

Cite this: *Chem. Sci.*, 2023, 14, 2447

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 24th November 2022
Accepted 3rd February 2023

DOI: 10.1039/d2sc06497a

rsc.li/chemical-science

Metal-free photosensitized radical relay 1,4-carboimination across two distinct olefins†

Guangying Tan,[‡] Fritz Paulus,[‡] Alessia Petti, Maxim-Aleksa Wiethoff, Anna Lauer, Constantin Daniliuc and Frank Glorius *

Intermolecular carboamination of olefins offers a powerful platform for the rapid construction of structurally complex amines from abundant feedstocks. However, these reactions often require transition-metal catalysis, and are mainly limited to 1,2-carboamination. Herein, we report a novel radical relay 1,4-carboimination across two distinct olefins with alkyl carboxylic acid-derived bifunctional oxime esters *via* energy transfer catalysis. The reaction is highly chemo- and regioselective, and multiple C–C and C–N bonds were formed in a single orchestrated operation. This mild and metal-free method features a remarkably broad substrate scope with excellent tolerance of sensitive functional groups, therefore providing easy access to structurally diverse 1,4-carboiminated products. Moreover, the obtained imines could be easily converted into valuable biologically relevant free γ -amino acids.

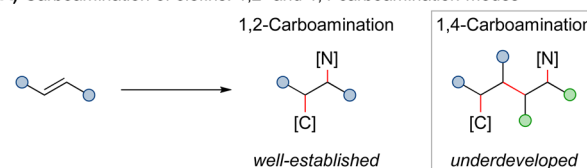
Introduction

Nitrogen-containing organic molecules are widely found in natural products, agrochemicals, pharmaceutical agents, and functional materials.¹ Consequently, the selective incorporation of amine functionalities into small molecules has received considerable attention in recent years.² In this context, the carboamination of olefins represents a vibrant research area in organic synthesis, as such transformations allow for the simultaneous installation of C–C and C–N bonds across simple olefins in a single operation, thereby constructing complex molecules in a modular manner from abundant feedstocks.^{3,4} However, despite significant achievements made over the past decades, some fundamental issues still remain to be solved in this field. First, these reactions often require transition-metal catalysis, rendering them costly and environmentally harmful. Second, the current studies are mainly limited to 1,2-carboamination of olefins, namely introducing carbon and amine functionalities across one olefin at its vicinal positions (Scheme 1A). Undoubtedly, from a synthetic perspective, the development of controllable remote 1,*n*-carboamination across more than one olefin to modularly access more structurally diverse amines, ideally under mild and metal-free conditions, is highly desirable.

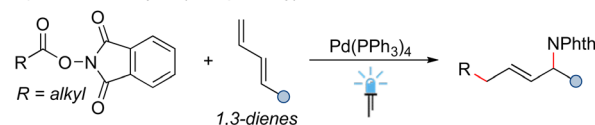
Compared to the vigorous growth and abundant achievements in 1,2-carboamination chemistry of olefins, remote

carboamination reactions are so far rarely developed. Comparatively few examples are transition-metal (Pd, Rh or Cu)-catalyzed 1,4-carboaminations of 1,3-dienes.⁵ Moreover, with

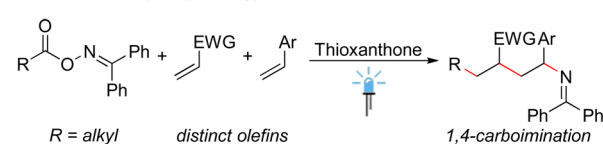
(A) Carboamination of olefins: 1,2- and 1,4-carboamination modes



(B) Our previous work: Photoinduced 1,4-carboimination of 1,3-dienes via palladium catalysis (SET pathway)



(C) This work: Photosensitized radical relay 1,4-carboimination across two distinct olefins (EnT pathway)



✓ Metal free ✓ Broadly applicable to natural products and drugs
✓ Modular build-up of complexity ✓ Rapid access to diverse γ -amino acids

Scheme 1 The development of 1,4-carboamination of olefins. (A) Carboamination of olefins: 1,2- and 1,4-carboamination modes. (B) Our previous work: photoinduced 1,4-carboimination of 1,3-dienes via palladium catalysis (SET pathway). (C) This work: photosensitized radical relay 1,4-carboimination across two distinct olefins (EnT pathway). SET: single electron transfer. EnT: energy transfer. NPhth: phthalimido.

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstraße 36, 48149 Münster, Germany. E-mail: glorius@uni-muenster.de

† Electronic supplementary information (ESI) available. CCDC 2207448. For ESI and crystallographic data in CIF or other electronic format see DOI: <https://doi.org/10.1039/d2sc06497a>

‡ Equal contribution.

the development of photochemistry,⁶ modern visible light-mediated methods for 1,4-carboaminations have recently gradually emerged.^{7–9} In a notable example, Sarlah and coworkers demonstrated an elegant strategy for the stepwise *syn*-1,4-carboamination of simple arenes by the combination of photoinduced cycloaddition and palladium-catalyzed ring-opening substitution.⁷ Very recently, we have realized a palladium-catalyzed 1,4-carboimination of 1,3-dienes with alkylcarboxylic acid-derived bifunctional reagents through a single electron transfer (SET) approach mediated by visible light (Scheme 1B).⁸ Based on this strategy, the palladium-catalyzed three component 1,4-carboamination of 1,3-dienes with haloalkanes and nitrogen nucleophiles has been subsequently achieved by other groups and us.⁹ Although these reactions are versatile, they require the use of transition metals (especially palladium), as catalysts. Moreover, the utilization of unstable 1,3-dienes as starting materials further restricts the general appeal of these protocols.

