Chemical Science

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: H. Fu, Z. Wang, S. Li, L. Zhu, X. Wang, H. Wang and B. Han, *Chem. Sci.*, 2025, DOI: 10.1039/D4SC08607D.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemical-science

COMMUNICATION

View Article Online
DOI: 10.1039/D4SC08607D

Journal Name COMMUNICATION

Photocatalytic 1,3-Difluoroalkylcarboxylation of Alkenes by Triple Kinetic-Controlled Radical Self-Ordering

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Hong Fu, Zuo-Shuai Wang, Si-Jia Li, Lin-Yuan Zhu, Xiao-Jian Wang, Hong-Chen Wang, and Bing Han*

A transition metal-free protocol for the unsymmetrical radical 1,3-difunctionalization of alkenes has been established for the first time in the form of 1,3-difluoroalkylcarboxylation by a photocatalytic radical three-component reaction of allyl formates, trifluoroacetanilides, and cesium formate. This reaction employs formate as the carboxylating reagent and trifluoroacetanilide as the difluoroalkylating reagent via C-F bond activation. As a result, a series of previously inaccessible unsymmetrical difluorinated adipic acid derivatives can be easily and efficient prepared. Mechanism studies reveal that a triple-kinetic controlled radical self-ordering is the key core for this unique reaction. This radical sorting involves fast initiation of CO_2 radical anion and its chemoselective addition and reduction, followed by the slow generation of fluoroalkyl radical and its chemo-/regioselective addition. Notably, this strategy is also suitable for the 1,3-difluoroalkylcarboxylation of unsymmetrical and cyclic alkenes by diastereoselectively constructing two or three consecutive stereocenters.

As a common chemical with a wide range of sources, the diverse conversion of olefin provides a convenient and practical way to obtain high value-added functional molecules. Among them, 1,2-difunctionalization is the one of most representative modes, which affords a convenient method for simultaneously introducing two functional groups and has received extensive attention.[1] Both symmetrical and unsymmetrical 1,2-difunctionalization have been fully developed by introducing two identical and different functional groups, respectively (Scheme 1A).[2,3] Recently, the 1,3-difunctionalization of olefin has gradually become a hot research topic because it provides a facile method to obtain useful 1,3-difunctionalized moiety by an unusual remote functionalization of alkene (Scheme 1B).[4] Several practical strategies have been established, which can be divided to 2-electron and 1-electron processes. Transition metal-hydride intermediates mediated olefin positional isomerization is the dominant method of the former, while the precious metal Pd and the coinage metal Ni have proven to be the most effective catalysts in the conversions.[5] A metal-free 2e process is also developed by using high-valence iodine as the oxidizing reagent, which undergoes ionic rearrangement facilitated by $I^{(III)}$, leading to 1,3-difluorination of olefins.[6] On the other hand, with the emergence of more and more efficient and controllable radical initiation methods, olefin 1,3-difunctionalization involving the 1-electron process has been gradually developed. An elegant approach is to use radical 1,2-functional group (FG) migration as a key link to realize a variant 1,3-difunctionalization in the form of 1,2,3-trifunctionalization.[7] Some successful cases employ the 1,2-boron,[7a] 1,2-acyl,[7b-d] and 1,2-aryl[7e] migrations, respectively. In addition, the radical addition/elimination/re-addition (AERA) strategy has also proven to be a promising protocol.[8] Consequently, some symmetric 1,3-difunctionalizations are realized, such as dicarboxylation,[8a] difluroalkyllation,[8b] diaminoalkylation[8c] and diphosphination.[8d] Although these approaches enrich the profile of olefin 1,3-difunctionalization, most are limited to symmetrical pattern, while the unsymmetrical, especially for the 1e-process, is still an unrealized goal.

Since the radical AERA strategy affords a viable method for the symmetrical 1,3-difunctinalization, it is expected to be applied to an unsymmetrical way as well. Despite this anticipation, it faces a formidable challenge that the process is bound to involve the multiple competitive reactions due to two different radicals would be employed. These competitions appear as the disordered radical addition of two radicals with substrate alkenes and the derived alkene intermediates as well as the undesired radical cross-coupling.[9] Thus, both symmetrical and unsymmetrical 1,3-difunctionalizations and the unwanted cross-coupled adducts would be produce as a complex mixture. To obtain the desired 1,3-unsymmetrical product while avoiding the formation of other byproducts, a hypothesis of triple kinetic-controlled process was proposed, which depends on several factors (Scheme 1C). First, a significant rate difference is necessary for the generation of two kinds of radicals to be

