



Cite this: *Chem. Sci.*, 2022, 13, 7256

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

Received 22nd April 2022
Accepted 27th May 2022

DOI: 10.1039/d2sc02277j

rsc.li/chemical-science

Three-component carboacylation of alkenes via cooperative nickelphotoredox catalysis†

Dingyi Wang^a and Lutz Ackermann^{ID} *^{ab}

Various commercially available acyl chlorides, aldehydes, and alkanes were exploited for versatile three-component 1,2-carboacylations of alkenes to forge two vicinal C–C bonds through the cooperative action of nickel and sodium decatungstate catalysis. A wealth of ketones with high levels of structural complexity was rapidly obtained *via* direct functionalization of C(sp²)/C(sp³)–H bonds in a modular manner. Furthermore, a regioselective late-stage modification of natural products showcased the practical utility of the strategy, generally featuring high resource economy and ample substrate scope.

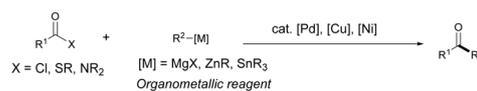
Introduction

Alkenes have found widespread applications for the rapid construction of diverse bioactive molecules and functionalized polymers.¹ In this context, alkene difunctionalization has undergone impressive progress during the last decade.^{2,3} Recently, cooperative nickelphotoredox catalysis has attracted increasing attention by installing two functional groups onto C=C double bonds to achieve the 1,2-difunctionalization of alkenes under mild reaction conditions, which was elegantly explored by Nevado,⁴ Molander,⁵ Aggarwal,⁶ Rueping,⁷ Martin,⁸ Studer,⁹ Koh¹⁰ among others.^{11,12} For instance, the groups of Kong¹³ and Molander^{5a} disclosed two elegant approaches for the carboacylation of alkenes through the activation of aliphatic C–H bonds *via* cooperative nickelphotoredox catalysis. Despite the indisputable advances, direct 1,2-carboacylations of alkenes for the preparation of ketones *via* nickelphotoredox catalysis is underdeveloped.

Alkene 1,2-difunctionalizations by means of the direct 1,2-carboacylation can access carbonyl compounds, which are prestigious structural motifs and represent important pharmacophores existing in many drug molecules such as ibuprofen, ketoprofen, and naproxen.¹⁴ Most of the traditional methods are based on preformed organometallic reagents, which are typically not compatible with electrophilic sensitive functional groups (Scheme 1A).¹⁵ Moreover, the multistep synthesis significantly decreases the efficiency and resource economy of these syntheses.¹⁶ Recently, efficient strategies have surfaced to achieve direct 1,2-carboacylations of alkenes,^{17,18} and especially, N-heterocyclic carbene (NHC)-catalyzed radical-

based 1,2-carboacylations of alkenes have witnessed major momentum (Scheme 1B).^{19,20} However, key synthesis challenges remain: (a) pre-activated alkyl and acyl substrates are required, which translate into the low atomic economy; (b) limited radical precursors including alkyl halides, redox-active esters and cyclobutanone oxime esters served as alkyl resources; (c)

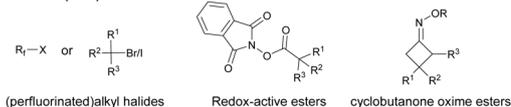
A) Transition-Metal-catalyzed Cross-Coupling with Acyl Electrophiles



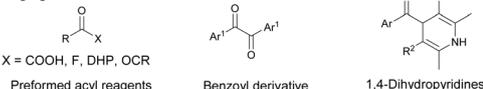
B) NHC-Catalyzed Carbocarbonylation of Alkenes



Radical source (R¹-X)



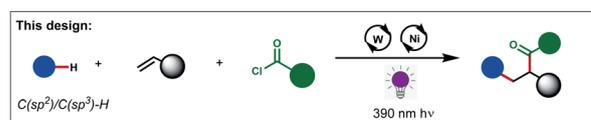
Acylating agents



Limitations:

- pre-activated alkyl substrates reduced atomic economy
- limited radical sources (perfluoroalkyl and tertiary alkyl groups)
- preparation of acyl reagents via multi-step synthesis

C) Ni/Photo-Cocatalyzed Carbocarbonylation via Direct Activation of C(sp²)/C(sp³)-H Bonds



- Excellent chemo- & regio-selectivity
- Commercially available, abundant materials
- Tertiary/secondary/primary radicals
- Modular access to diversified ketone derivatives

Scheme 1 Synthetic approaches to carbonyl compounds.

