienone using several radical-based reactions (Scheme 1B). Professor Lei said: “The development of an enantioselective synthetic route to these compounds is very challenging. Gratifyingly, after extensive experimentation of enantioselective polyene cyclization methods, the enantioselective synthesis was achieved by using MacMillan’s organocatalytic radical cation bicyclization.” Another challenge faced by the authors was to construct the ent-kaurane bicyclo[3.2.1]octene framework. After extensive conditions screening, the desired ent-kaurane-type skeleton was obtained as a sole product via regioselective 1,6-dienyne reductive radical cyclization. “In our previous work, the reductive radical cyclization occurred exclusively at the C11 position to form the jungermannenone-type scaffold in the presence of a C12 hydroxy group,” said Professor Lei, who continued: “Interestingly, when the C12-OH was converted into the oxidized ketone, the radical cyclization occurred at the C8 position exclusively, instead of occurring at the C11 position. Further mechanistic studies using density functional theory (DFT) calculations showed that the regioselectivity is mainly controlled by geometric factors.”

Then the biomimetic transformation of ent-kaurane to jungermannenone skeleton was investigated. Unfortunately, initial extensive attempts to convert biosynthetically ent-kaurane-type into jungermannenone-type scaffolds on model substrates via a carbocatonic rearrangement were unsuccessful. Professor Lei said: “To our delight, we finally achieved the interconversion between ent-kauranes and jungermannenones via a photoinduced rearrangement of bicyclo[3.2.1]octene.” A detailed previous mechanistic study had suggested that this photoinduced skeletal rearrangement possibly occurred via 1,3-acyl migration involving a cage radical pair or a bi-radical intermediate. Professor Lei remarked: “The interconversion between dihydrokauradienone and (-)-jungermannenone C also occurred smoothly promoted by sunlight, which indicated that ent-kaurane-type and jungermannenone-type diterpenoids are biosynthetically interrelated via this photoinduced radical rearrangement, which was previously thought to be a carbocation rearrangement. We therefore speculate that dihydrokauradienone is most likely a natural product.”

Furthermore, a series of structurally diverse ent-kaurane-type and jungermannenone-type diterpenoids or analogues and sesquiterpenoids also underwent this late-stage photoinduced skeleton rearrangement smoothly (Scheme 1C). “These transformations show that the photochemical rearrangements are highly functional-group-tolerant, so allylic alcohols, acids, primary and tertiary alcohols, lactones and enamide can all be present,” explained Professor Lei, who continued: “Careful examinations were conducted case by case to improve the yields. We discovered the optimal wavelengths didn’t correlate with the UV absorption data of the substrates. The computed study indicated that the...”
Scheme 1  (A) Proposed carbocationic biosynthetic pathway of isodon diterpenoids. (B) Protecting-group-free synthesis of isodon diterpenoids (+)-ent-kauradienone and (–)-jungermannenone C. (C) Late-stage photoinduced skeletal rearrangements of terpenoids.
photochemical rearrangement is not a thermodynamic equilibrium.”

Professor Lei concluded: “The enantioselective and protecting-group-free synthesis of (+)-ent-kauradienone and (−)-jungermannenone C were achieved in 12 and 14 steps, respectively, relying on three radical-based reactions, including a late-stage photoinduced radical rearrangement. Further applications of the late-stage rearrangements to various diterpenoids show good functional-group compatibility and suggest they are possibly involved in the biosynthetic pathways. We hope the photochemical 1,3-acyl migration will find more applications in natural products synthesis. Our work, together with previous examples contributed by other groups, is expected to spur more interest in radical chemistry for natural products synthesis.”

REFERENCES


About the authors

Benke Hong received his B.Sc. degree in pharmaceutical engineering from Liaoning University (P. R. of China). In 2011, he joined Professor Xiaoguang Lei’s group to start his Ph.D. studies on natural product synthesis. After receiving his Ph.D. in 2016, he is currently staying in the same group as a research assistant. His research project focuses on isodon diterpenoids total synthesis.

Weilong Liu received his B.Sc. degree in chemistry at Beijing Normal University (P. R. of China) in 2010. He then began his Ph.D. research under the supervision of Professor Xiaoguang Lei at Peking University (P. R. of China). He received his Ph.D. in 2015 and then joined BeiGene (P. R. of China) as a research investigator. In 2017, he moved to Geneva University (Switzerland) to conduct postdoctoral research with Professor Nicolas Winssinger.

Jin Wang was born in Jiangsu (P. R. of China) in 1995. He received his B.Sc. degree in chemistry from Nanjing University (P. R. of China). He commenced his Ph.D. studies under the supervision of Professor Xiaoguang Lei at Peking University (P. R. of China) in 2017, focusing on total synthesis of natural products.