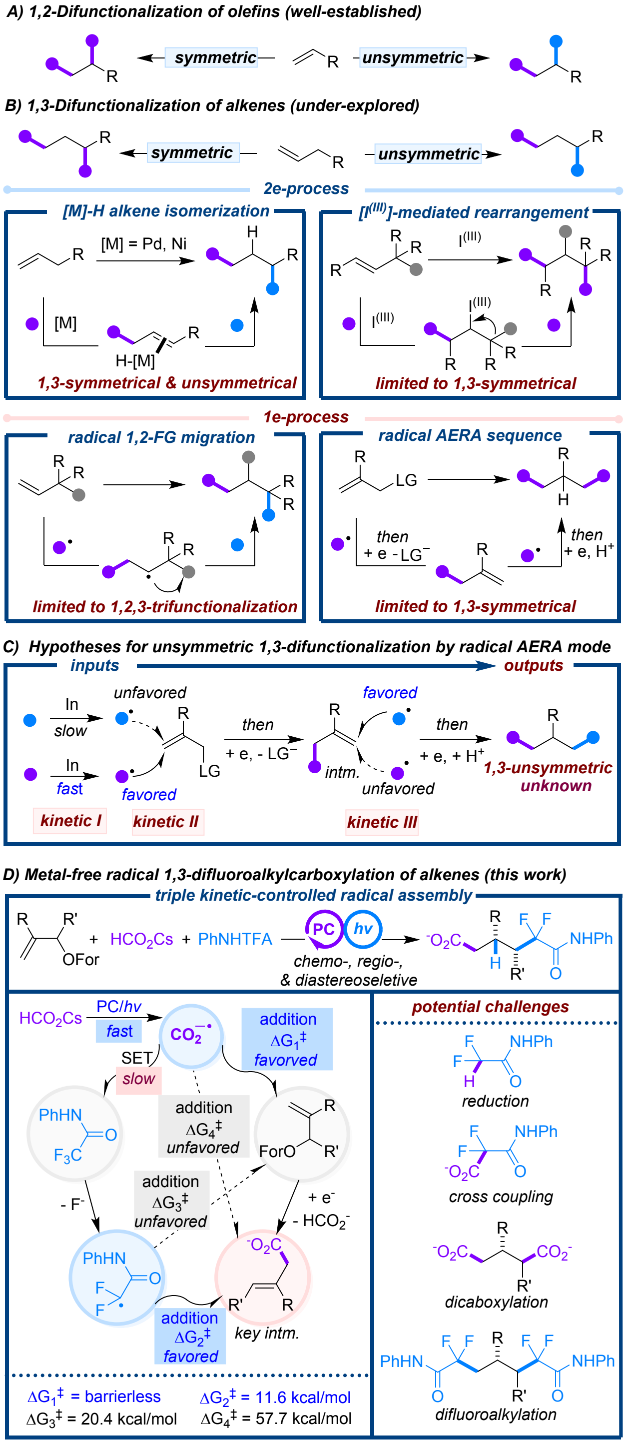
---

* State Key Laboratory of Applied Organic Chemistry (SKLAOC), College of Chemistry and Chemical Engineering, Lanzhou University, 222 South Tianshui Road, Lanzhou, 730000, People's Republic of China, Email: hanb@lzu.edu.cn

† Footnotes relating to the title and/or authors should appear here.

Supplementary Information available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/D4SC08607D



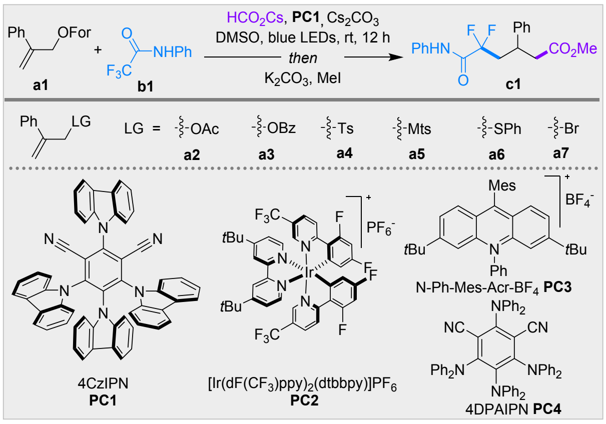
Scheme 1. 1,3-Didunctionalization of olefins

introduced (kinetic I). Secondly, the radical species produced first should have a faster addition rate than another radical species formed slowly to the substrate alkene in order to form a single intermediate alkene (kinetic II). Thirdly, the slowly formed radical should have the kinetic selectivity of preferential addition to the derived intermediate alkene rather than the substrate alkene (kinetic III). Finally, the cross coupling between these two radicals should be much slower than their addition to the corresponding alkenes.

Herein, we realize the hypothesis in the form of radical 1,3-difluoroalkylcarboxylation of olefins by a photocatalytic three-component reaction of allyl formates, trifluoroacetanilides, and cesium formate (Scheme 1D). To the best of our knowledge, this protocol represents the first successful example for the unsymmetrical 1,3-difunctionalization under the 1e-process. This approach initiates from the photocatalytic oxidation of formate to generate carbon dioxide radical anion ($CO_2^{\cdot-}$),[10] which preferentially reacts with allyl formates by fast radical addition. The nascent tertiary radical would be converted to the key intermediate but-3-enoate by subsequent reduction and further elimination of formate anion.[11,8b] With the consumption of allyl formate and the accumulation of but-3-enoate, $CO_2^{-\bullet}$ begins to reduce trifluoroacetanilide to difluoroacetanilide radical by C-F bond activation.[12] The latter preferentially adds onto but-3-enoate rather than allyl formate by taking advantage of kinetic rate difference. Finally, the radical 1,3-difluoroalkylcarboxylation is achieved by such a triple kinetic amplification process. As a result, a series of previously inaccessible unsymmetrical difluorinated adipic acid derivatives are easily prepared by this convenient photocatalytic multi-component reaction. Adipic acid derivatives are very useful structural units and play important roles in organic synthesis and polymerization.[13] In this context, this protocol not only successfully extends the radical AERA sequence to olefin 1,3-unsymmetrical difunctionalization, but also provides a simple method toward to such significant moieties.

The study was commenced by stirring allyl formate **a1**, trifluoroacetanilide **b1**, cesium formate, cesium carbonate in dimethylsulfoxide (DMSO) under the irradiation of blue LEDs (425 nm, 30 W) at room temperature under argon atmosphere. When 4CzIPN was used as the photocatalyst, the 1,3-difluoroalklcarboxylation took place smoothly and gave the desired product **c1** in 60% yield (entry 1). Formate was proved to be the best leaving group (LG) since when **a2**-**a7** containing groups such as OAc, OBz, Ts, trimethylphenylsulphonyl (Mts), thiophenyl, and Br were tested, the reaction gave unsatisfactory yields (entries 2-4).[14] When sodium formate was used instead of cesium formate as the reactant and reductant, the reaction yield was reduced to 41% (entry 5). Cesium carbonate was essential for an efficient reaction as the yield of **c1** dropped dramatically in the absence of it (entry 6). When DMF was used instead of DMSO, **c1** was only obtained in 28% yield (entry 7). Other photocatalysts such as $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (**PC2**), *N*-Ph-Mes-Acr-BF_4 (**PC3**), and 4DPAIPN (**PC4**) were also tested, but they were ineffective except for **PC4** which provided **c1** in 52% yield (entries 8-10). The usage amount of **b1** also influenced the reaction efficiency as when its amount was decreased to 3 equiv. and 1.5 equiv., the yield of **c1** was reduced to 51% and 23%, respectively (entries 11 and 12). In addition, the yield of **c1** could be slightly increased to 68% when the reaction was performed under CO_2 atmosphere (entry 13), whereas no reaction took place when the reaction was conducted under CO_2 atmosphere without the addition of cesium formate (entry 14), implying that cesium formate is crucial for an efficient reaction and CO_2 atmosphere is only conducive to promoting the reaction but was not a decisive factor. Notably, no reaction occurred when the reaction performed without **PC1** or without light irradiation (entries 15 and 16).