Seeking to address these limitations, we herein disclose an unprecedented radical relay 1,4-carboimination across two distinct olefins with alkyl carboxylic acid-derived bifunctional oxime esters *via* energy transfer (EnT) catalysis¹⁰ (Scheme 1C). This mild and metal-free reaction is highly chemo- and regio-selective, and multiple C–C and C–N bonds were formed in a single operation in an orchestrated manner. Moreover, due to the direct utilization of two distinct olefins as starting materials,

this method provides modular access to structurally diverse 1,4-carboaminated products, which could be easily converted into valuable biologically relevant free γ -amino acids.¹¹

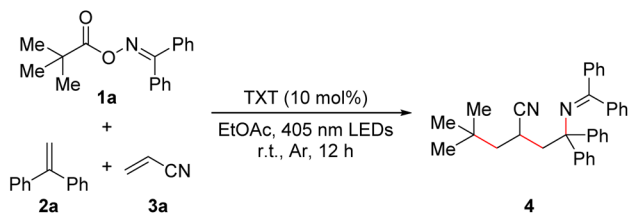
Results and discussion

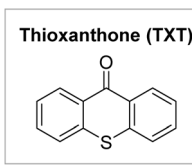
Reaction development

Bifunctional reagents have gained a preeminent role within organic synthesis, thanks to their versatility, atom economy, and efficient activation modes.¹² Recently, we and others have identified a class of benzophenone-based oxime esters as a suitable bifunctional source for supplying both carbon- and nitrogen-centered radicals through energy transfer catalysis.^{13–15} Our investigation commenced with the reaction of benzophenone *O*-pivaloyl oxime (**1a**), ethene-1,1-diylbenzene (**2a**), and acrylonitrile (**3a**) under visible-light-sensitized conditions (Table 1).

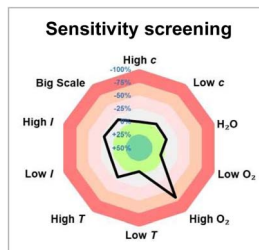
To our delight, after a systematic evaluation of the reaction parameters, the best yield for the desired product **4** reached 63% under the optimized reaction conditions: **1a** (0.3 mmol, 1.5 equiv.), **2a** (0.2 mmol, 1.0 equiv.), **3a** (0.4 mmol, 2.0 equiv.), and thioxanthone (10 mol%) in EtOAc (0.1 M, 2.0 mL), and irradiation with 18 W blue LEDs ($\lambda_{\text{max}} = 405 \text{ nm}$) under argon atmosphere at room temperature for 12 h (Table 1, entry 1). Control experiments demonstrated that both thioxanthone and blue light ($\lambda_{\text{max}} = 405 \text{ nm}$) were indispensable for this reaction

Table 1 Optimization of the reaction conditions^{a,b}

		
Entry	Variation	Yield ^b [%]
1	None	63, 60 ^c
2	w/o TXT	N.R.
3	w/o light	N.R.
4	450 nm LEDs	N.R.
5	CH ₂ Cl ₂ as solvent	56
6	Acetone as solvent	54
7	MeCN as solvent	57
8	DCE as solvent	48
9	[Ir-F] ^d (1.0 mol%) instead of TXT and 450 nm LEDs	50
10	EtOAc (0.05 M)	53
11	1.5 equiv. of 3a	58
12	1.0 equiv. of 1a , 2.0 equiv. of 2a and 3a	53



Thioxanthone (TXT)



Sensitivity screening

^a Standard conditions: **1a** (0.3 mmol, 1.5 equiv.), **2a** (0.2 mmol, 1.0 equiv.), **3a** (0.4 mmol, 2.0 equiv.), and thioxanthone (10 mol%) in EtOAc (0.1 M, 2.0 mL), irradiation with 18 W blue LEDs ($\lambda_{\text{max}} = 405 \text{ nm}$) under argon atmosphere at room temperature for 12 h. ^b NMR yields are given. ^c Isolated yield. ^d [Ir-F] = [Ir(dF(CF₃)ppy)₂(dtbbpy)](PF₆).



(Table 1, entries 2 and 3). As expected, the reaction did not proceed when switching to a blue light with a wavelength maximum of 450 nm (Table 1, entry 4). This protocol appeared to be relatively robust regarding the choice of solvents, as replacing EtOAc with CH₂Cl₂, acetone, MeCN, or DCE still provided **4** in similar yields (Table 1, entries 5–8). In addition, [Ir(dF(CF₃)ppy)₂(dtbbpy)](PF₆) proved to be a suitable catalyst for the reaction as well, giving product **4** in 50% yield (Table 1, entry 9). Other variations from the standard conditions, such as decreasing the concentration of the reaction or changing the substrate ratio, led to slightly diminished yields of product **4** (Table 1, entries 10–12). Furthermore, a reaction condition-based sensitivity screening was conducted, showing that the reaction was relatively robust towards moisture, light intensity, scale-up, and small changes in concentration and temperature, but sensitive towards high oxygen level (Table 1, see ESI† for the details).¹⁶

Mechanistic analysis

In order to obtain insights into the underlying reaction mechanism, we conducted a series of mechanistic experiments. Only trace amounts of **4** were observed when conducting the standard reaction in the presence of TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl), and compound **5** was detected in the reaction mixture by high-resolution mass spectrometry (Fig. 1A). Furthermore, the reaction was carried out under direct excitation conditions (irradiation at 365 nm instead of 405 nm; no photocatalyst), delivering product **4** in 38% NMR yield (see ESI† for the details). These results are consistent with an energy transfer-based radical pathway and an initial radical attack of the generated carbon-centered radical **B** to **3a**. Subsequently, we turned our attention towards the corresponding two-component 1,2-carboiminations of alkenes **2a** or **3a** with oxime ester **1a** (Fig. 1B). Both reactions delivered the corresponding 1,2-carboiminated products (**6** and **7**) in good yields, even though these compounds were only observed as minor side products in the three-component reaction of **1a**, **2a**, and **3a** (see ESI† for the details). To further probe the origin of the regioselectivity observed for the assembly of **4**, we conducted preliminary kinetic studies on both two-component reactions. The initial formation of **7** was found to be more than twice as fast than the formation of **6** (Fig. 1C), which is a hint that the formation of **4** might initiate with fast radical attack to **3a**. Lastly, the quantum yield of the reaction of **1a**, **2a**, and **3a** was determined. A value of 0.40 was obtained, rendering a pure radical chain mechanism unlikely (Fig. 1D).^{15c} However, a mixed radical chain/radical recombination mechanism cannot be ruled out.

