

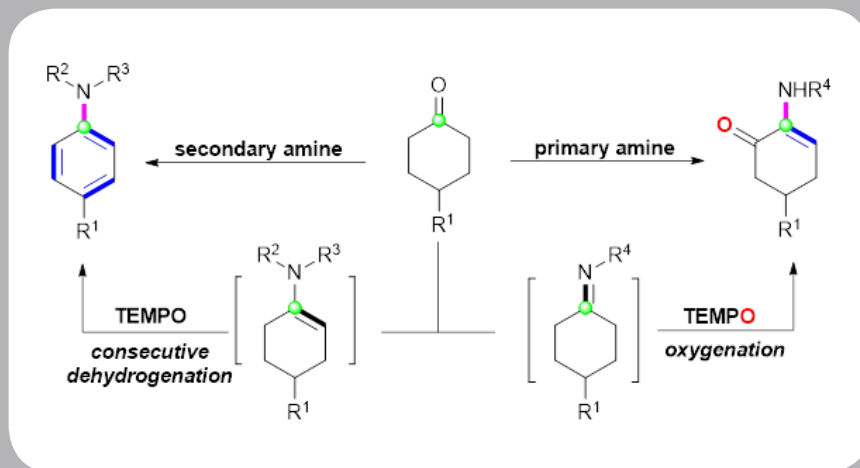
# Synform

People, Trends and Views in Chemical Synthesis

2019/03

## Differentiation between Enamines and Tautomerizable Imines in the Oxidation Reaction with TEMPO

Highlighted article by X. Jie, Y. Shang, Z.-N. Chen, W. Zhuang, W. Su



### Contact

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## Dear Readers,

This March issue of SYNFORM is particularly rich for two main reasons: (1) it has five articles instead of the usual four; (2) it celebrates two new members of the Thieme Chemistry family: Professor Cristina Nevado (University of Zurich, Switzerland), who joins the *Science of Synthesis* Editorial Board, and Professor Hideki Yorimitsu (Kyoto University, Japan), who is the newest addition to the SYNTHESIS Editorial Board. We would like to welcome Cristina and Hideki and wish them a fruitful and exciting cooperation with our team! Their interviews follow another interview, with the Young Career Focus protagonist Subhas Chandra Pan (India), which opens the issue. We then move on to a Literature Coverage article on the ground-breaking photoredox sunlight-promoted addition of CO<sub>2</sub> to imines developed in collaboration and published in *Nat. Commun.* by the groups of Xinyuan Fan (P.R. China) and Patrick Walsh (USA). Finally, the last article remains in the area of imines, in this case tautomerizable to enamines, which – remarkably – can be differentiated by oxidation with TEMPO, leading to different products.

Enjoy your reading!



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### Contact

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## Young Career Focus: Dr. Subhas Chandra Pan (Indian Institute of Technology Guwahati, India)

**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. Subhas Chandra Pan (Indian Institute of Technology Guwahati, India).

### Biographical Sketch



Dr. S. C. Pan

**Subhas Chandra Pan** was born in 1980 in West Bengal (India). He obtained his BSc degree with honours in chemistry from the University of Calcutta (India) in 2001 and stood first in chemistry honours. Then he received his MSc degree in 2004 from the Indian Institute of Science, Bangalore (India), achieving the highest mark of the year for chemistry. During his MSc thesis he worked in Prof.

Goverdhan Mehta's laboratory on the total synthesis of epoxyquinone natural products and successfully synthesized the natural products jesterone, torreyanic acid, ambuic acid and yanuthone A. He obtained his PhD in 2008 summa cum laude under the guidance of Prof. Benjamin List at the Max-Planck-Institut für Kohlenforschung, Mülheim an der Ruhr (Germany). During his PhD, he developed a novel variant of the Strecker reaction, namely the asymmetric acylcyanation of imines using chiral thiourea catalysts. He also discovered a catalytic three-component Ugi reaction using phenyl phosphinic acid as the catalyst. Then he began postdoctoral work at Harvard University (USA) in the group of Prof. E. J. Corey, where he focused on the catalytic asymmetric Kulinkovich reaction. Consequently, in 2009 he carried out his second postdoctoral study at the Scripps Research Institute, Florida (USA) with Prof. Glenn C. Micalizio and conducted research on the synthesis of gepotidacin analogues. In 2011, he joined the Indian Institute of Technology Guwahati (India) as assistant professor and was promoted to associate professor in 2015. His research interests comprise metal and organocatalytic diastereo- and enantioselective reactions and natural products synthesis. He received the DAE Young Scientist Research Award in 2012 and a Thieme Chemistry Journal Award in 2018.

### INTERVIEW

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

**Dr. Pan** During my PhD studies, I became fascinated with asymmetric organocatalysis, which has established itself as a powerful method for the synthesis of chiral molecules. My independent research is focused mainly on the convenient catalytic asymmetric syntheses of different carbocyclic and heterocyclic frameworks. We are also interested in the synthesis of natural products and other bioactive molecules utilizing our methodology.

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

**Dr. Pan** I became interested in organic synthesis during my undergraduate studies at Ramakrishna Mission Vidya-mandira, Belur Math under the University of Calcutta. In my college days, I was taught by excellent organic chemistry teachers and solving organic chemistry problems was enjoyable. Then in my Master's studies at the Indian Institute of Science, Bangalore, I was fortunate to work on total synthesis of natural products under the guidance of Prof. Goverdhan Mehta. During this period, I became confident in performing organic reactions on the bench and thinking about organic research problems. During my PhD, I worked on asymmetric organocatalysis and became really interested in constructing chiral organic molecules.