Table 1. Optimization of the Reaction Conditions



entry	variation of conditions [a]	yield [b]
1	None	60%
2	**a2** instead of **a1**	23%
3	**a3**, **a4**, **a6**, **a7** instead of **a1**	<10%
4	**a5** instead of **a1**	26%
5	HCO_2Na instead of HCO_2Cs	41%
6	without Cs_2CO3	45%
7	DMF instead of DMSO	28%
8	**PC2** instead of **PC1**	Trace
9	**PC3** instead of **PC1**	Trace
10	**PC4** instead of **PC1**	52%
11	3 eq of **b1**	51%
12	1.5 eq of **b1**	23%
13	**under CO_2 atmosphere**	**68%**
14	CO_2 atmosphere instead of HCO_2Cs	NR
15	without **PC1**	NR
16	in dark	NR

[a]Reaction conditions: **a1** (0.2 mmol, 1 eq), **b1** (4 eq), HCO_2Cs (2 eq), Cs_2CO_3(0.5 eq), 4CzIPN (**PC1**, 2 mol %), DMSO (3 mL), Ar, blue LEDs (425 nm, 30 W), rt, 12 h; then MeI (0.3 mL) and K_2CO_3 (1.0 mmol), rt, 4 h. [b] Isolated yield.

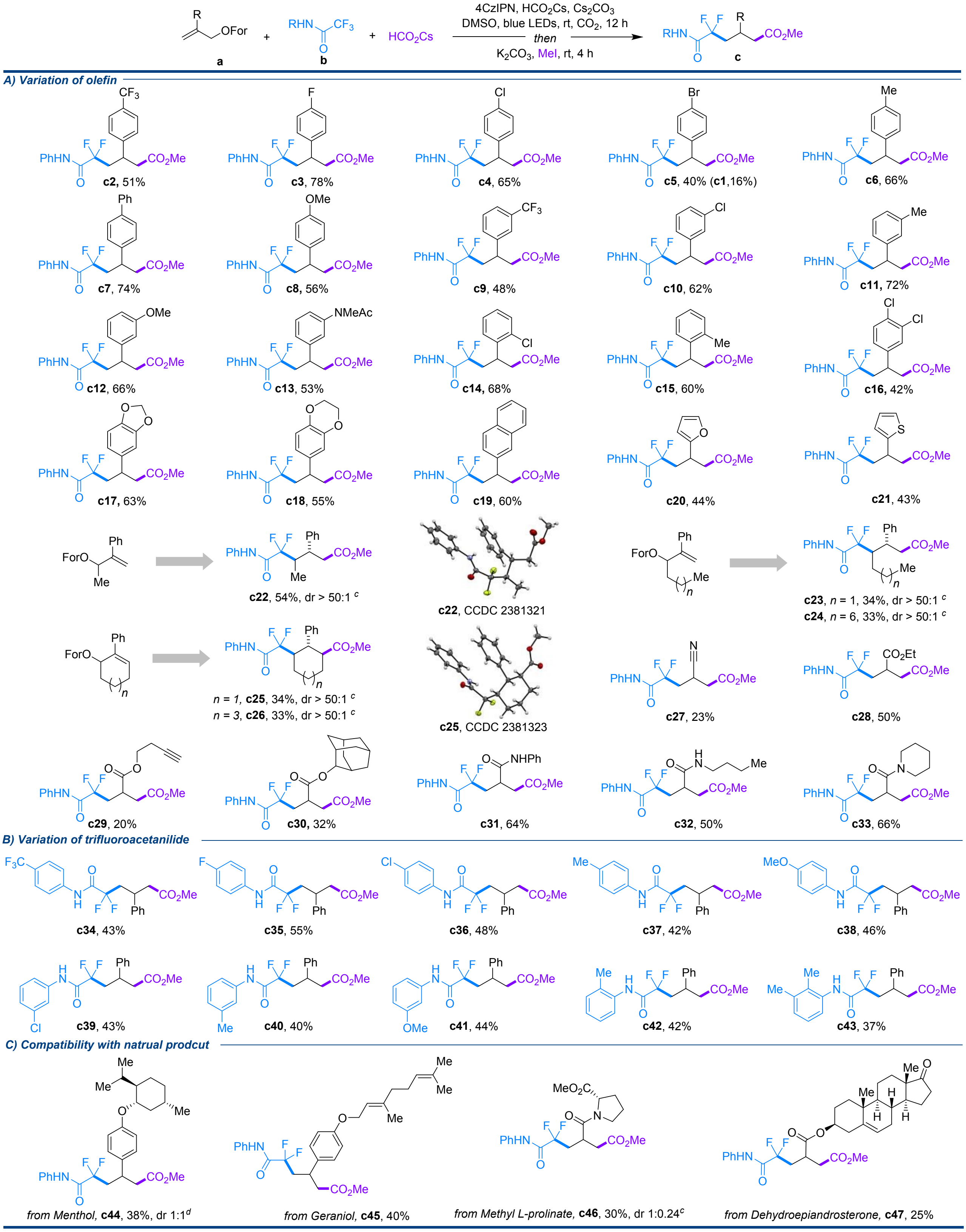
With the optimal conditions in hand (entry 13 in Table 1), the reaction scope was explored and the results are shown in Scheme 2. Allyl formate was first investigated (Scheme 2A). 2-Phenylallyl formates bearing para-substituents with a wide range of electronic properties such as trifluoromethyl, fluorine, chlorine, bromine, methyl, phenyl, and methoxy were all converted smoothly in the reaction, providing the desired products **c2**-**c8** in good yields. Among them, when *para*-bromophenyl incorporated allyl formates was involved in the reaction, besides the normal product **c5** was obtained in 40% yield, **c1** was also formed in 16% yield. Apparently, the reason for **c1** formation can be attributed to the fact that **c5** is prone to further reductive debromination under the conditions.[15] In addition, *meta*-substituted 2-phenylallyl formates bearing electron-deficient or electron-donating groups such as trifluoromethyl, chlorine, methyl, methoxy, acetamido on the phenyl ring exhibited good compatibility with the protocol, delivering products **c9**-**c13** in moderate to good yields. Similarly, this approach was also suitable for *ortho*-substituted phenyl counterpart, as demonstrated in the cases **c14** and **c15**, producing the corresponding products in good yields. Notably, olefin containing disubstituted phenyl moieties such as 2,3-dichlorophenyl, 3,4-piperonyl, 3,4-ethylenedioxyphenyl were also good candidates for the transformation, affording products **c16**-**c18** in good yields. Besides phenyl, other aromatics and heteroaromatics such as naphthalene, furan and thiophene incorporated olefins were also well tolerated in the tactic, giving **c19**-**c21** in moderate yields. Significantly, when unsymmetrical alkenes with different chain lengths were subjected to the reaction, the regio- and diastereoselective 1,3-difluoroalkylcarboxylation took place smoothly as well, providing products **c22**-**c24** in moderate yields as a single diastereomer. The structure and the *anti*-configuration of **c22** were confirmed by the X-ray diffraction study. The excellent regioselectivity of the unsymmetrical olefin indicates that the addition of $CO_2^{-\bullet}$ rather than difluoroalkyl radical onto allyl formate is the priority step. In addition, cyclic alkenes such as cyclohexene and cyclooctene incorporated allyl formates were also suitable for this protocol. By regio- and diastereoselective processes, **c25** and **c26** were produced as a single diastereomer with three continuous chiral centers in 34% and 33% yields, respectively. The structure and the adjacent *trans*-configuration of continuous three stereocenters of **c25** were also confirmed by the X-ray diffraction study. It is noteworthy that when the aromatic ring moiety of allyl formates was replaced by electron deficient groups such as cyano, esters and amides, the reaction was also converted smoothly and provided the corresponding products **c27**-**c33** in moderate to good yields. The functional group tolerance of this approach is also fully demonstrated by the incorporation of functional groups such as ester, amides, and alkyne into the allyl moiety.