^aInstitut für Organische und Biomolekulare Chemie and Wöhler Research Institute for Sustainable Chemistry, Georg-August-Universität Göttingen, Tammannstraße 2, 37077 Göttingen, Germany. E-mail: Lutz.Ackermann@chemie.uni-goettingen.de

^bDZHK (German Centre for Cardiovascular Research), Germany

† Electronic supplementary information (ESI) available. See <https://doi.org/10.1039/d2sc02277j>



preformed complex acyl reagents are required. To overcome these major limitations, it is hence highly desirable to develop new, alternative strategies that provide efficient access to substituted carbonyl compounds. In this context, acyl chlorides and aldehydes are inexpensive, abundant and easily available commodity chemicals and can serve as suitable acyl sources for the direct transformation of alkenes.^{21,22} Their transformation in one single-step operation is appealing but challenging. In sharp contrast, we, herein, present a photochemical nickel-catalyzed approach for the preparation of functionalized carbonyl compounds, using acyl chlorides as acyl reagent to incorporate simultaneously and with excellent selectivity two different carbon fragments onto alkenes (Scheme 1C). This method exhibits broad substrate scope, it is compatible with carbonyl radicals from various aldehydes and with diverse tertiary/secondary/primary alkyl radicals, indeed contrasting with previous reports.

Results and discussion

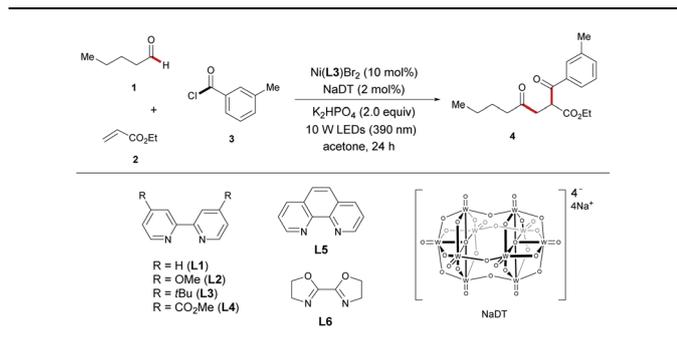
To identify the ideal reaction conditions for the envisioned carboacylation of alkenes reaction, we chose three commercial reagents, namely valeraldehyde (**1**), ethyl acrylate (**2**) and 3-methyl-benzoyl chloride (**3**), as the substrates (Table 1). After a careful investigation of all reaction parameters (more details see the ESI[†]), we arrived at the optimized conditions, involving

2 mol% sodium decatungstate (NaDT) and 10 mol% Ni(dtbbpy)Br₂, along with K₂HPO₄ as the base under blue LED (10 W) irradiation in acetone (0.2 M) at 30 °C for 24 h, furnishing the dicarbonylation product **4** in 71% isolated yield (Table 1, entry 1). Comparable photocatalyst tetrabutylammonium decatungstate (TBADT) resulted in a lower yield (entry 2). This result shows that ion pairing could be an important factor to modulate the reactivity in ionic photoredox catalysts.²³ Differently substituted 2,2'-bipyridines, such as ligands **L1**, **L2** or **L4**, led to dramatic erosions in yield (entry 3). In addition, employing phenanthroline (**L5**) or bisoxazole (**L6**) as ligand gave no conversion, showing that the backbone of the ligand had a great impact on the reactivity for the catalyst (entry 4). Replacing K₂HPO₄ with other bases, like K₃PO₄ or Na₂HPO₄, was found to be less efficient to the product yield (entries 5 and 6). Only small traces or even no products could be observed when the reaction was carried out using other solvents (entries 7–9). Reducing the amount of aldehyde from 5 equiv. to 4 equiv. had a little impact on the reaction outcome (entry 10). In addition, reducing alkene to 1 equiv. led to dramatic erosions in yield (entry 11). Control experiments confirmed that the alkene carbonylations did not occur without the nickel catalyst, the photocatalyst or light (entry 12).