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

**Dr. Pan** Organic synthesis is a fundamental and eternal science for the development of medicines, materials, cosmetics, and fragrances, among others. One of the major challenges in organic synthesis from the environmental point of view is

to generate less waste, or even no waste at all. Thus, atom- and step-economic approaches should be developed for the synthesis of a particular molecule. Catalytic domino or cascade reactions have emerged as powerful approaches for the synthesis of complex molecular frameworks in a single step. Another challenge is to prepare different enantiomers or diastereomers of a product from a single starting material. In this case, stereodivergent catalysis is a dominant method for the synthesis of a library of stereoisomers.

**SYNFORM** Your research group is active in the area of asymmetric synthesis and natural product synthesis. Could you tell us more about your research and its aims?

**Dr. Pan** One major focus of our research is to prepare bioactive privileged cyclic structural motifs via an asymmetric organocatalytic domino strategy. We have employed bidentate reactants for this purpose. In recent years we have developed convenient syntheses of multi-substituted tetrahydrofurans, tetrahydropyrans, pyrrolidines, imidazolidines, coumarins, pyrazolones, etc. We have also explored  $\alpha$ -nitro ketones as nitro-containing acyl transfer reactants. A range of bidentate substrates such as unsaturated pyrazolones,  $\gamma$ -hydroxyenones and 2-hydroxycinnamaldehydes were engaged in the reaction with  $\alpha$ -nitro ketones. Also, in a few cases, we have carried out theoretical investigations to understand the detailed mechanism. We would like to apply our methodology in natural products synthesis in the near future.

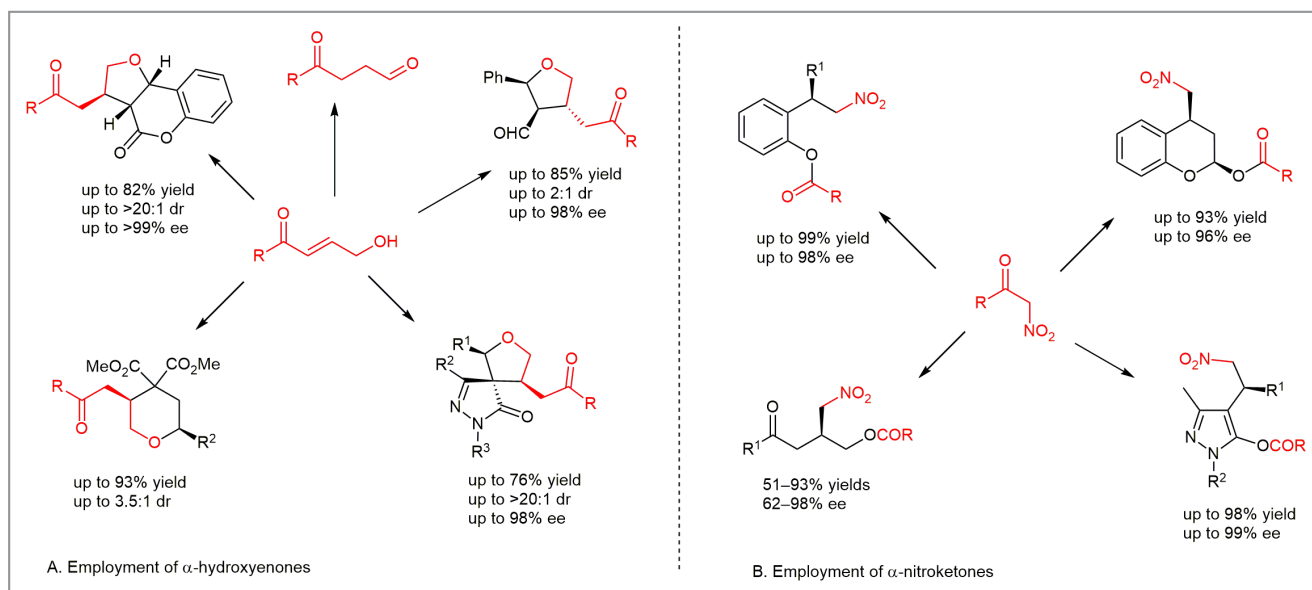
**SYNFORM** What is your most important scientific achievement to date and why?

**Dr. Pan** This is a tough question and difficult to choose a particular accomplishment. At the beginning of my career, we developed an organocatalytic redox isomerization of electron-deficient alcohols, which was accepted as an abstract in organic chemistry portal. Later, we explored  $\alpha$ -nitro ketones in a range of asymmetric transformations. We found that the higher reactivity of  $\alpha$ -nitro ketones relative to nitroalkanes is beneficial for undergoing challenging conjugate addition reactions. Lastly, I would like to thank my co-workers for their enthusiasm, hard work and dedication, and funding agencies for their support.

*Matthew Fanak*

## REFERENCES

- (1) K. Mondal, B. Mondal, S. C. Pan *J. Org. Chem.* **2016**, *81*, 4835–4840.
- (2) R. Maity, C. Gharui, A. K. Sil, S. C. Pan *Org. Lett.* **2017**, *19*, 662–665.
- (3) M. Balha, B. Mondal, S. C. Sahoo, S. C. Pan *J. Org. Chem.* **2017**, *82*, 6409–6416.
- (4) S. Mukhopadhyay, U. Nath, S. C. Pan *Adv. Synth. Catal.* **2017**, *359*, 3911–3916.