Next, the scope of the trifluoroacetamides was tested as shown in Scheme 2B. *N*-Phenylamides containing *para*-substituents with a variety of electronic properties such as CF_3, F, Cl, Me, MeO were all suitable for the conversion, providing the corresponding products **c34**-**c38** in moderate yields. In addition, *N*-phenylamides containing *meta*-/*ortho*-substituents were also good partner for this method, as illustrated in cases **c39**-**c43**. To investigate the compatibility of the protocol for complex skeleton, some allyl formates containing natural products such terpene, amino acid, and steroid were tested in the approach as well. As illustrated in Scheme 2C, scaffolds of menthol, geraniol, *L*-proline, and dehydroepiandrosterone were all compatible in the reaction, producing the corresponding products **c44**-**c47** in moderate yields.

To further prove the practicability of this strategy, a gram-scale preparation reaction was conducted as shown in Scheme 3. When the reaction was carried out on 6 mmol scale of **a1**, the reaction also successfully proceeded and gave the product **c1** in 1.19 g with 57% yields. The usefulness of the product was also demonstrated by the subsequent

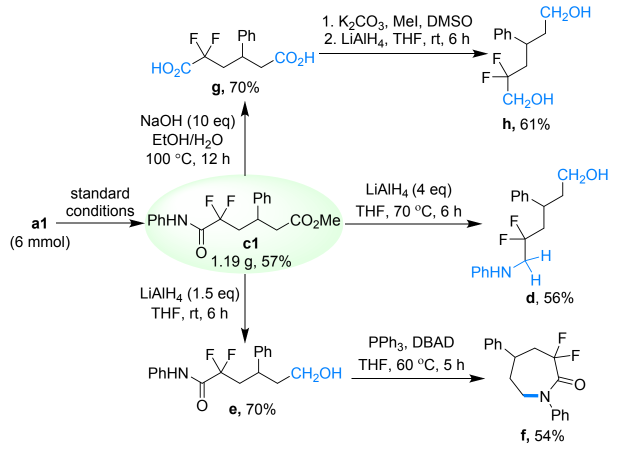
View Article Online
DOI: 10.1039/D4SC08607D

Scheme 2. Exploration of Substrate Scope [a, b]



[a] Reaction conditions: **a** (0.2 mmol, 1 eq), **b** (4 eq), HCO_2Cs (2 eq), Cs_2CO_3(0.5 eq), 4CzIPN (2 mol %), DMSO (3 mL), CO_2 (1 atm), blue LEDs (425 nm, 30 W), rt, 12 h; then MeI (0.3 mL), K_2CO_3 (2.0 mmol), rt, 4 h. [b] Isolated yield. [c] The diastereomer ratio was determined by ^1H NMR. [d] The diastereomer ratio was determined by ^{19}F NMR.