Houhua Li was born in Jiangxi (P. R. of China) in 1985. He studied carbohydrate chemistry under the supervision of Professor Xinshan Ye during his B.Sc. and M.Sc. at Peking University (P. R. of China). In 2009, he moved to National Institute of Biological Sciences (NIBS) in Beijing (P. R. of China) and worked with Professor Xiaoguang Lei on the synthesis of lycopodium alkaloids. He received his Ph.D. under the supervision of Professor Clément Mazet at the University of Geneva (Switzerland) in 2016 and then conducted postdoctoral work with Professor Herbert Waldmann at the Max Planck Institute of Molecular Physiology (Germany). Since 2019, he has been an assistant professor at the School of Pharmaceutical Sciences in Peking University. His research interests lie mainly in the chemistry and biology of bioactive natural products.

Xiaoguang Lei was born and raised in Beijing, P. R. of China. He obtained B.Sc. degree in chemistry at Peking University (P. R. of China) in 2001. He then moved to Boston (USA) and conducted his Ph.D. research studies on natural product synthesis and chemical biology under the supervision of Professor John. A. Porco at Boston University. He received his Ph.D. in 2006, and then moved to New York City (USA) and joined Professor Samuel J. Danishefsky’s group at Columbia University (USA) as a postdoctoral fellow in bioorganic chemistry. In early 2009, he returned to China, and started his independent research career as a Principal Investigator and Director of Chemistry Center at the National Institute of Biological Sciences (NIBS) in Beijing (P. R. of China). In early 2014, he received a tenured professorship from Peking University (P. R. of China), and moved his research group to the College of Chemistry there. He also joined the Peking-Tsinghua Center for Life Science as a senior PI. The major research areas of Professor Lei’s laboratory are chemical biology, natural product total synthesis and medicinal chemistry.
The question of how life might have originated is still one of the most intriguing and unsolved mysteries for mankind. The RNA-world is so far the most influential hypothesis among many others, which posits that life emerged from RNA,” said Professor Thomas Carell (Ludwig-Maximilians-Universität, Munich, Germany), whose research group is interested in shedding some light on this fascinating issue. He added: “Since the pioneering work of Leslie Orgel in the 1970s, many groups have failed to produce all four letters of the RNA alphabet under plausible early Earth conditions.”

Nucleosides contain a glycosidic bond that connects the sugar with the nucleobase. Formation of this bond is very challenging especially in water. In a previous publication (Science 2016, 352, 833–836), Professor Carell’s group was able to show that purine nucleoside formation is relatively easy if one employs more nucleophilic nucleobase precursors. “At the same time, you achieve full regioselectivity for the naturally occurring N-9 isomers,” said Professor Carell, who continued: “In our new work we show that amazing chemistry can happen if you introduce N–O bonds into prebiotic chemistry, which leads to a completely novel pathway to pyrimidine nucleosides and even the corresponding nucleotides. The N–O bond mutually protects two functional groups, an amine and an aldehyde. Only upon reductive cleavage of the N–O bond are both functional groups released to form the pyrimidine heterocycle. Reduction is highly efficient in the presence of catalytic amounts of Fe(II) and thiols.”

Even more exciting is the group’s observation that pyrimidine chemistry is compatible with their previously reported purine route. “This allowed us for the first time to form all four Watson–Crick building blocks under identical conditions from small atmospheric and volcanic molecules,” said Professor Carell. He continued: “The next challenge is now to connect these building blocks to form RNA polymers. This should be feasible because we also observe the nucleoside-5′-diphosphates as activated RNA building blocks.”

Besides the canonical RNA building blocks, nature uses a plethora of modified nucleosides. Of interest are amino acid modified nucleosides – molecules between genotype and phenotype. Professor Carell explained: “We have already shown that these molecules can form from simple chemistry and therefore might represent molecular fossils of an early Earth. This could explain how the first peptides were made by means of RNA, which would shift the view from a pure RNA-world to an RNA-peptide co-evolution.”

Professor Carell concluded: “Beyond prebiotic chemistry, our new publication and the presented pyrimidine pathway may be applicable in pharmaceutical industry for the synthesis of nucleoside analogues as anti-viral compounds.”