Based on these experiments and our previous studies,^{13,14} a mechanistic analysis of the selective 1,4-carboimination of **1a**, **2a**, and **3a** was developed (Fig. 1E, see ESI† for details). The reaction initiates with an energy transfer-enabled homolysis of **1a** to provide the persistent N-centered iminyl radical **A** and the transient C-centered alkyl radical **B**, which are of ambiphilic and nucleophilic properties, respectively. Then, steered by polarity matching, persistent radical effects (PRE),¹⁷ and

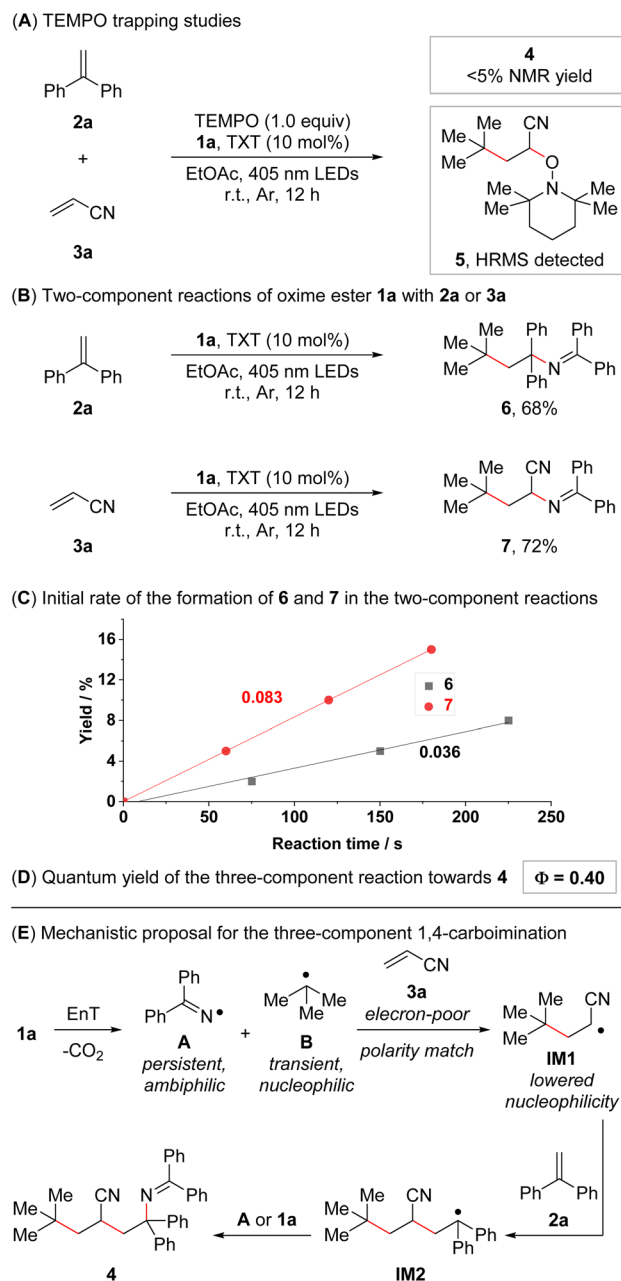
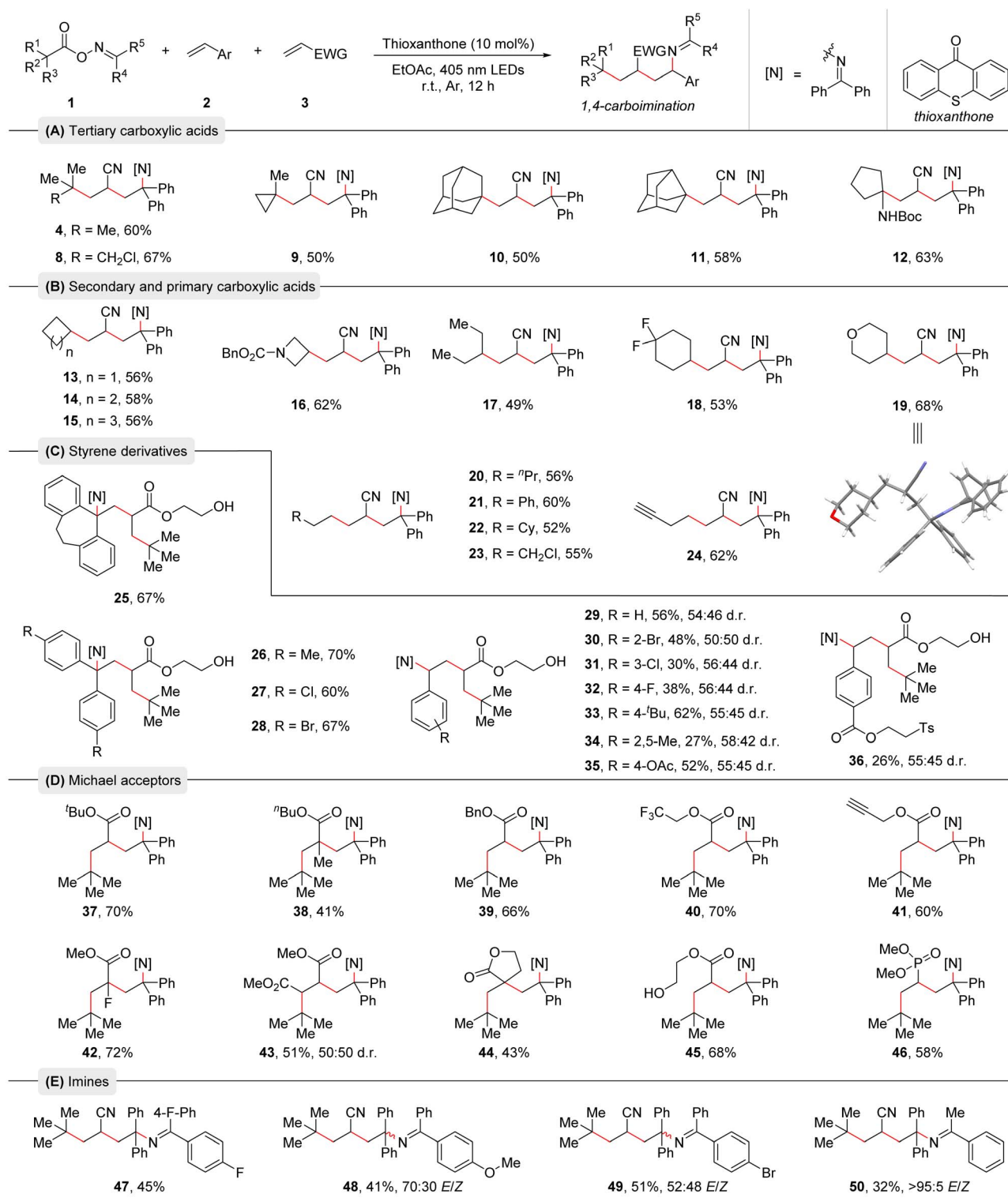