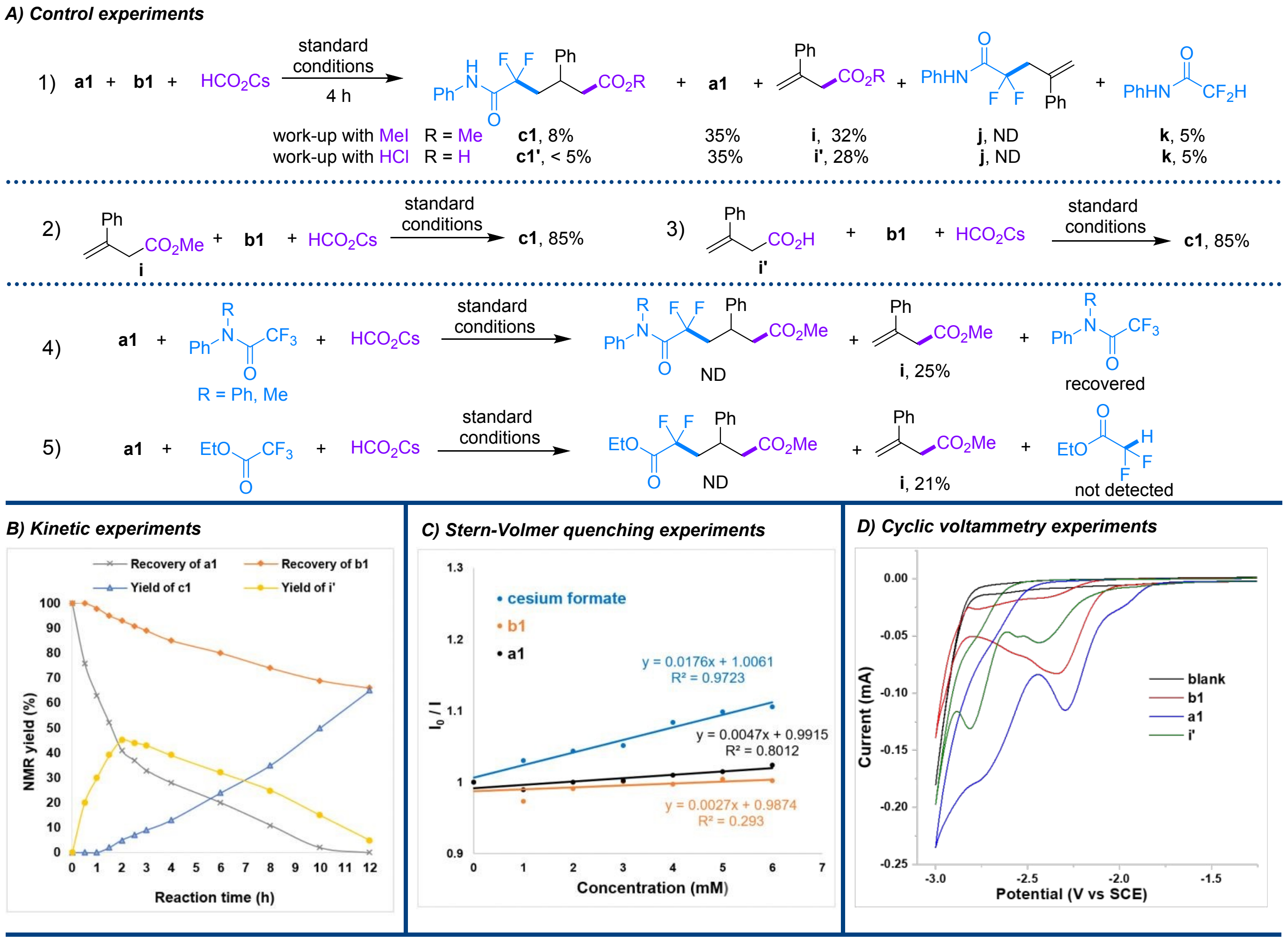
View Article Online
DOI: 10.1039/D4SC08607D



Scheme 3. Gram-scale synthesis and follow-up conversions

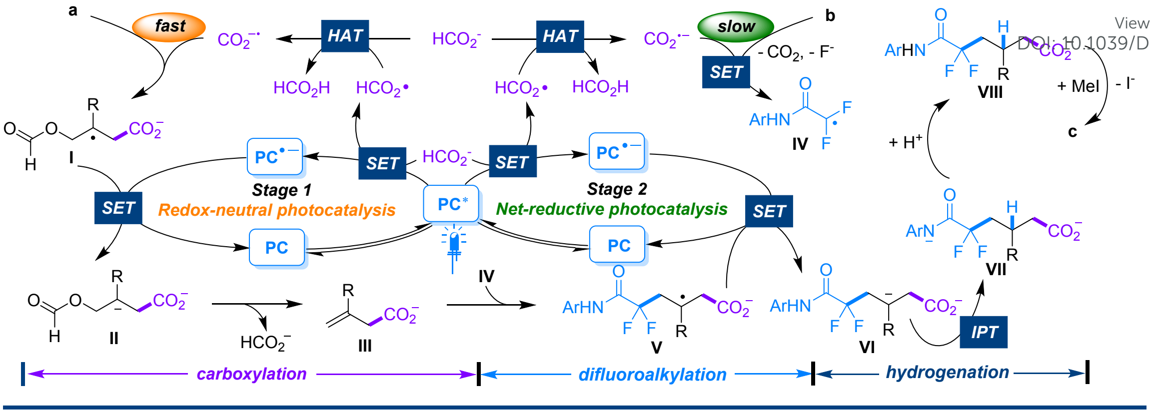
derivatization to provide some difluoro-containing key intermediates as shown in Scheme 3. When **c1** was treated with different amounts of $LiAlH_4$ under room temperature or heating, the gradient reduction of **c1** could be easily achieved by generating fully and partially reductive deoxygenation products **d** and **e** in 56% and 70% yields, respectively. The latter could be further converted to *α*, *α*-difluoro-*N*-phenylcaprolactam **f** in 54% yield under Mitsunobu reaction conditions. Hydrolysis of **c1** under basic conditions gave *α*, *α*-difluoro-adipic acid **g** in 70% yield, which could be further reduced to *α*, *α*-difluorohexanediol **h** in 61% yields.

To further understand the mechanism of this reaction, control experiments, fluorescence quenching experiments and kinetic experiments were performed as shown in Scheme 4. When the sample reaction time was shortened to 4 hours under the standard conditions, **c1** was obtained in only 8% yield and **a1** was recovered in 35% yield, accompanied by the formation of methyl but-3-enoate **i** and difluoroacetanilide **k** in 32% and 5% yields, respectively (Scheme 4A-1). In addition, when the aforementioned reaction was treated with HCl as the work-up process, the corresponding but-3-enoic acid **i'** was also obtained in 28% yield. By treating ester **i** or acid **i'** with **b1** under the standard conditions, the desired product **c1** was obtained in 85% yield in both reactions (Scheme 4A-2 and 3). Apparently, but-3-enoate is the key intermediate of the reaction, which is produced by the fast addition of the generated $CO_2^{-\bullet}$ onto allyl formate. In addition, the formation of a tiny amount of **k** and **c1** also implies that fluoroalkyl radical is slowly produced and preferred to add onto the intermediate alkene but-3-enoate rather than to add allyl formate. This view is also confirmed by the undetection of another possible intermediate **j**. However,



Scheme 4. Mechanistic studies

View Article Online
DOI: 10.1039/D4SC08607D



Scheme 5. Proposed mechanism.