After having established the optimized reaction conditions, we next assessed the generality of acyl chlorides **3** in this cooperative catalysis (Table 2). A wide range of acyl chlorides **3** reacted successfully, affording the 1,4-dicarbonyl compounds (**4**–**23**) in moderate yields. The cooperative catalysis was shown to be amenable for both electron-donating substituents such as methyl, methoxy and thiomethyl, as well as electron-withdrawing substituents, including trifluoromethyl, ester and cyano groups (**4**–**15**). Acyl chlorides with halogen groups in the *meta* or *para* position, including F, Cl, Br and chloromethyl, as well as various heteroaryl chlorides, were perfectly compatible, providing an opportunity for further late-stage transformations. Notably, dialkyl carbamoyl chloride like dimethylcarbamoyl chloride were tolerated as well (**24**). Under otherwise identical reaction conditions, aliphatic acyl chlorides failed thus far to deliver the three-component products.

Thereafter, we turned our attention to the reactivity of aldehydes **1** (Table 2). A variety of aliphatic aldehydes with different groups were hence probed, showing good reactivity to afford the desired products **25**–**30**. Interestingly, (hetero) aromatic aldehydes were also successfully transformed into the corresponding products **31**–**34**. Subsequently, we explored the generality of this dual metallaphotoredox for different alkene **2** types as reaction partners with aldehydes and acyl chlorides. A broad range of acrylates with different groups was examined. The different electronic and steric configurations of the ester group of alkenes also have shown good tolerance in this photocatalysis (**35**–**39**). Furthermore, it was demonstrated that our strategy was not only applicable to acrylates. Indeed, it also enabled difunctionalization of other electron-deficient olefins, including methyl vinyl ketone (**40**), acrylonitrile (**41**), *N*-methylmaleimide (**42**) and phenyl vinyl sulfone (**43**). In order to further demonstrate the potential of the dual catalysis, the complex acrylate derived from the natural hormone estrone was