Fig. 1 Mechanistic studies and mechanistic proposal. (A) TEMPO trapping experiment. Reaction conditions: **1a** (0.15 mmol, 1.5 equiv.), **2a** (0.1 mmol, 1.0 equiv.), **3a** (0.2 mmol, 2.0 equiv.), thioxanthone (TXT, 10 mol%), and TEMPO (0.1 mmol, 1.0 equiv.) in EtOAc (0.1 M, 1.0 mL), 18 W blue LEDs ($\lambda_{\text{max}} = 405 \text{ nm}$), r.t., 12 h. (B) Two-component reactions of **1a** with **2a** or **3a**. Reaction conditions: **1a** (0.3 mmol, 1.5 equiv.), **2a** or **3a** (0.2 mmol, 1.0 equiv.), and thioxanthone (10 mol%) in EtOAc (0.1 M, 2.0 mL), 18 W blue LEDs ($\lambda_{\text{max}} = 405 \text{ nm}$), r.t., 12 h. Isolated yields given. (C) Initial course and rate of the reaction between **1a** and **2a** and the reaction between **1a** and **3a** (see ESI† for the details). (D) Quantum yield of the reaction between **1a**, **2a**, and **3a** (see ESI† for the details). (E) Mechanistic proposal for the intermolecular 1,4-carboimination of **2a** and **3a** with **1a**.

a higher concentration of **3a** compared to **2a**, the nucleophilic C-centered alkyl radical **B** preferentially adds to electron poor olefin **3a** to form an α -cyano-containing C-centered alkyl radical



Table 2 Scope of alkyl carboxylic acid-derived bifunctional oxime esters and olefins^{a,b}

^a Reaction conditions: Oxime esters **1** (0.3 mmol, 1.5 equiv.), styrene derivatives **2** (0.2 mmol, 1.0 equiv.), Michael acceptors **3** (0.4 mmol, 2.0 equiv.), and thioxanthone (10 mol%) in EtOAc (0.1 M, 2.0 mL), irradiation with 18 W blue LEDs ($\lambda_{\text{max}} = 405$ nm) under argon atmosphere at room temperature for 12 h. ^b Isolated yields are given. The d.r. and E/Z values were determined by ¹H NMR analysis.