Figure 1 Unified synthesis of pyrimidine and purine RNA building blocks
About the authors

Thomas Carell received his prediploma and diploma from the Universities of Münster and Heidelberg (Germany). In 1993, he obtained his doctorate with Prof. H. A. Staab at the Max-Planck Institute of Medical Research. After postdoctoral training with Prof. J. Rebek at MIT (Cambridge, USA) he moved to the ETH Zürich (Switzerland) to start his independent research. He accepted a full professor position for Organic Chemistry at the Philipps-Universität in Marburg (Germany) in 2000 and moved in 2004 to his current position at the Ludwig-Maximilians-Universität (LMU) in Munich (Germany), where he heads a research group in chemical biology. Thomas Carell is a member of the German National Academy Leopoldina and of the Berlin-Brandenburgische Academy of Arts and Sciences. He is the recipient of the Cross of Merit from the Federal Republic of Germany and of the Leibniz Award of the DFG. He has been a member of the board of BASF SE since 2019.

Sidney Becker received his B.Sc. and M.Sc. in chemistry and business studies from the University of Zurich (Switzerland), where he completed his Master’s thesis in the group of Prof. John Robinson. As a PhD student, he joined the laboratory of Prof. Thomas Carell at the Ludwig Maximilians University Munich (Germany). He is now working as a postdoctoral researcher in the group of Prof. Shankar Balasubramanian at the University of Cambridge (UK).

Jonas Feldmann graduated from Ludwig Maximilians University Munich (Germany) with a B.Sc. in chemistry and biochemistry (2015), and an M.Sc. in biochemistry (2018). As a visiting graduate student, he joined the group of Prof. Yitzhak Tor at UC San Diego (USA). He then started his PhD in the group of Prof. Thomas Carell (Ludwig-Maximilians-Universität, Munich, Germany), focusing on the prebiotic synthesis of RNA nucleotides.

Stefan Wiedemann received his B.Sc. degree in chemistry and biochemistry from Ludwig Maximilians University, Munich (Germany) in 2016, and his Master’s degree in chemistry from the same university in 2018. Afterwards, he started his PhD in the group of Prof. Carell in prebiotic chemistry.
Young Career Focus: Prof. Chris Slootweg (Van ’t Hoff Institute for Molecular Sciences, University of Amsterdam, The Netherlands)

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 Prof. Chris Slootweg (Van ’t Hoff Institute for Molecular Sciences, University of Amsterdam, The Netherlands).

Biographical Sketch

Chris Slootweg studied physical organic chemistry at Vrije Universiteit Amsterdam (The Netherlands), main-group chemistry at the University of Sussex (UK) and homogeneous catalysis at the University of Amsterdam (The Netherlands) for his undergraduate and MSc degrees. He completed his PhD on highly strained organophosphorus compounds with Koop Lammertsma at Vrije Universiteit Amsterdam in 2005 before taking up a postdoctoral position with Peter Chen at ETH Zürich (Switzerland) until 2006. Now he is an associate professor at the Van ’t Hoff Institute for Molecular Sciences, University of Amsterdam (The Netherlands).

SYNFORM When did you get interested in synthesis?

Prof. J. C. Slootweg My interest in chemistry was sparked by determining the identity of the minerals that I found in nature. Crystals of pyromorphite (Figure 1), the first phosphorus-containing mineral to be discovered, were displayed on the cover of my PhD thesis (2005) to reflect my quest for novel, structurally unique organophosphorus compounds. Growing crystals is still a key facet of my research. I love to create novel synthetic methodologies, to unravel mechanistic insights aiming for transferable understanding, as well as to develop scalable recycling methods.

INTERVIEW

SYNFORM What is the focus of your current research activity?

Prof. J. C. Slootweg The mission of my laboratory at the Van ’t Hoff Institute for Molecular Sciences of the University of Amsterdam is to educate students at the intersection of fundamental physical organic chemistry, main group chemistry and circular chemistry. I find it most exciting to combine state-of-the-art computational chemistry with synthetic chemistry to facilitate the discovery of new concepts, processes and unique species.

Figure 1 Pyromorphite [Pb₅(PO₄)₃Cl] (Gongcheng, Guangxi, China) was the first phosphorus-containing mineral, and was discovered in 1779. In 1813, it was named after the Greek words for “fire” and “form”, since after being melted, a sample will begin to take on a crystalline shape during cooling. (Photograph by Willem Dijkstra)
SYNFORM What do you think about the modern role and prospects of organic synthesis?

Prof. J. C. Slootweg Organic synthesis has always used fossil feedstocks as a resource and in recent years has also exploited the use of renewable resources, such as biomass. The next synthetic challenge will be to use waste as a resource for the development of novel (and existing) chemical products and processes, which will contribute to realizing a circular economy and securing our sustainable future. Only by reusing, recovering and recycling our valuable resources can we overcome material scarcity and solve environmental problems.