Table 1 Optimization of reaction conditions^a

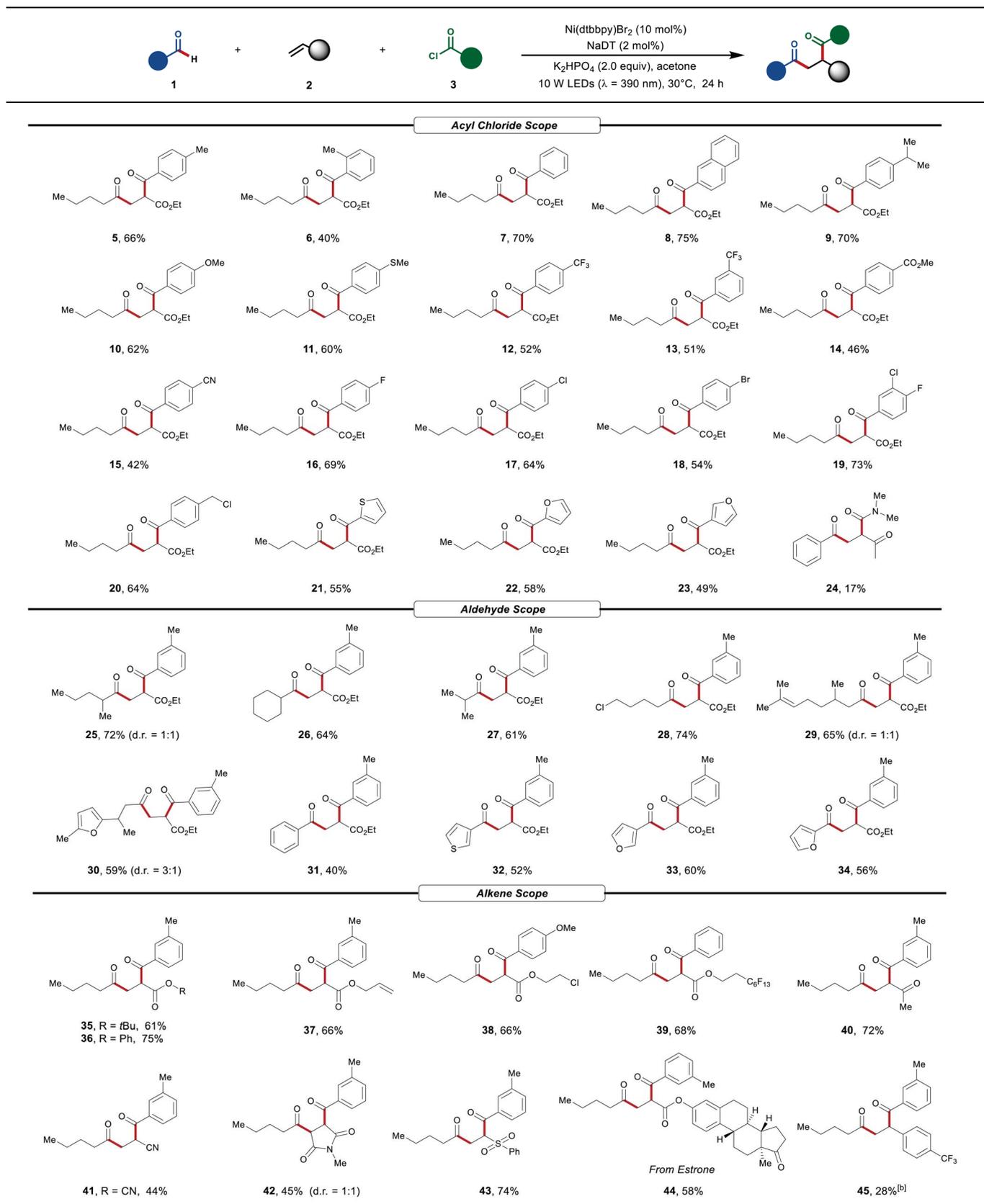


Entry	Variation from "standard conditions"	Yield ^b /[%] ^c
1	None	76 (71) ^c
2	TBADT instead of NaDT	59
3	L1 , L2 or L4 instead of L3	26, 36, 15
4	L5 or L6 instead of L3	0
5	K ₃ PO ₄ instead of K ₂ HPO ₄	42
6	Na ₂ HPO ₄ instead of K ₂ HPO ₄	27
7	MeCN instead of acetone	11
8	DCM instead of acetone	Trace
9	DMSO instead of acetone	0
10	4 equivalents of valeraldehyde were used	70
11	1 equivalent of ethyl acrylate were used	59
12	Absence of NaDT, Ni or light	0

^a Reaction conditions: **1** (1 mmol), **2** (0.4 mmol), **3** (0.2 mmol), Ni(**L3**)Br₂ (10 mol%), NaDT (2 mol%), K₂HPO₄ (0.4 mmol) in acetone (0.2 M) at 30 °C under irradiation of LEDs (10 W, λ = 390 nm) for 24 hours.

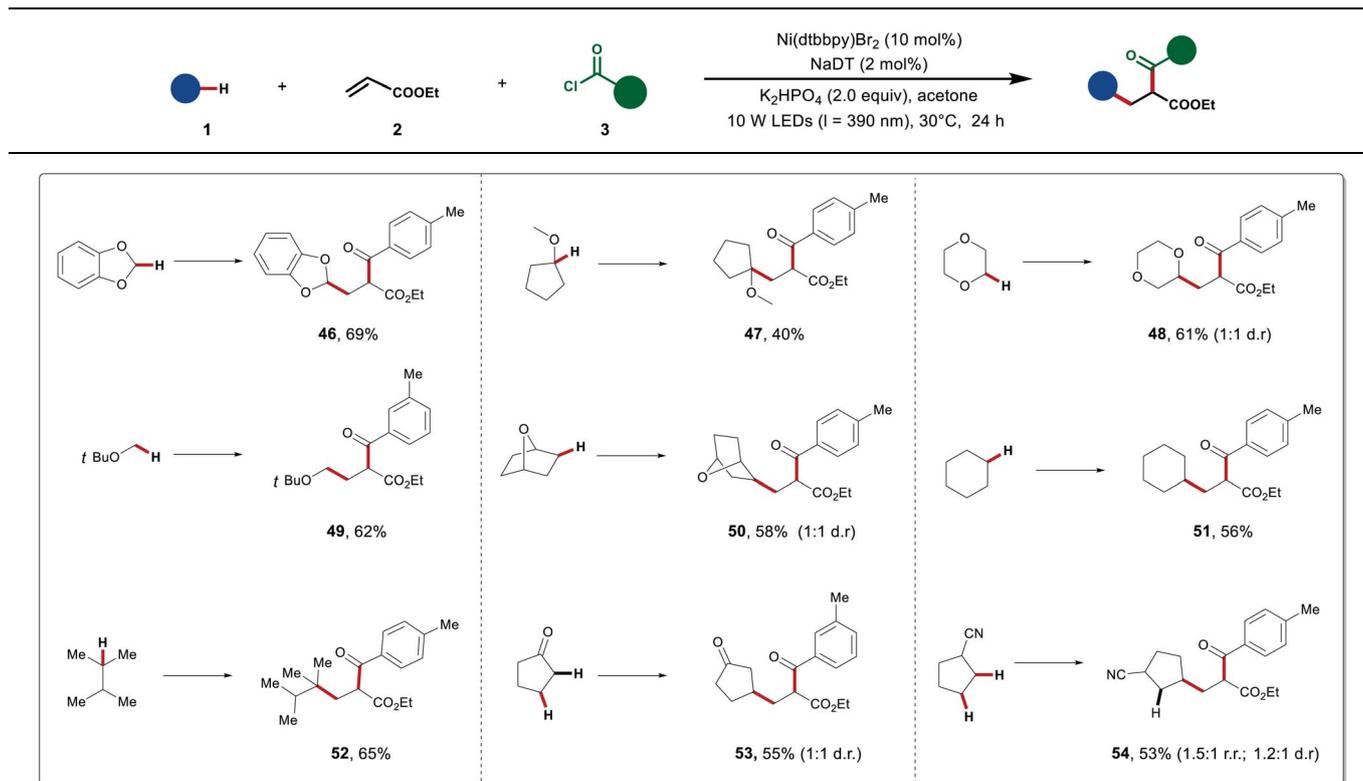
^b GC yield with *n*-dodecane as internal standard. ^c Isolated yield.