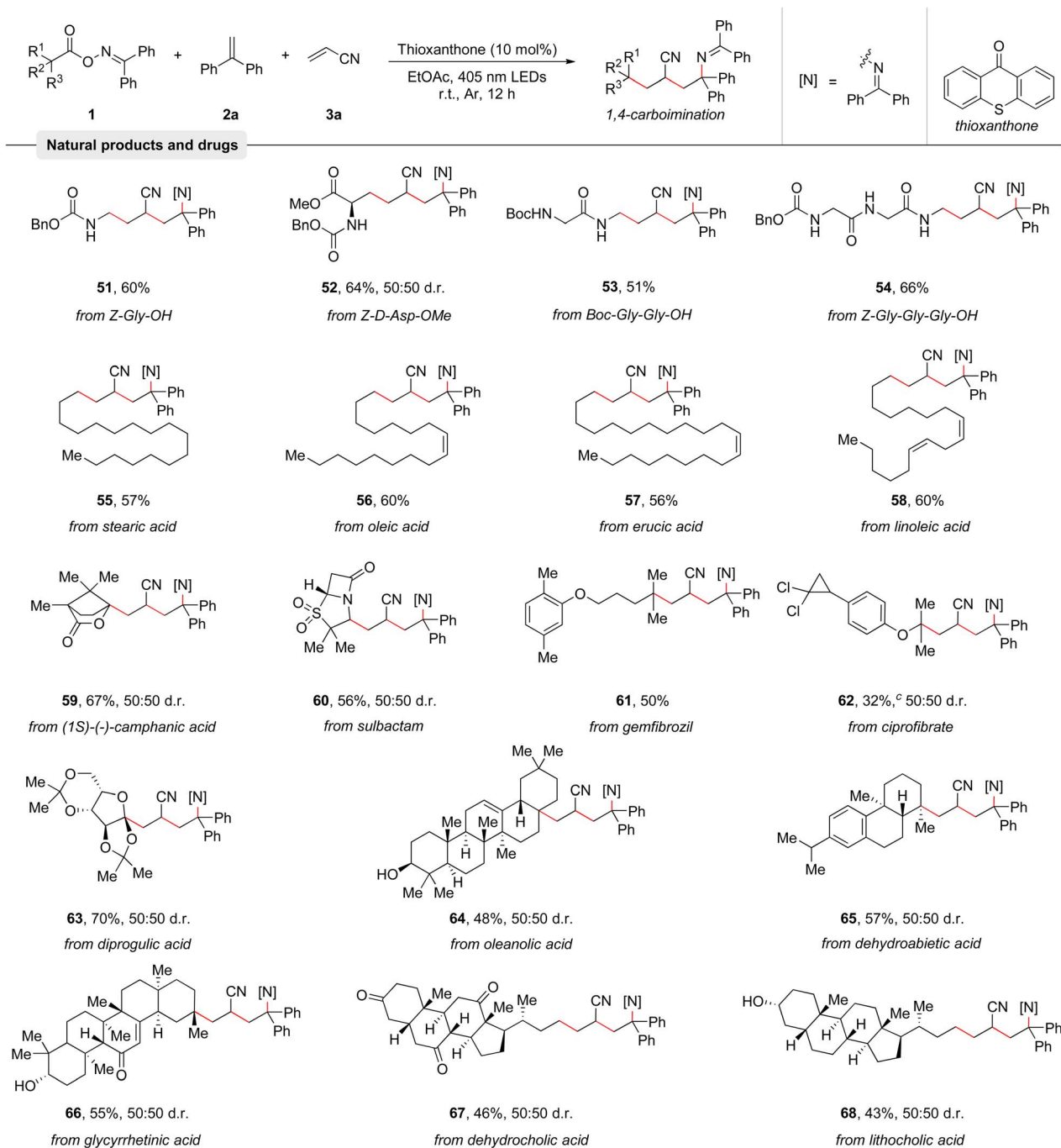


with reduced nucleophilicity (**IM1**). Subsequently, addition of **IM1** to **2a** gives another benzyl stabilized C-centered alkyl radical (**IM2**), which is further trapped by the persistent N-centered iminyl radical **A** to furnish the desired 1,4-carboimination product **4** via radical recombination. Alternatively, due to low concentrations of the radical species and a relatively high

concentration of oxime ester **1a**, **IM2** can form product **4** via radical attack to oxime ester **1a** and subsequent fragmentation, representing a radical chain mechanism.^{15c,18}

This mechanism is therefore related to our previous work, in which we used oxime carbonates as a source for electrophilic oxygen-centered radicals to achieve a three-component 1,4-

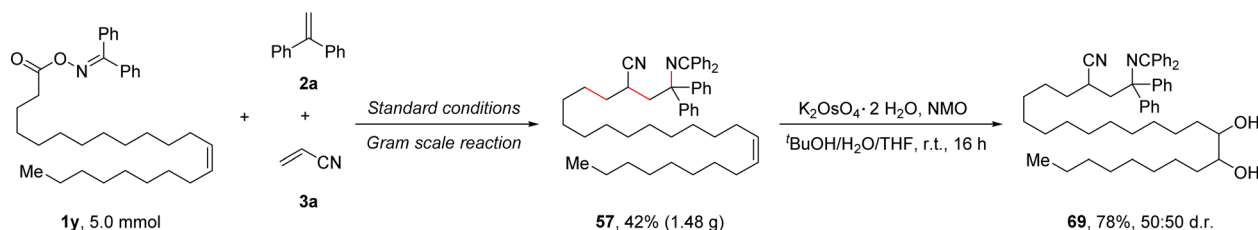
Table 3 Modification of natural products and drugs^{a,b}



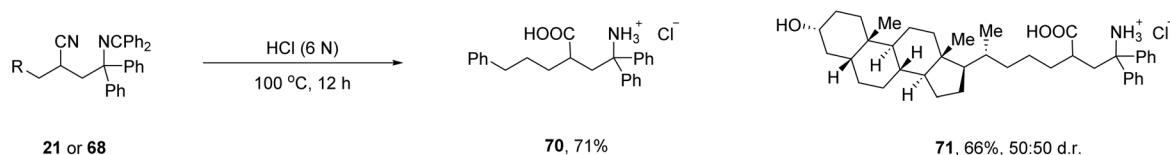
^a Reaction conditions: oxime esters **1** (0.3 mmol, 1.5 equiv.), ethene-1,1-diylidibenzene **2a** (0.2 mmol, 1.0 equiv.), acrylonitrile **3a** (0.4 mmol, 2.0 equiv.), and thioxanthone (10 mol%) in EtOAc (0.1 M, 2.0 mL), irradiation with 18 W blue LEDs ($\lambda_{\text{max}} = 405 \text{ nm}$) under argon atmosphere at room temperature for 12 h. ^b Isolated yields are given. The d.r. values were determined by ¹H NMR analysis. ^c Oxime ester **1ad** (0.2 mmol, 1.0 equiv.), ethene-1,1-diylidibenzene **2a** (0.4 mmol, 2.0 equiv.), acrylonitrile **3a** (0.4 mmol, 2.0 equiv.) were used.



