

## Asymmetric Three-Component Olefin Dicarbofunctionalization Enabled by Photoredox and Copper Dual Catalysis

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Alkenes are among the most privileged and versatile compounds in organic synthesis, because a diverse range of functional groups can be readily introduced across the C=C  $\pi$  system by using many well-established and versatile vicinal di-functionalization reactions. In this context, one of the most investigated and fundamental transformations is the intermolecular three-component alkene vicinal di-carbo-functionalization (DCF) reaction, which allows for the installation of two different carbon fragments.

The group of Professors Jia-Rong Chen and Wen-Jing Xiao at Central China Normal University (Wuhan, P. R. of China) has been interested in visible-light photoredox-controlled reactions of iminyl nitrogen radicals. "In recent years, chiral copper catalysis laid the foundations of a new and robust platform for the development of asymmetric radical-mediated alkene DCF reactions, providing a robust and powerful method towards the construction of diverse C–C and C–heteroatom bonds,<sup>1,2</sup>" said Professor Chen. "However, despite the broad synthetic applicability of these methods, the intrinsic redox potential window of copper catalysts, which is critical to the generation of radicals, results in certain limitations concerning the range of accessible radical precursors." Recently, Professors Chen and Xiao developed a generally applicable visible-light-driven copper-catalyzed radical cross-coupling reaction of cyanoalkyl carbon radicals, which enables the synthesis of diverse distantly functionalized alkyl nitriles.<sup>3</sup> In this article, they reported an intermolecular, enantioselective three-component radical vicinal DCF reaction of olefins by merger of radical addition and cross-coupling chemistry, under photoredox and copper dual catalysis (Scheme 1).

"The reaction exhibits a remarkably wide substrate scope, and a range of styrene derivatives with electron-donating (e.g., Me, <sup>t</sup>Bu, Ph) or electron-withdrawing (e.g., F, Cl, Br, OAc, Bpin) functional groups are well tolerated, furnishing the corresponding products in good yields and stereoselectivity," said Professor Chen, who continued: "This protocol can also be successfully extended to biologically relevant molecules and pharmaceutically derived styrene analogues. For instance, alkenes derived from estrone, febuxostat, and simple amino acids, reacted well to give the desired acylcyanation products with good stereoselectivity." Besides that, the group also demonstrated that the catalytic system could also be success-

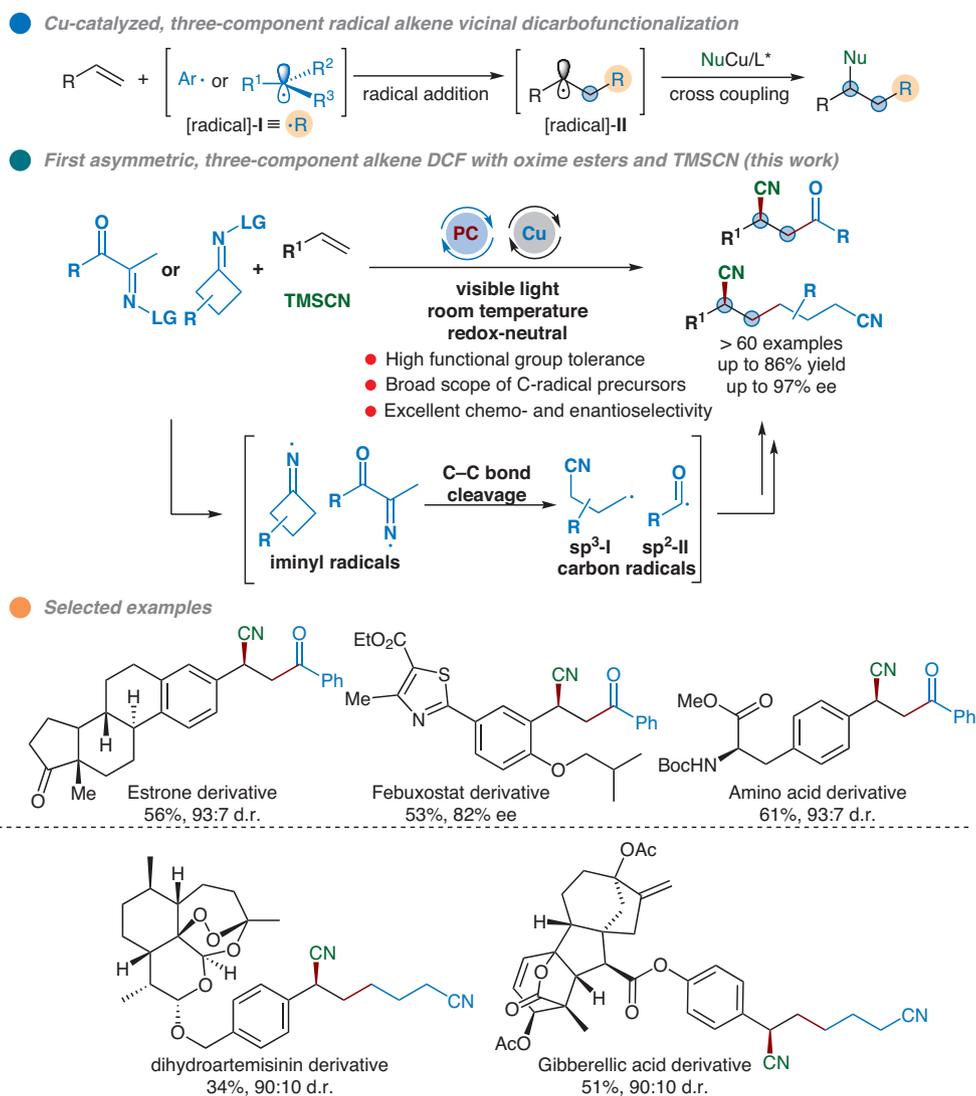
fully extended to the reaction of cycloketone-derived oxime esters, alkenes, and TMS-CN. "A representative set of oxime esters bearing a variety of functional groups, which can be easily prepared in two steps from the relevant ketone precursors, underwent the reaction successfully," said Professor Chen, who continued by explaining that diverse further transformations of the chiral  $\beta$ -cyano ketones and alkyldinitriles to chiral amides, aliphatic amines and esters were successfully realized, and gram-scale synthesis could be easily achieved.

Professor Chen concluded: "We have developed an intermolecular, highly enantioselective three-component radical vicinal DCF reaction of alkenes, using oxime esters and TMS-CN, by exploiting the potential of dual photoredox and copper catalysis. This three-component reaction proceeds under mild conditions, and demonstrates broad substrate scope and high functional group tolerance, providing a general approach to optically active  $\beta$ -cyano ketones and alkyl-dinitriles."

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### REFERENCES

- (1) F. Wang, P. Chen, G. Liu *Acc. Chem. Res.* **2018**, *51*, 2036–2046.
- (2) Z.-L. Li, G.-C. Fang, Q.-S. Gu, X.-Y. Liu *Chem. Soc. Rev.* **2020**, *49*, 32–48.
- (3) X.-Y. Yu, Q.-Q. Zhao, J. Chen, W.-J. Xiao, J.-R. Chen *Acc. Chem. Res.* **2020**, *53*, 1066–1083.



**Scheme 1** Catalytic asymmetric, three-component di-carbo-functionalization (DCF) reactions of alkenes with oxime esters and TMSCN: reaction design and selected examples

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