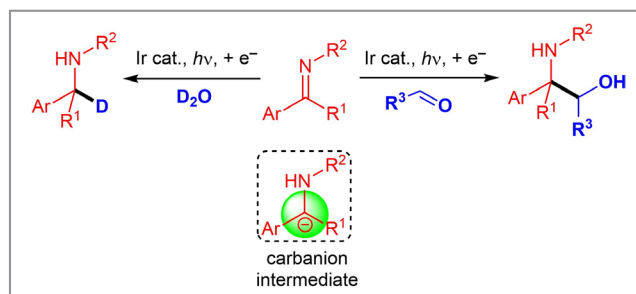


# Sunlight-Promoted CO<sub>2</sub> Transformations: Synthesis of $\alpha$ -Amino Acids with Imines

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

The importance of  $\alpha$ -amino acids is broadly documented in synthesis, catalysis, protein science and biomedical research. Efficient chemical synthesis of  $\alpha$ -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  $\alpha$ -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.

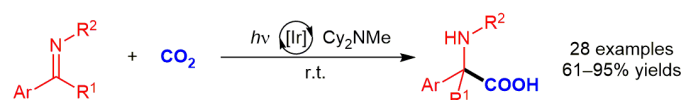
Professor Xinyuan Fan (Nanjing Tech University, P. R. of China), Professor Patrick Walsh (University of Pennsylvania, USA, Honorary Professor at Nanjing Tech University, P. R. of China) and their co-workers previously demonstrated that benzophenone ketimines, which are conventionally electrophilic, exhibit 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)



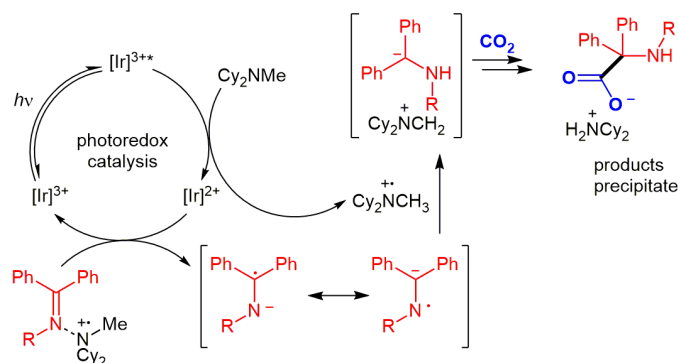
**Scheme 1** Previously reported Umpolung imine transformations by photoredox catalysis

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).”

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



**b)** plausible mechanism



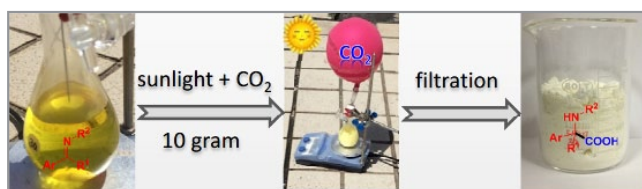
**Scheme 2** CO<sub>2</sub> fixation with imines by photoredox catalysis

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).”

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 Fanke*



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

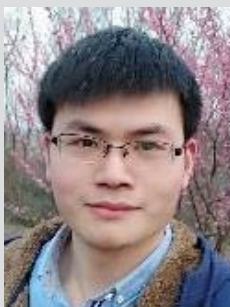
“To summarize,” said Professor Fan, “we developed a simple and efficient method to synthesize  $\alpha$ -amino acid derivatives using  $\text{CO}_2$  and imines by harvesting the energy of sunlight. The advantages of this method include: 1) mild conditions (room temperature, atmospheric pressure of  $\text{CO}_2$ , 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

## About the authors



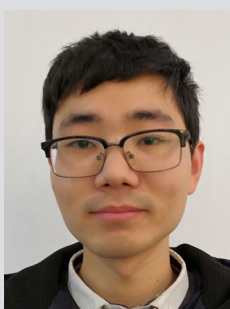
Prof. X. Fan

**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

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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).