(A) Gram scale synthesis and dihydroxylation of product 57



(B) Deprotection of selected products to generate the corresponding free amino acids



Scheme 2 Synthetic applications. (A) Gram scale synthesis and dihydroxylation of product 57. (B) Deprotection of selected products to generate the corresponding free amino acids. NMO: *N*-methylmorpholine *N*-oxide.

oximation.¹⁸ In both cases, the desired regioselectivity was achieved by rational reaction design based on the philicity of the generated radicals and the polarity of the olefins. Notably, the different philicities of carbon- and oxygen-centered radicals cause a different order of building block assembly depending on the selected reagent.

Synthetic scope

With the optimized reaction conditions in hand, we conducted an additive-based robustness screening to initially assess the reaction's functional group compatibility. The obtained results highlighted the outstanding tolerance of heterocycles and functional groups and already hinted towards the broadness of the substrate scope (see ESI† for the details).¹⁹ Next, the substrate scope with respect to the three reaction partners was examined (Table 2). First, a range of alkyl carboxylic acid-derived bifunctional oxime esters was explored. Tertiary alkyl carboxylic acids smoothly underwent this radical relay 1,4-carboimination reaction, providing the corresponding products in moderate to good yields (Table 2A, 4 and 8–12). Notably, these reactions were highly chemo- and regioselective, and two quaternary carbon centers were easily created, demonstrating the appeal of our method in building complex molecules. Then, a series of secondary and primary carboxylic acids was tested (Table 2B, 13–24). Various cyclic and acyclic carboxylic acids were all well compatible with this protocol, delivering the desired products in moderate to good yields. The structure of product 19 was further confirmed by X-ray crystallography (Table 2B).²⁰ Subsequently, we turned our attention to the compatibility of olefins. As shown in Table 2C, diverse styrene derivatives with different electron-donating or electron-withdrawing substituents in various positions of the aromatic ring were found to be effective substrates for this 1,4-carboimination reaction, producing the corresponding products in moderate to good yields (Table 2C, 25–36). Functional groups such as bromide, acetoxy and an ester containing a tosyl group

were well tolerated, offering opportunities for further functionalization. Moreover, a series of Michael acceptors such as acrylates and vinyl phosphate were also suitable for this transformation (Table 2D, 37–46). Satisfactorily, a variety of sensitive functional groups like alkenyl fluoride, trifluoromethyl, alkynyl, ester, phosphonate, and even a free alcohol were well tolerated in this method. Due to polar mismatch, electron rich and unactivated olefins were not suitable for this protocol. We further tested oxime esters with different imine moieties leading to products 47–50. Benzophenone-derived oxime esters containing fluoride, bromide, or methoxy groups were tolerated. Notably, an acetophenone-derived oxime ester delivered product 50 in moderate yield with well-controlled *E/Z*-selectivity.

Among various potential carbon-centered radical precursors, alkyl carboxylic acids represent an ideal starting material as these stable compounds are abundant, cheap, and are found in numerous natural products and pharmaceuticals.²¹ To demonstrate the broad applicability of the protocol, its capability to couple structurally complex natural products and pharmaceuticals with olefins 2a and 3a was investigated. As summarized in Table 3, many amino acids and peptides such as Z-Gly-OH (51), Z-D-Asp-OMe (52), Boc-Gly-Gly-OH (53), and Z-Gly-Gly-Gly-OH (54) were examined, giving the corresponding products in good yields. Moreover, a series of naturally occurring alkyl carboxylic acids including stearic acid (55), oleic acid (56), erucic acid (57), and linoleic acid (58) smoothly reacted with olefins 2a and 3a to afford good yields of the 1,4-carboimination products. Notably, the contained C–C double bonds remained untouched. (1S)-(–)-Camphanic acid (59) and diprogulic acid (63) were also smoothly engaged in the 1,4-carboimination reaction. Pharmaceuticals like sulbactam (60), gemfibrozil (61), and ciprofibrate (62) were successfully utilized as well, generating the desired imines in good yields. Finally, various complex steroid molecules, such as oleanolic acid (64), dehydroabiatic acid (65), glycyrrhetic acid (66), dehydrocholic



acid (**67**), and lithocholic acid (**68**) were also suitable for this transformation. Overall, these examples clearly highlight the broadness of the developed reaction and its compatibility with complex molecules.

To further demonstrate the synthetic practicality of this protocol, a gram scale reaction of **1y**, **2a**, and **3a** was performed, affording the desired product **57** in 42% yield (1.48 g). Dihydroxylation of product **57** was conducted,⁸ furnishing product **69** in 78% yield (Scheme 2A). Treating selected 1,4-carboimination products (**21** or **68**) with 6 N HCl at 100 °C for 12 h provided the corresponding biologically relevant free γ -amino acids (**70** and **71**), further highlighting the utility of this method (Scheme 2B).

Conclusions

In summary, we have developed a novel radical relay 1,4-carboimination across two distinct olefins with alkyl carboxylic acid-derived bifunctional oxime esters. Metal-free energy transfer catalysis enables the well-choreographed, highly chemo- and regioselective formation of three bonds in one single operation. The presented protocol is characterized by a remarkably broad substrate scope with excellent tolerance of sensitive functional groups, therefore allowing for the modular construction of a large variety of highly complex imines which could be easily converted into valuable biologically relevant free γ -amino acids. We believe that this work will be of interest to the synthetic community, and will inspire researchers to further explore other remote 1,*n*-difunctionalization reactions.

Data availability

The authors declare that the data supporting the findings of this study are available within the paper and the ESI,[†] as well as from the authors upon request.