SYNFORM Could you tell us more about your group’s areas of research and your aims?

Prof. J. C. Slootweg While my previous research endeavours targeted solely closed-shell (two-electron) processes in main-group chemistry, currently my laboratory also generates radicals on purpose and studies their redox chemistry and one-electron reactivity. This presents a unique possibility to advance, for example, the single-electron reduction of CO₂ as a productive strategy for carbon–carbon bond formation under mild conditions and propel the use of the CO₂ radical anion as a reactive intermediate in organic synthesis. Furthermore, driven by “how can I as a chemist contribute to sustainability”, I explore circular chemistry (see below), which offers a holistic systems approach for the bottom-up development of molecular and materials chemistry to combat global sustainability issues.

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

Prof. J. C. Slootweg To promote life-cycle thinking and circularity in chemistry, I developed the concept of circular chemistry and formulated the corresponding 12 principles (Nature Chem. 2019, 11, 190–195; Figure 2). Circular chemistry aims to replace today’s linear ‘take–make–dispose’ approach with circular processes, which optimize resource efficiency across chemical value chains and enable a closed-loop, waste-free environment. By making chemical processes truly circular, molecules and materials can be repurposed near-indefinitely, resulting in energy as the only input. Chemistry is all about making molecules and materials and the principles of green chemistry provide an enabling framework for optimizing their synthesis and production. After their use, these molecules and materials ultimately need to be reused, recovered and/or recycled. To promote the development of molecules and materials from waste, circular chemistry highlights that chemistry is all about remaking molecules and materials too.

In Amsterdam, we develop sustainable phosphorus chemistry using waste phosphates as resource to produce high-grade phosphate products, such as specialty fertilizers and flame-retardants (Figure 3). SusPhos, now also a UvA spin-off, presents an ideal showcase for circular chemistry, since we contribute to solving environmental crises caused by a surplus of phosphates in the environment and make valuable products at the same time.

Figure 2 The twelve principles of circular chemistry (reproduced with permission from Nature Chem. 2019, 11, 190)

Figure 3 Steven Beijer, SusPhos researcher, showing phosphate waste (right) that are used as resource to make value-added phosphate products (left). (Photograph by Rogier Chang)
It is my desire to develop in the short term a Circular Technologies Center that uses chemistry as enabling tool to target the conservation of critical raw materials (element scarcity) as well as contributes to solving pressing waste problems. Such a Circular Technologies Center will, for the first time, combine design, synthesis and catalysis with the environmental fate and impact of current products targeting safe by design (no persistent, bio-accumulative, and toxic compounds; green chemistry) and design for re-use, recovery and recycling (circular chemistry).

[Signature]

Matteo Tancola
Late-Stage Trifluoromethylthiolation of Benzylic C–H Bonds

*Nat. Commun.* **2019**, DOI: 10.1038/s41467-019-12844-9

It is estimated that over 20% of small-molecule drugs on the market contain at least one fluorine atom. The trifluoromethyl group – which is a xenobiotic function, not yet found in any naturally available compound – is also encountered in a number of drugs, generally as an aromatic substituent but sometimes connected to a heteroatom such as oxygen or sulfur. Due to its strongly electron-withdrawing characteristics and high lipophilicity, the selective introduction of trifluoromethythio group (SCF₃) into organic and pharmaceutical molecules can improve their cell membrane permeability and metabolic stability of the target molecules. Hence, synthetic strategies for introducing an SCF₃ group in organic molecules entailing versatility, diversity and availability are highly desirable in the arsenal of synthetic chemists.

In a recent paper, the group of Professor Jin Xie and Professor Chengjian Zhu at Nanjing University (Nanjing, P. R. of China) developed an organophotoredox-catalyzed reaction for site-selective benzylic C–H bond trifluoromethylthiolation of a wide variety of alkyl arenes and heteroarenes. “Currently, the regioselectivity of the reaction relies mainly on the physicochemical properties (e.g., exchange constants and polarity) of intermolecular hydrogen-atom-transfer (HAT) reagents or oxidants in terms of C–H bond dissociation energy and electronic properties,” Professor Xie and co-authors pointed out. They continued: “Hence, in this paper we reported the development of a metal-free, photoredox inner-sphere HAT process which predictably generates, from natural products or drug derivatives, a benzylic radical which can be tri-

### Scheme 1 Photoredox-catalyzed trifluoromethylthiolation of benzylic C–H bonds

#### a.

![A. 73% (98:2)](image1)

**A.** 73% (98:2)

#### b.

![B. 76%](image2)

**B.** 76%

![C. 57%](image3)

**C.** 57%

![D. 72% (98:2)](image4)