when ethyl trifluoroacetate and *N,N*-disubstituted trifluoroacetanilide were were used instead of **b1** for the reaction under standard conditions, they were totally recovered and only the intermediate i was obtained (Scheme 4A-4 and 5). These results suggest that the N-H moiety of **b** is critical for the reaction as it is probably involved in the spin-centre shift promoted reductive defluorination of trifluoroacetanilide[12] and final intramolecular proton transfer.[16] Apparently, such a triple kinetic-controlled reaction is crucial for the efficient unsymmetrical 1,3-difunctionalization, which is also confirmed by the reaction rate curves as illustrated in Scheme 4B. Moreover, the fluorescence quenching experiments showed that the excited **PC1*** could be significantly quenched by cesium formate but be hardly quenched by **a1** and **b1** (Scheme 4C). These results not only indicate that the reaction begins from the photoredox of formate by the excited state of **PC1**, but also verifies that $CO_2^{-\bullet}$ is produced first in the reaction. Different from Yu's strategy of in-situ formed formate as carboxylation reagent derived from the reduction of CO_2 by sacrificing equivalent Ph_3SiH[7e], formate is used directly as the carboxylation regent as well as the reductant in this study. Despite cyclic voltammogram illustrated in Scheme 4D imply that **a1** ($E_{1/2}$ = -2.13 V vs SCE) could also be continuously reduced by $CO_2^{-\bullet}$ ($E_{1/2}$ = -2.2 V vs SCE) to allylic carbanion to further add to CO_2 to form the key intermediate but-3-enoate (see SI for a possible alternative path), this process is obviously not a significant path because, just as shown in Entry 1 of Table 1, the reaction could also occur efficiently without CO_2. This result indicates that the formation of but-3-enoate is more like to experience the addition of $CO_2^{-\bullet}$ to allylic formate rather than to be reduced by it. In addition, the obtained reductive potentials of **b1** ($E_{1/2}$ = -2.18 V vs SCE) and but-3-enoate ($E_{1/2}$ = -2.30 V vs SCE) suggest that the former could be indeed reduced by $CO_2^{-\bullet}$ whereas the reduction of the latter looks not easy. In addition, DFT (density functional theory) calculation results also confirm the proposed kinetic-controlled process as the addition of $CO_2^{-\bullet}$ onto allyl formates is barrierless, but its addition onto the intermediate but-3-enoate is a very difficult process with an extremely high energy barrier of 57.7 kcal/mol. On the contrary, the addition of fluoroalkyl radical onto but-3-enoate is favorable and only needs to cross an energy barrier of 11.6 kcal/mol, while its addition onto allyl formates is unfavorable and needs to across an energy barrier of 20.4 kcal/mol (See SI for DFT calculation in detail).

Based on our experimental observations and previous literature reports,[16,17,8b] Scheme 5 illustrates a plausible mechanism involving a two-stage photocatalytic cycle. The reaction is initiated by a photooxidation of formate ($E_{1/2}$ = +0.93 V vs SCE for HCO_2^-/ $HCO_2^\bullet$)[10c] by the excited **PC1*** ($E_{1/2}$ = +1.35 V vs SCE for $PC^*/PC^{-\bullet}$)[18] to produce $PC^{-\bullet}$ and formoxyl radical by a single-electron transfer (SET) process. A hydrogen atom transfer (HAT) between formoxyl radical and formate would form formic acid and $CO_2^{-\bullet}$. The latter adds rapidly onto the substrate **a** by a barrierless process to provide the radical intermediate **I**. **I** would be further reduced by $PC^{-\bullet}$ to the carboanion intermediate **II**, which immediately eliminates formate by C-O bond cleavage to yield the intermediate **III** accompanied by the regeneration of PC (Stage 1). On the other hand, with the consumption of substrate **a** and the accumulation of the intermediate **III**, $CO_2^{-\bullet}$ begins to reduce substrate **b**. By a SET reduction and the subsequent defluorination-facilitated spin-centre transfer, **b** is converted to the radical **IV**. **IV** tends to add onto the key intermediate **III** to provide radical **V**, which is further reduced by $PC^{\bullet-}$ to give the intermediate **VI** (Stage 2). **VI** immediately undergoes intramolecular proton transfer (IPT) [16] from the tethered N-H to the carboanion center to form the intermediate **VII**, which subsequently abstracts a proton from the surroundings to yield the intermediate **VIII**. Finally, after treatment with MeI, **VIII** is methylated to produce the desired product **c**.

In summary, a transition-metal free protocol for the 1,3-difluoroalkylcarboxylation of alkenes has been established for the first time by a photocatalytic three-component reaction of allyl formates, trifluoroacetanilides, and cesium formate. This approach employs 4CzIPN as the cheap organic photocatalyst, formate as the carboxylating reagent, and trifluoroacetanilides as the difluoroalkylating reagent. Consequently, a series of structurally useful difluorinated adipic acid derivatives were efficiently produced. This chemistry represents the first successful example for the unsymmetrical 1,3-difunctionalization of alkenes under 1e-process as well as the first unsymmetrical extension for the radical AERA strategy. A triple-kinetic controlled radical self-ordering is the crucial core to the success of the protocol, which contains the sequential production of $CO_2^{-\bullet}$ and difluoromethylaniline radical and their chemo-/regioselective additions on alkenes. This strategy not only broadens the boundary of radical AERA strategy but also provides a new tactic for the unsymmetrical 1,3-difunctinalization of olefins. Other 1,3-unsymmetrical difunctionalization of olefins are being explored in our groups.

Data availability

The supporting information includes all experimental details, including synthesis and characterization of all starting materials and products reported in this study, and mechanistic studies. NMR spectra of all products reported are included as well.

Author contributions

B.H. and H.F. conceived and directed the project. H.F., S.L., L.Z., X.W. and H.W. performed experiments. H.F., S.L., L.Z. and X.W. prepared the Supplementary Information. Z.W. performed the DFT calculations and drafted the DFT parts. B.H. wrote the paper. All authors discussed the results and commented on the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We thank The National Natural Science Foundation of China (Nos. 22471109, 22171118, and 21873041) and The Science and Technology Major Program of Gansu Province of China (22ZD6FA006, 23ZDFA015, and 24ZD13FA017) for financial support.