Author contributions

G. T., F. P. and F. G. conceived the project; G. T., F. P. and A. P. performed the experiments and analyzed the data; M.-A. W. and A. L. prepared some of the starting materials; C. D. characterized the X-ray structure of **19**; G. T., F. P. and F. G. wrote the manuscript with contributions from all authors; F. G. supervised the project.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We thank the Alexander von Humboldt Foundation (G. T.; A. P.) and the Deutsche Forschungsgemeinschaft (Leibniz Award, F. G.; GRK 2678-437785492, F. P.) for supporting this work.

Notes and references

- 1 A. Ricci, *Amino Group Chemistry: From Synthesis to the Life Sciences*, Wiley-VCH, Weinheim, 2008.
- 2 For selected reviews, see: (a) J. P. Wolfe, S. Wagaw, J.-F. Marcoux and S. L. Buchwald, *Acc. Chem. Res.*, 1998, **31**, 805; (b) J. F. Hartwig, *Nature*, 2008, **455**, 314; (c) T. E. Müller, K. C. Hultsch, M. Yus, F. Foubelo and M. Tada, *Chem. Rev.*, 2008, **108**, 3795; (d) M.-L. Louillat and F. W. Patureau, *Chem. Soc. Rev.*, 2014, **43**, 901; (e) J. Jiao, K. Murakami and K. Itami, *ACS Catal.*, 2016, **6**, 610; (f) Y. Park, Y. Kim and S. Chang, *Chem. Rev.*, 2017, **117**, 9247.
- 3 For selected recent reviews on carboamination of olefins, see: (a) H. Jiang and A. Studer, *Chem. Soc. Rev.*, 2020, **49**, 1790; (b) X. Chen, F. Xiao and W.-M. He, *Org. Chem. Front.*, 2021, **8**, 5206; (c) K. Hirano and M. Miura, *J. Am. Chem. Soc.*, 2022, **144**, 648.
- 4 For selected examples on intermolecular 1,2-carboamination of olefins, see: (a) D. N. Mai and J. P. Wolfe, *J. Am. Chem. Soc.*, 2010, **132**, 12157; (b) K. Weidner, A. Giroult, P. Panchaud and P. Renaud, *J. Am. Chem. Soc.*, 2010, **132**, 17511; (c) H. Zhang, W. Pu, T. Xiong, Y. Li, X. Zhou, K. Sun, Q. Liu and Q. Zhang, *Angew. Chem., Int. Ed.*, 2013, **52**, 2529; (d) D. Prasad Hari, T. Hering and B. König, *Angew. Chem., Int. Ed.*, 2014, **53**, 725; (e) A. Faulkner, J. S. Scott and J. F. Bower, *J. Am. Chem. Soc.*, 2015, **137**, 7224; (f) J. Cheng, X. Qi, M. Li, P. Chen and G. Liu, *J. Am. Chem. Soc.*, 2015, **137**, 2480; (g) T. Piou and T. Rovis, *Nature*, 2015, **527**, 86; (h) S. Kawamura, H. Egami and M. Sodeoka, *J. Am. Chem. Soc.*, 2015, **137**, 4865; (i) J.-S. Lin, X.-Y. Dong, T.-T. Li, N.-C. Jiang, B. Tan and X.-Y. Liu, *J. Am. Chem. Soc.*, 2016, **138**, 9357; (j) A. Lerchen, T. Knecht, C. G. Daniliuc and F. Glorius, *Angew. Chem., Int. Ed.*, 2016, **55**, 15166; (k) Y.-Y. Liu, X.-H. Yang, R.-J. Song, S. Luo and J.-H. Li, *Nat. Commun.*, 2017, **8**, 14720; (l) Z. Liu, Y. Wang, Z. Wang, T. Zeng, P. Liu and K. M. Engle, *J. Am. Chem. Soc.*, 2017, **139**, 11261; (m) B. Qian, S. Chen, T. Wang, X. Zhang and H. Bao, *J. Am. Chem. Soc.*, 2017, **139**, 13076; (n) J. Davies, N. S. Sheikh and D. Leonori, *Angew. Chem., Int. Ed.*, 2017, **56**, 13361; (o) A. Bunescu, T. M. Ha, Q. Wang and J. Zhu, *Angew. Chem., Int. Ed.*, 2017, **56**, 10555; (p) Y. Zhang, H. Liu, L. Tang, H.-J. Tang, L. Wang, C. Zhu and C. Feng, *J. Am. Chem. Soc.*, 2018, **140**, 10695; (q) T. M. Monos, R. C. McAtee and C. R. J. Stephenson, *Science*, 2018, **361**, 1369; (r) X. Bao, T. Yokoe, T. M. Ha, Q. Wang and J. Zhu, *Nat. Commun.*, 2018, **9**, 3725; (s) S. N. Gockel, T. L. Buchanan and K. L. Hull, *J. Am. Chem. Soc.*, 2018, **140**, 58; (t) H. Xiao, H. Shen, L. Zhu and C. Li, *J. Am. Chem. Soc.*, 2019, **141**, 11440; (u) Y. Moon, B. Park, I. Kim, G. Kang, S. Shin, D. Kang, M.-H. Baik and S. Hong, *Nat. Commun.*, 2019, **10**, 4117; (v) H. Jiang, G. Seidler and A. Studer, *Angew. Chem., Int. Ed.*, 2019, **58**, 16528; (w) H. Jiang, X. Yu, C. G. Daniliuc and A. Studer, *Angew. Chem., Int. Ed.*, 2021, **60**, 14399.
- 5 For transition metals-catalyzed 1,4-carboamination of 1,3-dienes, see: (a) B. A. Patel, J. E. Dickerson and R. F. Heck, *J. Org. Chem.*, 1978, **43**, 5018; (b) B. A. Patel, L.-C. Kao,