**D.** 72% (98:2)

#### c.

![E. 53%](image5)

**E.** 53%

![F. 89%](image6)

**F.** 89%

![G. 38%](image7)

**G.** 38%

![H. 46%](image8)

**H.** 46%

![I. 51%](image9)

**I.** 51%

![J. 63% Pirfenidone analogue](image10)

**J.** 63% Pirfenidone analogue

![K. 62% Celestidole analogue](image11)

**K.** 62% Celestidole analogue

![L. 71% Epiandrosterone analogue](image12)

**L.** 71% Epiandrosterone analogue

![M. 69%](image13)

**M.** 69%
fluoromethylthiolated, avoiding the use of oxidants and HAT reagents.”

Excitingly, this protocol shows an excellent site-selectivity (Figure 1a) and a broad substrate scope (Figure 1b). “In addition, late-stage trifluoromethylthiolation of drugs and synthesis of the benzophenone benzyl trifluoromethyl sulfides were successfully achieved (Figure 1c). Finally, continuous flow chemistry further demonstrates the synthetic practicability,” remarked the authors.

Professors Xie and Zhu concluded by mentioning some future prospects: “This photoredox inner-sphere HAT process can be applied in benzylic C–H bond functionalization processes and our lab is currently investigating this enantioselective synthesis strategy.”

About the authors

**Jin Xie** is currently an associate professor at Nanjing University (P. R. of China). He was born in Chongqing, P. R. of China, in 1985. He received his Bachelor’s degree from Northeast Forestry University (P. R. of China) in 2008, and his Ph.D. in 2013 from Nanjing University working under the direction of Prof. Chengjian Zhu. From 2014 to 2017, he was a postdoctoral research associate in the group of Prof. A. S. K. Hashmi at Heidelberg University (Germany). In 2017, he returned to Nanjing University to start his independent career. His current research interests are the development of diverse catalysis concepts, focusing on organometallic chemistry (bimetallic catalysis) and synergistic catalysis in radical chemistry. He obtained several awards, such as the 1000-youth talent plan of China, Thieme Chemistry Journals Award, Jiangsu Funds for Distinguished Young Scholars and Outstanding Reviewer for ChemComm.

**Chengjian Zhu** was born in Henan, P. R. of China, in 1966. He obtained his Ph.D. from the Shanghai Institute of Organic Chemistry (CAS, P. R. of China) in 1996. He joined Nanjing University (P. R. of China) as an associate professor in 2000 and has been a professor there since 2003. His present research interests lie in visible-light photoredox catalysis.

**Wentao Xu** was born in Hubei Province, P. R. of China, in 1990. He received his Bachelor’s degree from the Hefei University of Technology (P. R. of China) in 2014 and his Master’s degree from the same university in 2017, under the supervision of Prof. Huajian Xu. He is currently conducting his Ph.D. studies under the supervision of Prof. Jin Xie and Prof. Chengjian Zhu at Nanjing University (P. R. of China).

**Wenliang Wang** was born in Shanghai, P. R. of China, in 1998. He studied for his Bachelor’s degree in 2015–2019 at Shandong University (P. R. of China) with Prof. Bo Wu. Since 2019, he has been a Ph.D. candidate at Nanjing University (P. R. of China) under the supervision of Prof. Jin Xie.

**Tao Liu** was born in Jiangxi, P. R. of China, in 1997. Since 2016, he has been an undergraduate at Nanjing University (P. R. of China). In 2018, he joined Prof. Xie’s group under the National College Students’ Innovation and Entrepreneurial Training Program.
Coming soon

- Literature Coverage
  Ketones and Aldehydes as Alkyl Radical Equivalents for C–H Functionalization of Heteroarenes

- Literature Coverage
  Expedient Synthesis of (E)-Hydrazone Esters and 1H-Indazole Scaffolds through Heterogeneous Single-Atom Platinum Catalysis

- Literature Coverage
  Modular Synthesis of α-Fluorinated Arylmethanes via Desulfonylative Cross-Coupling

Further highlights

Synthesis | Short Review: Transition-Metal-Catalyzed Suzuki–Miyaura Type Cross-Coupling Reactions of π-Activated Alcohols
(by S. Ruchirawat, J. S. M. Samec, and co-workers)

Synlett | Account: Benziodoxole-Derived Organosulphonates: The Strongest Hypervalent Iodine Electrophiles and Oxidants
(by V. V. Zhdankin and co-workers)

Synfacts | Synfact of the Month in category “Metals in Synthesis”: Copper-Mediated Late-Stage Fluorination of Arenes Using Photoredox Catalysis

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