Scheme 1

- (5) S. Mukhopadhyay, S. C. Pan *Chem. Commun.* **2018**, 54, 964–967.
- (6) B. Mondal, M. Balha, S. C. Pan *Asian J. Org. Chem.* **2018**, 7, 1788–1792.
- (7) B. Mondal, S. C. Pan *Adv. Synth. Catal.* **2018**, 360, 4348–4353.
- (8) C. Gharui, D. Behera, S. C. Pan *Adv. Synth. Catal.* **2018**, 360, 4502–4508.

## Editorial Board Focus: Professor Cristina Nevado (University of Zürich, Switzerland)

**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 Professor Cristina Nevado (University of Zürich, Switzerland) who joined the Editorial Board of Science of Synthesis with effect of July 2018.

### Biographical Sketch



Prof. C. Nevado

**Cristina Nevado** was born in 1977 in Madrid (Spain), where she graduated in chemistry at the Autónoma University in 2000. In October 2004 she received her PhD in organic chemistry at the same university working with Prof. Antonio M. Echavarren in the cyclization of enzymes catalyzed by platinum and gold complexes. In December 2006 she joined the group of Prof. Alois Fürstner at the Max-Planck-Institut für Kohlenforschung (Germany) where she was part of the team who conquered the first total synthesis of lejimalide B, a marine macrolide possessing a very sensitive architecture. In May 2007 she started her independent career as an Assistant Professor of Organic Chemistry at the University of Zürich. In 2011, Cristina was awarded the Chemical Society Reviews Emerging Investigator Award and the Thieme Chemistry Journal Award in recognition of her contributions in the field of synthetic organic chemistry. In 2012 she received an ERC Junior Investigator grant and has been awarded the Werner Prize of the Swiss Chemical Society. In 2013 she became Full Professor. Among her many contributing roles to the community, Cristina is currently Senior Associate Editor for ACS Central Science and for Organic Syntheses. Rooted in the wide area of organic chemistry, her research program is focused on complex chemical synthesis and new organo-metallic reactions.

### INTERVIEW

**SYNFORM** Please comment on your role as a Member of the Editorial Board of Science of Synthesis.

**Prof. Nevado** I am truly excited to join the Editorial Board of Science of Synthesis and eager to work with its distinguished members to further promote and expand the capabilities that SoS provides to the synthetic community at large.

**SYNFORM** How do you describe the value of a product such as Science of Synthesis to the chemistry community?

**Prof. Nevado** Science of Synthesis represents a 'go-to' source in order to get familiar with fundamental topics in organic chemistry, providing an up-to-date compilation of the most important developments in the field. For students, SoS is also a very good source to get familiar with a particular theme, to get background information to prepare review or introductory materials as well as to assess whether or not a new transformation they might have discovered has a potential niche and thus deserves to be further explored. Furthermore, within SoS, structural searches and experimental procedures are available online, which represents a truly valuable asset for any experimentalist.

**SYNFORM** What do you think about the modern role and prospects of synthetic chemistry, in particular its importance in and for the pharmaceutical industry?

**Prof. Nevado** Synthetic chemistry has an important role to play in modern societies. We need materials with highly tailored properties, agrochemicals with accurate application profiles and also new drugs with more selective modes of

action. Thus, the quest for novel synthetic methods that can produce the desired outcomes in a timely, cost-effective and sustainable manner is now peaking.

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

**Prof. Nevado** Our group embraces a truly multidisciplinary research program with three distinct focal areas: late transition metal catalysis and mechanistic understanding of organometallic reactions, complex natural product synthesis and the design and development of chemical probes to answer biological questions. We truly believe in the power of synthesis and organic molecules to impact multiple fields.

**SYNFORM** *You are a leading researcher with regard to synthetic organic and organometallic chemistry. Could you tell us more about how important you perceive this particular topic to be?*

**Prof. Nevado** A shrinking pool of natural resources requires creative solutions to which chemistry can significantly contribute. Catalysis in its multiple forms (homogeneous, heterogeneous, bio-, photo- and electro-) is one of the central areas to tackle some of these highly challenging goals. Further, mechanistic understanding and application of cutting-edge analytical tools will be key not only to optimizing existing methods, but more importantly, to developing unprecedented ones to match current and future needs with minimal environmental impact and maximum added value.





## Editorial Board Focus: Professor Hideki Yorimitsu (Kyoto University, Japan)

**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 Professor Hideki Yorimitsu (Kyoto University, Japan) who joined the Editorial Board of *Synthesis* with effect of January 2019.