- N. A. Cortese, J. V. Minkiewicz and R. F. Heck, *J. Org. Chem.*, 1979, **44**, 918; (c) J. M. O'Connor, B. J. Stallman, W. G. Clark, A. Y. L. Shu, R. E. Spada, T. M. Stevenson and H. A. Dieck, *J. Org. Chem.*, 1983, **48**, 807; (d) H. Bao, L. Bayeh and U. K. Tambar, *Chem. Sci.*, 2014, **5**, 4863; (e) T. Pinkert, T. Wegner, S. Mondal and F. Glorius, *Angew. Chem., Int. Ed.*, 2019, **58**, 15041.
- 6 For selected reviews and book on photochemistry, see: (a) J. M. R. Narayanam and C. R. J. Stephenson, *Chem. Soc. Rev.*, 2011, **40**, 102; (b) J. Xuan and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 6828; (c) C. K. Prier, D. A. Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322; (d) K. L. Skubi, T. R. Blum and T. P. Yoon, *Chem. Rev.*, 2016, **116**, 10035; (e) M. Silvi and P. Melchiorre, *Nature*, 2018, **554**, 41; (f) C. R. J. Stephenson, T. Yoon and D. W. C. MacMillan, *Visible Light Photocatalysis in Organic Chemistry*, Wiley-VCH, Weinheim, 2018.
- 7 For stepwise dearomative 1,4-carboaminations, see: (a) M. Okumura, A. S. Shved and D. Sarlah, *J. Am. Chem. Soc.*, 2017, **139**, 17787; (b) C. Tang, M. Okumura, Y. Zhu, A. R. Hooper, Y.-H. Lee and D. Sarlah, *Angew. Chem., Int. Ed.*, 2019, **58**, 10245.
- 8 H.-M. Huang, M. Koy, E. Serrano, P. M. Pflüger, J. L. Schwarz and F. Glorius, *Nat. Catal.*, 2020, **3**, 393.
- 9 (a) H.-M. Huang, P. Bellotti, P. M. Pflüger, J. L. Schwarz, B. Heidrich and F. Glorius, *J. Am. Chem. Soc.*, 2020, **142**, 10173; (b) P. Bellotti, M. Koy, C. Gutheil, S. Heuvel and F. Glorius, *Chem. Sci.*, 2021, **12**, 1810; (c) H.-M. Huang, P. Bellotti, S. Kim, X. Zhang and F. Glorius, *Nat. Synth.*, 2022, **1**, 464; (d) Z.-L. Liu, Z.-P. Ye, Y.-X. Chen, Y. Zheng, Z.-Z. Xie, J.-P. Guan, J.-A. Xiao, K. Chen, H.-Y. Xiang and H. Yang, *Org. Lett.*, 2022, **24**, 924; (e) C. Fu, Z. Zhang, Y. Li, D. Gao, Z.-N. Cui and Z. Li, *Chem. Commun.*, 2022, **58**, 5614.
- 10 For selected reviews on energy transfer catalysis, see: (a) F. Strieth-Kalthoff, M. J. James, M. Teders, L. Pitzer and F. Glorius, *Chem. Soc. Rev.*, 2018, **47**, 7190; (b) Q.-Q. Zhou, Y.-Q. Zou, L.-Q. Lu and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2019, **58**, 1586; (c) F. Strieth-Kalthoff and F. Glorius, *Chem.*, 2020, **6**, 1888.
- 11 P. Spiteller, *Amino acids, peptides and proteins in organic chemistry*, Wiley-VCH, Weinheim, 2009.
- 12 H.-M. Huang, P. Bellotti, J. Ma, T. Dalton and F. Glorius, *Nat. Rev. Chem.*, 2021, **5**, 301.
- 13 T. Patra, P. Bellotti, F. Strieth-Kalthoff and F. Glorius, *Angew. Chem., Int. Ed.*, 2020, **59**, 3172.
- 14 G. Tan, M. Das, H. Keum, P. Bellotti, C. Daniliuc and F. Glorius, *Nat. Chem.*, 2022, **14**, 1174.
- 15 (a) P.-J. Xia, F. Liu, Y.-M. Pan, M.-P. Yang and Y.-Y. Yang, *Org. Chem. Front.*, 2022, **9**, 2522; (b) X. Wang, Y. Chen, P. Liang, J.-Q. Chen and J. Wu, *Org. Chem. Front.*, 2022, **9**, 4328; (c) J. Majhi, R. K. Dhungana, Á. Rentería-Gómez, M. Sharique, L. Li, W. Dong, O. Gutierrez and G. A. Molander, *J. Am. Chem. Soc.*, 2022, **144**, 15871.
- 16 L. Pitzer, F. Schäfers and F. Glorius, *Angew. Chem., Int. Ed.*, 2019, **58**, 8572.
- 17 For reviews on PRE effect, see: (a) H. Fische, *Chem. Rev.*, 2001, **101**, 3581; (b) D. Leifert and A. Studer, *Angew. Chem., Int. Ed.*, 2020, **59**, 74.
- 18 G. Tan, F. Paulus, Á. Rentería-Gómez, R. F. Lalisce, C. G. Daniliuc, O. Gutierrez and F. Glorius, *J. Am. Chem. Soc.*, 2022, **144**, 21664.
- 19 T. Gensch, M. Teders and F. Glorius, *J. Org. Chem.*, 2017, **82**, 9154.
- 20 CCDC 2207448 (19)[†]
- 21 (a) N. Rodríguez and L. J. Goossen, *Chem. Soc. Rev.*, 2011, **40**, 5030; (b) C. P. Johnston, R. T. Smith, S. Allmendinger and D. W. C. MacMillan, *Nature*, 2016, **536**, 322; (c) T. Qin, J. Cornella, C. Li, L. R. Malins, J. T. Edwards, S. Kawamura, B. D. Maxwell, M. D. Eastgate and P. S. Baran, *Science*, 2016, **352**, 801.