Notes and references

1 For selected reviews, see: (a) H.-M. Huang, P. Bellotti, J. Ma, T. Dalton, F. Glorius, *Nat. Rev. Chem.*, 2021, **5**, 301–321; (b) H. Jiang, A. Studer, *Chem. Soc. Rev.*, 2020, **49**, 1790–1811; (c) L. M. Wickham, R. Giri, *Acc. Chem. Res.*, 2021, **54**, 3415– 3437; (d) S. Zhu, X. Zhao, H. Li, L. Chu, *Chem. Soc. Rev.*, 2021, **50**, 10836– 10856; (e) J. Derosa, O. Apolinar, T. Kang, V. T. Tran, K. M. Engle, *Chem. Sci.*, 2020, **11**, 4287–4296; (f) X. Bao, J. Li, W. Jiang, C. Huo, *Synthesis*, 2019, **51**, 4507–4530.

2 For selected works, see: (a) N. Fu, G. S. Sauer, S. Lin, *J. Am. Chem. Soc.*, 2017, **139**, 15548–15553; (b) Q. Wu, A. Roy, E. Irran, Z.-W. Qu, S. Grimme, H. F. T. Klare, M. Oestreich, *Angew. Chem. Int. Ed.*, 2019, **58**, 17307–17311; (c) B. Tian, P. Chen, X. Leng, G. Liu, *Nat. Catal.*, 2021, **4**, 172–179; (d) T. Ju, Y.-Q. Zhou, K.-G. Cao, Q. Fu, J.-H. Ye, G.-Q. Sun, X.-F. Liu, L. Chen, L.-L. Liao, D.-G. Yu, *Nat. Catal.*, 2021, **4**, 304–311; (e) L. Liu, M. C. Aguilera, W. Lee, C. R. Youshaw, M. L. Neidig, O. Gutierrez, *Science*, 2021, **374**, 432–439; (f) X. Hu, I. Cheng-Sánchez, W. Kong, G. A. Molander, C. Nevado, *Nat. Catal.*, 2024, **7**, 655–665; (g) J. Z. Wang, W. L. Lyon, D. W. C. MacMillan, *Nature*, 2024, **628**, 104–109;

3 Our work for difunctionalization of olefins. (a) S.-Q. Lai, B.-Y. Wei, J.-W. Wang, W. Yu, B. Han, *Angew. Chem. Int. Ed.*, 2021, **60**, 21997–22003; (b) D. Wei, T. Liu, Y. He, B. Wei, J. Pan, J. Zhang, N. Jiao, B. Han, *Angew. Chem. Int. Ed.*, 2021, **60**, 26308– 6313; (c) D.-T. Xie, H.-L. Chen, D. Wei, B.-Y. Wei, Z.-H. Li, J.-W. Zhang, W. Yu, B. Han, *Angew. Chem. Int. Ed.*, 2022, **61**, e202203398; (d) S.-P. Hu, C.-H. Gao, T.-M. Liu, B.-Y. Miao, H.-C. Wang, W. Yu, B. Han, *Angew. Chem. Int. Ed.*, 2024, **63**, e202400168.

4 (a) R. K. Dhungana, R. R. Sapkota, D. Niroula, R. Giri, *Chem. Sci.*, 2020, **11**, 9757–9774; (b) D.-K. Wang, L. Li, Q. Xu, J. Zhang, H. Zheng, W.-T. Wei, *Org. Chem. Front.*, 2021, **8**, 7037–7049; (c) X. Ma, Q. Zhang, W. Zhang, *Molecules*, 2023, **28**, 3027–3072.

5 (a) H. Sommer, F. Juliá-Hernández, R. Martin, I. Marek, *ACS Cent. Sci.*, 2018, **4**, 153– 165; (b) Y. Li, D. Wu, H. Cheng, G. Yin, *Angew. Chem. Int. Ed.*, 2020, **59**, 7990–8003; (c) H.-Y. Tu, S. Zhu, F.-L. Qing, L. Chu, *Synthesis*, 2020, **52**, 1346– 1356; (d) W. Li, J. K. Boon, Y. Zhao, *Chem. Sci.*, 2018, **9**, 600–607; (e) Z. Wu, J. Meng, H. Liu, Y. Li, X. Zhang, W. Zhang, *Nat. Chem.*, 2023, **15**, 988–997.

6 (a) H. A. Sharma, K. M. Mennie, E. E. Kwan, E. N. Jacobsen, *J. Am. Chem. Soc.*, 2020, **142**, 16090–16096; (b) A. C. Dean, E. H. Randle, A. J. D. Lacey, G. A. M. Giorio, S. Doobary, B. D. Cons, A. J. J. Lennox, *Angew. Chem. Int. Ed.*, 2024, **63**, e202404666.

7 (a) K. Jana, A. Bhunia, A. Studer, *Chem.*, 2020, **6**, 512–522; (b) R. Liu, Y. Tian, J. Wang, Z. Wang, X. Li, C. Zhao, R. Yao, S. Li, L. Yuan, J. Yang, D. Shi, *Sci. Adv.*, 2022, **8**, eabq8596.; (c) H.-Z. Xiao, B. Yu, S.-S. Yan, W. Zhang, X.-X. Li, Y. Bao, S.-P. Luo, J.-H. Ye, D.-G. Yu, *Chin. J. Catal.*, 2023, **50**, 222–228; (d) G. Zhao, S. Lim, D. G. Musaev, M.-Y. Ngai, *J. Am. Chem. Soc.*, 2023, **145**, 8275-8284. (e) H.-Z.Xiao, B. Yu, S.-S. Y, W.Z, X.-X. L, Y. B, S.-P. Luo, J.-H. Ye, D.-G. Yu, *Chin. J. Catal.*, 2023, **50**, 222–228.