### Biographical Sketch



Prof. H. Yorimitsu

**Hideki Yorimitsu** was born in Kochi, Japan, in 1975. He obtained his B.Eng. and Ph.D. in 1997 and 2002, respectively, from Kyoto University (Japan) under the supervision of Professor Koichiro Oshima. He then served as a JSPS postdoctoral fellow with Professor Eiichi Nakamura at the University of Tokyo (Japan). He became an Assistant Professor in 2003 and an Associate Professor in 2008 in the Graduate School of Engineering, Kyoto University. He moved to the Department of Chemistry, Graduate School of Science in the same university in 2009 and became a Professor in 2015. He was also a visiting professor at the Institute for Molecular Science (Japan, 2014–2016) as well as a project leader of ACT-C, Japan Science and Technology Agency (Japan, 2012–2018), and is currently an Honorary International Chair Professor at the National Taipei University of Technology (Taiwan). His research program focuses on the development of new organic transformations for creating new molecules, phenomena, and concepts. He has received the Thieme Journals Award (2006), the Chemical Society of Japan Award for Young Chemists (2009), Mitsui Chemicals Catalysis Science Award of Encouragement (2011), Young Scientists' Prize from MEXT (2011), Mukaiyama Award (2016), and Negishi Award (2018).

### INTERVIEW

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

**Prof. Yorimitsu** Since I was a PhD candidate, I have been a big fan of Thieme journals. I naturally consider it a great honor to join the Thieme family as an Associate Editor of *Synthesis*. Under the leadership of Paul Knochel and in effective collaboration with the other excellent Associate Editors, I will be happy to contribute to the development of organic synthesis and to open up new avenues through the editorial activity.

The Thieme family has already been achieving successful generational change. On the *Synthesis* side, Franziska Schoenebeck and I have just joined, effective January 2019. I believe that the new editorial team considers organic synthesis to be as important as ever, with deeper sympathy and closer communication with young researchers and readers. I hope that the synthetic community will become more attractive than ever before.

I will serve as the Regional Editor for Japan and Korea mainly. Both countries are very strong in organic synthesis. To steadily strengthen the binational community, I will be very happy to support good research and researchers through my editorial activity. I wish to handle more submissions from these countries and to receive fruitful comments from reviewers, especially from the younger Japanese and Korean generations.

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

**Prof. Yorimitsu** I love to discover novel organic transformations, especially those which proceed via unexpected/beautiful reaction mechanisms, with high efficiency/selectivity, and/or to produce useful/unusual molecules. One of my favorite



research topics is aromatic metamorphosis, wherein a hetero-aromatic ring is converted into a different ring via partial disassembly and reconstruction of ring systems. For example, we invented transformations of dibenzothiophenes into triphenylenes, carbazoles, dibenzophospholes, etc. For details, please see our *Synlett* Account (*Synlett* **2016**, *27*, 1765–1774). I hope aromatic metamorphosis is a game-changing strategy in organic synthesis. Another favorite is the use of unsaturated onium cations, mainly sulfonium cations, in organic synthesis. For instance, we invented a metal-free regioselective C–H/C–H coupling producing biaryls from aryl sulfoxides and phenols. The key in this transformation is concomitant loss of the aromaticity of the two aromatic substrates via sulfonium-tethered intermediates. I will submit a manuscript about this sulfonium chemistry to *Synlett* in a couple of months.

**SYNFORM** *You are a leading researcher with regard to synthetic organic and organometallic chemistry. Could you tell us more about how important you perceive this particular topic to be?*

**Prof. Yorimitsu** The Sustainable Development Goals have been set by the United Nations. Some of the goals about environmental issues are essentially equivalent to goals about chemistry. Our society is based on organic molecules, and naturally thus on organic synthesis and organometallic chemistry, two key technologies of transforming organic molecules. More efficient, selective, and atom-economical transformations should be pursued. However, simply pursuing such environmental criteria would not be sufficient. Deep understanding of reaction mechanisms, physical organic chemistry of reactions and molecules, discovery of unexpected reaction outcomes, and synthesis of unusual molecules will often lead to quantum leaps in our chemical community. Our community should cherish curiosity-driven chemistry.

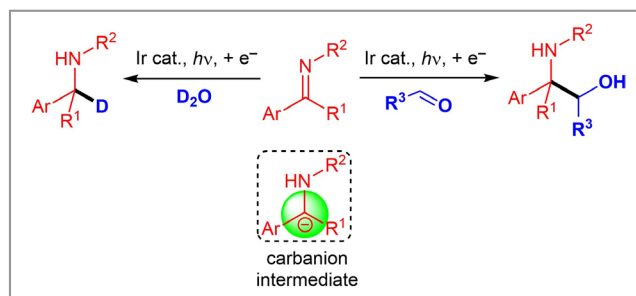


# Sunlight-Promoted CO<sub>2</sub> Transformations: Synthesis of α-Amino Acids with Imines

*Nat. Commun.* **2018**, *9*, 4936

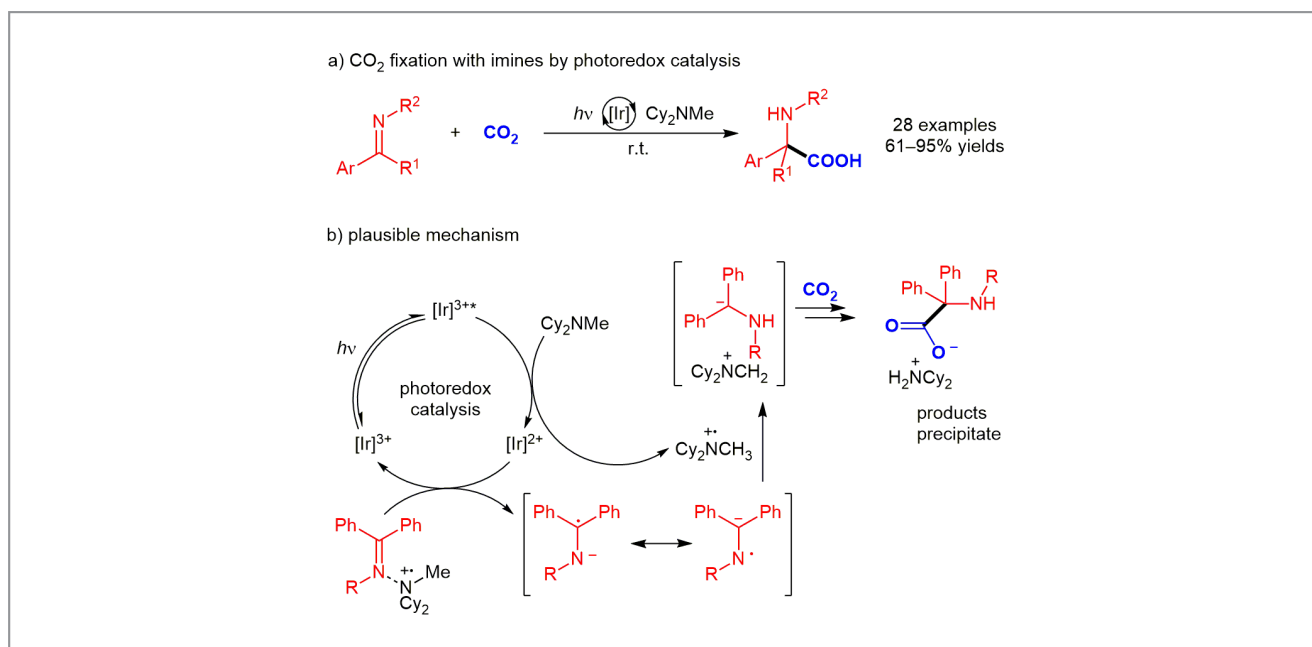
The importance of α-amino acids is broadly documented in synthesis, catalysis, protein science and biomedical research. Efficient chemical synthesis of α-amino acids has long been a pursuit of organic chemists. CO<sub>2</sub> is a nontoxic, abundant and renewable C1 synthon that is an ideal carboxyl source for the synthesis of α-amino acids. Due to its relatively inert nature, however, very strong nucleophilic reagents such as RMgX or RLi are usually required to attack CO<sub>2</sub> to form C–C bonds.

Professor Xinyuan Fan (Nanjing Tech University, P. R. of China), Professor Patrick Walsh (University of Pennsylvania, USA, Honorary Professor at Nanjing Tech University, P. R. of China) and their co-workers previously demonstrated that benzophenone ketimines, which are conventionally electrophilic, exhibit umpolung reactivity under photoredox catalytic conditions. Thus, in the presence of a sacrificial amine, photoredox catalyst and visible light, these ketimines were found to undergo single-electron reduction and H- abstraction to generate carbon-centered carbanions. “The carbanions ultimately abstract a proton from water (or deuterium from D<sub>2</sub>O)



**Scheme 1** Previously reported Umpolung imine transformations by photoredox catalysis

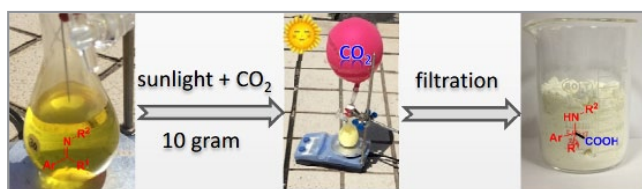
to afford reduction products in high yields (Scheme 1, left; *Org. Lett.* **2018**, *20*, 2433–2436),” explained Professor Fan. He continued: “The umpolung reactivity was further demonstrated in the cross-electrophile couplings between ketimines and aldehydes to afford useful amino alcohols (Scheme 1, right; *Org. Lett.* **2019**, *21*, 27–31).”



**Scheme 2** CO<sub>2</sub> fixation with imines by photoredox catalysis

The team next examined the synthesis of amino acids with the relatively inert electrophile  $\text{CO}_2$ , imine substrates and a sacrificial reductant ( $\text{Cy}_2\text{NMe}$ ) promoted by visible light energy. “Fortunately, the desired amino acid products were obtained in high yields after optimization of the reaction conditions (Scheme 2a),” said Professor Walsh. He continued: “Interestingly, we realized that the products precipitate from the solution during the reaction. Exploiting this observation, we developed a straightforward and efficient method to purify the products. A simple filtration of the reaction mixture enabled isolation of the amino acids, with the counterion  $[\text{H}_2\text{NCy}_2]^+$ . The proposed mechanism is outlined in Scheme 2b.”

Sunlight, as the most sustainable and renewable energy form on the surface of the Earth, is an attractive power source to drive chemical transformations. “Nature developed an exquisite and efficient method, the well-known photosynthesis, to harvest the energy of sunlight to convert  $\text{CO}_2$  and water into glucose, which supplies much of the biosphere with energy and chemical building blocks,” said Professor Fan. “The efficiency of this method encouraged us to explore the amino acid synthesis using sunlight energy instead of artificial light. And fortunately, we were very excited to find the same efficiency of the reaction under sunlight irradiation as artificial light generated in the laboratory.” He continued: “To further demonstrate the robust nature of this new transformation, we showed that this reaction could be easily scaled up to 10 grams without loss of yield, indicating its great practicality (Scheme 3).”