8 (a) Z. Yao, G. Li, Y. Zhou, L. Xu, D. Xue, *Adv. Synth. Catal.*, 2023, **365**, 224–229; (b) B. Yu, Y. Liu, H.-Z. Xiao, S.-R. Zhang, C.-K. Ran, L. Song, Y.-X. Jiang, C.-F. Li, J.-H. Ye, D.-G. Yu, *Chem.*, 2024, **10**, 938–951; (c) X.-Y. Wang, P. Xu, W.-W. Liu, H.-Q. Jiang, S.-L. Zhu, D. Guo, X. Zhu, *Sci. China Chem.*, 2024, **67**, 368–373; (d) H. Xin, L. Zhang, J. Liao, X.-H. Duan, X. Yang, L.-N. Guo, *Org. Lett.*, 2024, **26**, 6030–6034; (e) J.-X. Yu, Y.-Y. Cheng, X.-Y. Zeng, B. Chen, C.-H. Tung, L.-Z. Wu, *Org. Lett.*, 2024, **26**, 6809–6813; (f) W. Shan, Z. Wang, C. Gao, X. Li, W. Zhuang, R. Liu, C. Shi, H. Qin, X. Li, D. Shi, *Green Chem.*, 2024, **26**, 9749–9756.

9 (a) M. Uno, S. Sumino, T. Fukuyama, M. Matsuura, Y. Kuroki, Y. Kishikawa, I. Ryu, *J. Org. Chem.*, 2019, **84**, 9330– 9338; (b) H. Li, S. Chiba, *Chem. Catal.*, 2022, **2**, 1128–1142; (c) E. L. Saux, M. Zanini, P. Melchiorre, *J. Am. Chem. Soc.*, 2022, **144**, 1113–1118.

10 (a) J. Majhi, G. A. Molander, *Angew. Chem. Int. Ed.*, 2024, **63**, e202311853; (b) W. Xiao, J. Zhang, J. Wu, *ACS Catal.* 2023, **13**, 15991–16011; (c) Y. Huang, J. Hou, L.-W. Zhan, Q. Zhang, W.-Y. Tang, B.-D.Li, *ACS Catal.*, 2021, **11**, 15004– 15012; (d) S. N. Alektiar, J. Han, Y. Dang, C. Z. Rubel, Z. K. Wickens, *J. Am. Chem. Soc.*, 2023, **145**, 10991–10997; (e) S. N. Alektiar, Z. K. Wickens, *J. Am. Chem. Soc.*, 2021, **143**, 13022–13028.

11 (a) W. Zhang, S. Lin, *J. Am. Chem. Soc.*, 2020, **142**, 20661–20670; (b) F.-L. Haut, R.S. Mega, J. V. Estornell, R. Martin, *Angew. Chem. Int. Ed* 2023, **62**, e202304084; (c) S. Senapati, S. K. Parida, S. S. Karandikar, S. Murarka, *Org. Lett.*, 2023, **25**, 7900–7905.

12 (a) Y.-J. Yu, F.-L. Zhang, T.-Y. Peng, C.-L. Wang, J. Cheng, C. Chen, K. N. Houk, Y.-F. Wang, *Science*, 2021, **371**, 1232– 1240; (b) S.-S. Yan, S.-H. Liu, L. Chen, Z.-Y. Bo, K. Jing, T.-Y. Gao, B. Yu, Y. Lan, S.-P. Luo, D.-G. Yu, *Chem.*, 2021, **7**, 3099–3113; (c) M. W. Campbell, V. C. Polites, S. Patel, J. E. Lipson, J. Majhi, G. A. Molander, *J. Am. Chem. Soc.*, 2021, **143**, 19648–19654; (d) J.-H. Ye, P. Bellotti, C. Heusel, F. Glorius, *Angew. Chem. Int. Ed.*, 2022, **61**, e202115456.

View Article Online
DOI: 10.1039/D4SC08607D

13 (a) Y. Wan, J.-M. Lee, *ACS Catal.*, 2021, **11**, 2524−2560; (b) J. Rios, J. Lebeau, T. Yang, S. Li, M. D. Lynch, *Green Chem.*, 2021, **23**, 3172−3190; (c) J. Yang, J. Liu, H. Neumann, R. Franke, R. Jackstell, M. Beller, *Science*, 2019, **366**, 1514–1517.
14 (a) J. Zhang, Y. Li, R. Xu, Y. Chen, *Angew. Chem. Int. Ed.*, 2017, **56**, 12619 –12623; (b) K. Sun, M. Ueno, K. Imaeda, K. Ueno, M. Sawamura, Y. Shimizu, *ACS Catal.*, 2021, **11**, 9722−9728; (c) Y. Zhou, Y. Qin, Q. Wang, Z. Zhang, G. Zhu, *Angew. Chem. Int. Ed.*, 2022, **61**, e202110864; (d) X. Chen, X. Luo, P. Wang, *Tetrahedron Lett.*, 2022, **91**, 153646.
15 (a) A. J. Boyington, C. P. Seath, A. M. Zearfoss, Z. Xu, N. T. Jui, *J. Am. Chem. Soc.*, 2019, **141**, 4147−4153; (b) A. F. Chmiel, O. P. Williams, C. P. Chernowsky, C. S. Yeung, Z. K. Wickens, *J. Am. Chem. Soc.*, 2021, **143**, 10882−10889; (c) C. M. Hendy, G. C. Smith, Z. Xu, T. Lian, N. T. Jui, *J. Am. Chem. Soc.*, 2021, **143**, 8987−8992.
16 P. Lei, B. Chen, T. Zhang, Q. Chen, L. Xuan, H. Wang, Q. Yan, W. Wang, J. Zeng, F. Chen, *Org. Chem. Front.*, 2024, **11**, 458−465.
17 (a) A. M. Vasquez, J. A. Jr. Gurak, C. L. Joe, E. C. Cherney, K. M. Engle, *J. Am. Chem. Soc.*, 2020, **142**, 10477−10484; (b) Z. Wu, S. N. Gockel, K. L. Hull, *Nat. Commun.*, 2021, **12**, 5956; (c) J.-T. Li, G. Fang, G.-Y. Wu, C.-X. Zhuo, *ACS Catal.*, 2023, **13**, 12648−12655.
18 Y. Liu, X.-L. Chen, X.-Y. Li, S.-S. Zhu, S.-J. Li, Y. Song, L.-B. Qu, B. Yu, *J. Am. Chem. Soc.* 2021, **143**, 964−972.

View Article Online
DOI: 10.1039/D4SC08607D

The supporting information includes all experimental details, including synthesis and characterization of all starting materials and products reported in this study, and mechanistic studies. NMR spectra of all products reported are included as well.