**Scheme 3** Sunlight-mediated 10-gram-scale reaction

“To summarize,” said Professor Fan, “we developed a simple and efficient method to synthesize  $\alpha$ -amino acid derivatives using  $\text{CO}_2$  and imines by harvesting the energy of sunlight. The advantages of this method include: 1) mild conditions (room temperature, atmospheric pressure of  $\text{CO}_2$ , visible light), 2) operational simplicity (chromatography-free purification) and 3) environment-friendly characteristics (consumption of the greenhouse gas  $\text{CO}_2$ , use of sustainable sunlight energy).” Professor Walsh concluded: “There have been a number of groups involved in this area (see work from

Da-Gang Yu’s team: *Angew. Chem. Int. Ed.* **2018**, *57*, 13897). The next challenge will be to develop enantioselective versions of this reaction.”

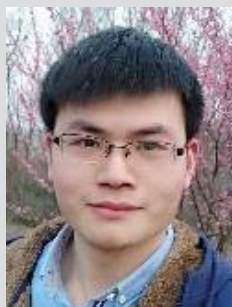
*Mattias Fanck*

## About the authors



Prof. X. Fan

**Xinyuan Fan** received his B.A. and M.A. degrees from Lanzhou University (P. R. of China) and his Ph.D. (2014) at the Institute of Chemical Research of Catalonia (Spain) with Prof. Miquel Pericas. He did postdoctoral research (2015–2017) with Prof. Peng Chen and Prof. Zhang-Jie Shi at Peking University (P. R. of China), after which he joined Nanjing Tech University (P. R. of China) as an associate professor. He is developing organic methods and bioorthogonal chemical tools.



R. Wang

**Rui Wang** is currently a Master's student in the Institute of Advanced Synthesis of Nanjing Tech University (P. R. of China). He is working on photoredox catalytic imine transformations under the supervision of Prof. Xinyuan Fan and Prof. Patrick J. Walsh.



X. Gong

**Xu Gong** received his B.A. from Nanjing Tech University (P. R. of China) in 2017, after which he joined the research group of Prof. Xinyuan Fan as a Master's student in the Institute of Advanced Synthesis of Nanjing Tech University. His research interests focus on photoredox catalytic CO<sub>2</sub> transformations.



M. Ma

**Mengyue Ma** received her B.A. from Liaocheng University (P. R. of China) in 2017. In the same year, she joined the research group of Prof. Xinyuan Fan as a Master's student in the Institute of Advanced Synthesis of Nanjing Tech University (P. R. of China). Her research interests focus on photoredox catalytic double-bond transformations.



Prof. P. J. Walsh

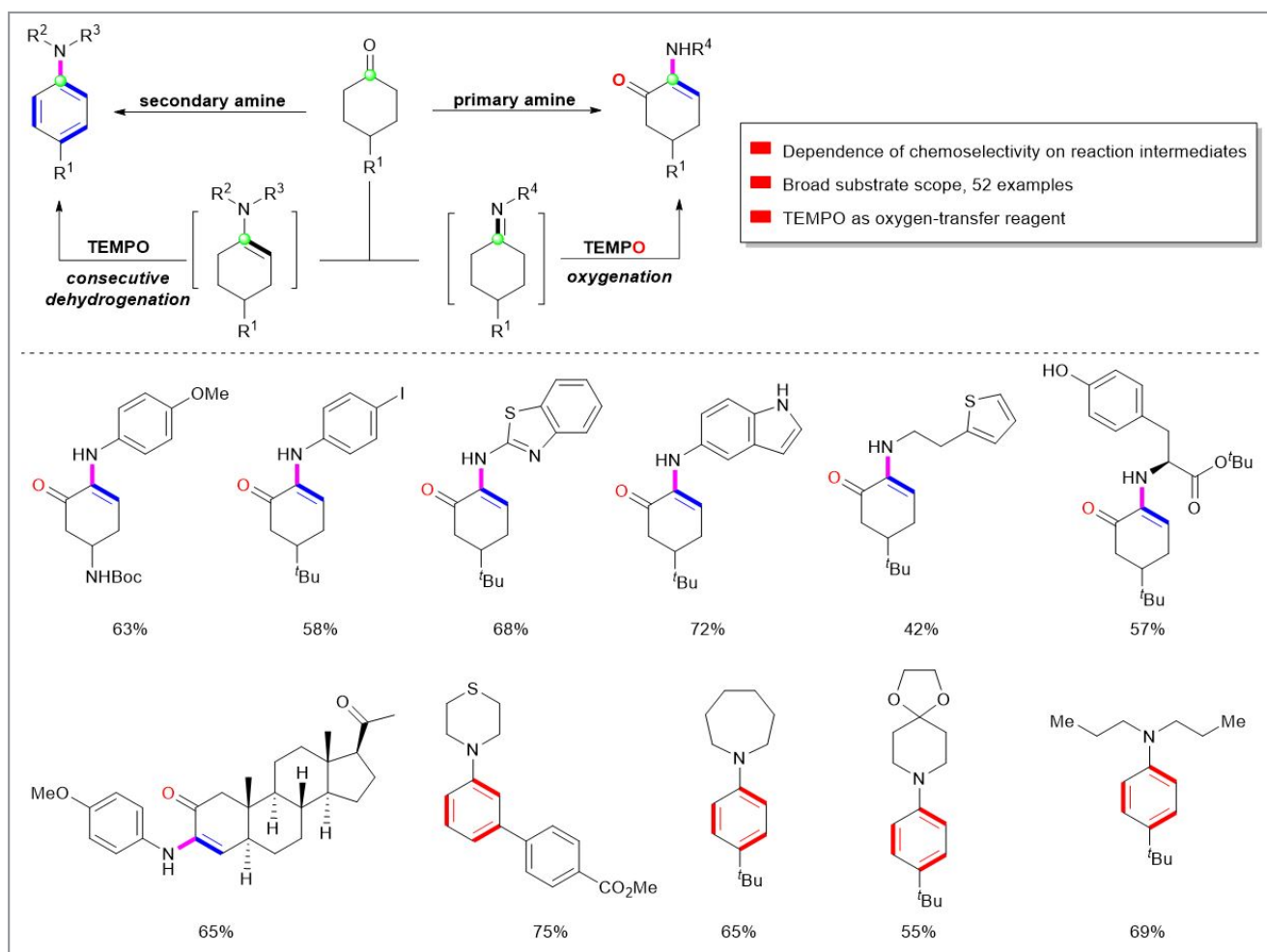
**Patrick J. Walsh** completed his B.A. at the University of California San Diego (USA), his Ph.D. at UC Berkeley (USA) with Prof. Robert G. Bergman (Ph.D., 1991), and a postdoc with Prof. K. B. Sharpless at the Scripps Institute (USA). From 1994–1999 he was an assistant professor at San Diego State University (USA) and professor at Centro de Graduados e Investigación, Instituto Tecnológico de Tijuana (Mexico, 1996–1999). In 1999 he moved to the University of Pennsylvania (USA) where he is the Alan G. MacDiarmid Professor. He is an Honorary Professor at Nanjing Tech University (P. R. of China).

# Differentiation between Enamines and Tautomerizable Imines in the Oxidation Reaction with TEMPO

*Nat. Commun.* **2018**, *9*, 5002

Imines and enamines are ubiquitously encountered intermediates in organic synthesis, especially in recently developed aminocatalysis reactions for the efficient and selective functionalization of aldehydes and ketones. Imines featuring  $\alpha$ -hydrogens are in equilibrium with their enamine tautomers. This imine–enamine tautomerism is the nitrogen analogue of keto–enol tautomerism, but with higher reactivity. This feature makes the tautomerizable imine resemble the reactivity of the corresponding enamine in organic trans-

formations. Although several examples have been reported on the utilization of this tautomerizable character of imines for organic synthesis, the exact difference in reactivity between the imine-derived enamine tautomer and the real enamine remains underdeveloped. In light of this, the research groups of Professor Weiping Su and Wei Zhuang at Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences (P. R. of China) collaborated to develop a unique model reaction pattern that could discriminate this subtle



discrepancy, affording molecular diversity depending on the chemistry of imine and enamine tautomers and offering an insight into their structure–reactivity relationship.

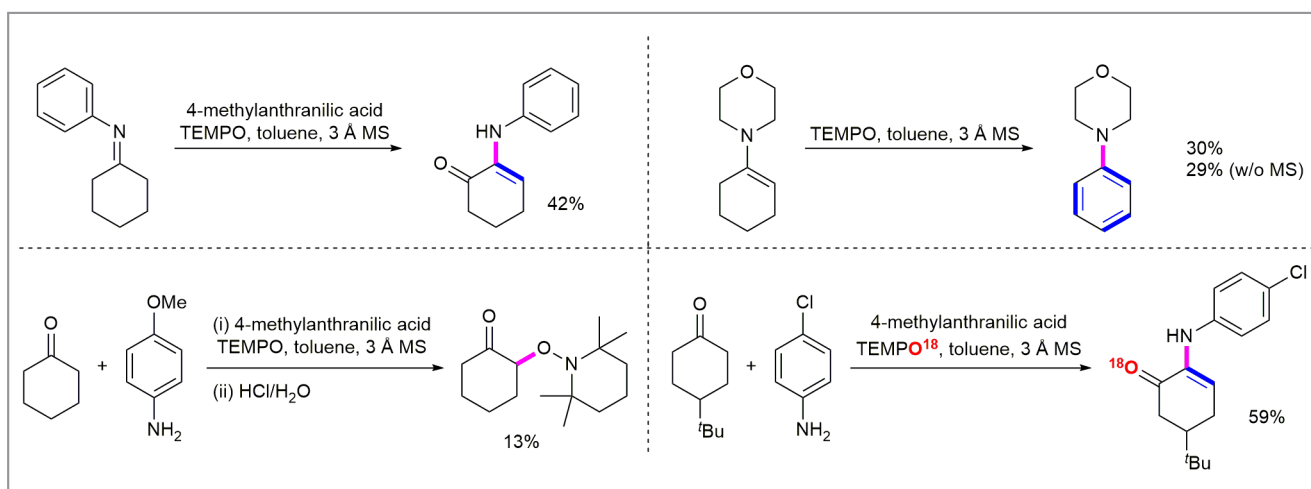
As a continuing interest in the oxidative transformations with TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) as oxidant in Professor Su's group, Dr. Xiaoming Jie initiated the investigation with reactions of amines, cyclohexanones and TEMPO. He explained: "It has been established that the outcome of the reaction is exclusively dependent on the amine species, in which a distinct difference could be exhibited between enamines and tautomerizable imines: i) when primary amines were used, the *in situ* generated tautomerizable imines gave rise to the formation of  $\alpha$ -amino enones, which are versatile synthetic intermediates for heterocycle synthesis; ii) conversely, when secondary amines were used, the *in situ* generated enamines led to the production of arylamines; the latter is orthogonal to the established strategy making use of transition-metal catalysts (Scheme 1)."

Dr. Yaping Shang made a contribution to the substrate scope development as well as experimental mechanism studies (Scheme 2). She explained: "I examined the reaction of presynthesized imine and enamine with TEMPO under standard reaction conditions, and obtained  $\alpha$ -amino enone and aryl amine, respectively, indicating that imine and enamine are indeed reaction intermediates. Moreover, both the isolated  $\alpha$ -aminoxylated ketone intermediate and the  $^{18}\text{O}$ -labeling experiment revealed that the oxygen atom in the  $\alpha$ -amino enone originated from TEMPO." In order to make further confirmations about the product structure, Dr. Xiaofeng Zhang characterized the structures of four representative compounds.

Dr. Zhe-Ning Chen and Prof. Wei Zhuang helped to conduct computational studies to give an in-depth understanding about the differences between imines and enamines in this transformation at a molecular level. They said: "The results demonstrate that the NH-containing enamine kinetically favors  $\alpha$ -radical formation by TEMPO-mediated hydrogen atom abstraction from the NH moiety and then 1,4-elimination to generate  $\alpha$ -amino enones. Whereas the NH-lacking enamine – derived from a secondary amine – prefers  $\beta$ -radical formation and subsequent consecutive  $\beta$ -elimination of H/TEMPO to deliver arylamines. Therefore, due to imine–enamine tautomerization, the  $\alpha$ -hydrogen-containing imine displays distinctly different reactivity in terms of regioselectivity and chemoselectivity relative to the enamine that lacks the NH moiety."

Prof. Su concluded: "This protocol offers a simple platform to combine the chemistry of imine and enamine together and to show their reactivity differences through distinctive product distribution under nearly identical reaction conditions. The underlying mechanism is interesting and we anticipate that our findings will provide valuable clues to enlighten more diverse reaction patterns based on the reactivity difference of tautomerizable imines and enamines. We will continue to investigate in this direction and are curious to see what we will discover in the future."

*Mattias Fankle*



**Scheme 2** Experimental mechanistic studies



## About the authors



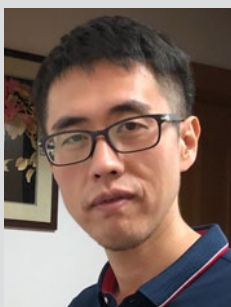
Dr. X. Jie

**Xiaoming Jie** was born and grew up in Hebei (P. R. of China). He earned a B.Sc. from Nanjing Agricultural University (P. R. of China). He completed his Ph.D. at Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences (P. R. of China) under the supervision of Prof. Weiping Su in 2013. He then continued to work in Prof. Su's group as a research assistant and was promoted to a research associate in 2016. At the end of 2017, he moved to Westfälische Wilhelms-Universität Münster (Germany) to carry out postdoctoral research with Prof. Gerhard Erker where he has focused on the synthesis and reactivity investigation of cyclic frustrated Lewis pairs.



Dr. Y. Shang

**Yaping Shang** was born and grew up in Inner Mongolia (P. R. of China). She received her B.Sc. from Inner Mongolia University for the Nationalities (P. R. of China) and her Ph.D. under the supervision of Prof. Weiping Su at Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences (P. R. of China) in 2013. She then worked as a research assistant in Prof. Su's group and was promoted to a research associate in 2018. Her research interests are radical-based dehydrogenation reactions and C–H activation reactions in pharmaceutical synthesis.



Prof. Z.-N. Chen

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Prof. W. Zhuang

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Prof. W. Su

**Weiping Su** graduated from Anhui Education Institute in 1987 and earned his Ph.D. at Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences in 1999 under the supervision of Prof. Maochun Hong. After one year of working as an assistant professor at the same institute, he moved to the United States to do postdoctoral studies with Prof. Richard H. Holm at Harvard University (2000–2001), Prof. Jin Li at Rutgers University (2001–2002), and Prof. John G. Verkade at Iowa State University (2002–2005). Then, he joined the faculty at Fujian Institute of Research on the Structure of Matter in 2006. His research interests include synthetic methodology, discoveries of metal-complex-based homogeneous catalysts and nanoparticle-based recyclable catalysts, and the structure-property relationships of catalysts.



## Coming soon

### Literature Coverage

#### Diarylmethane Synthesis through $\text{Re}_2\text{O}_7$ -Catalyzed Bimolecular Dehydrative Friedel–Crafts Reactions

### Name Reaction Bio

#### Mendeleev, Menshutkin and Beilstein: A New Generation Takes Over

### Editorial Board Focus

#### Interview with Franziska Schoenebeck (Germany)

## Further highlights

### Synthesis Review: Syntheses of Post Iboga Alkaloids

(by S. Han and co-workers)

### Synlett Account: Expanding the Porphycene Core: Modification and Metalation

(by J. L. Sessler and co-workers)

### Synfacts Synfact of the Month in category “Organo- and Biocatalysis”: Catalytic Deracemization of Allenes

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