Table 2 Scope of three-component dicarbonylation of alkenes ^a

^a Reaction conditions: **1** (1 mmol), **2** (0.4 mmol), **3** (0.2 mmol), Ni(dtbbpy)Br₂ (10 mol%), NaDT (2 mol%), K₂HPO₄ (0.4 mmol) in acetone (0.2 M) at 30 °C under irradiation of LEDs (10 W, λ = 390 nm) for 24 hours. Isolated yields. d.r., diastereomeric ratio. ^b 6.0 equivalents of aldehyde **1** and 4.0 equivalents of alkene **2** were used.

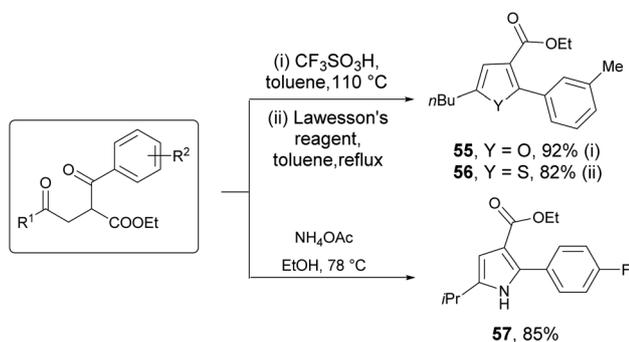


Table 3 Scope of three-component carbonylation of alkenes^a

^a General reaction conditions: **1** (2 mmol), **2** (0.4 mmol), **3** (0.2 mmol), Ni(dtbbpy)Br₂ (10 mol%), NaDT (2 mol%), K₂HPO₄ (0.4 mmol) in acetone (0.2 M) at 30 °C under irradiation of LEDs (10 W, λ = 390 nm) for 24 hours. Yields of isolated products. d.r., diastereomeric ratio; r.r., regioisomeric ratio.

subjected to the protocol (**44**). The reaction proceeded efficiently, affording the desired 1,4-diketone in 58% yield with excellent chemo- and regioselectivity, indicating its potential for late-stage functionalization of complex molecules. Under slightly modified conditions, this strategy was also applicable for dicarbonylation of styrenes bearing electron-withdrawing groups such as 4-(trifluoromethyl)styrene, giving **45** in 28% yield. But styrenes substrates containing electron-donating groups such as 4-methylstyrene and unactivated alkene like hex-1-ene were not tolerated.

Having established the 1,2-dicarbonylation, the suitability of this strategy to introduce simultaneously an alkyl group and a carbonyl group onto a double bond was studied, by employing hydrocarbons and acyl chlorides as the radical precursor and the acyl source, respectively (Table 3). Gratifyingly, when three-component carbonylation of alkenes was conducted with 1,3-benzodioxole, ethyl acrylate and 4-methylbenzoyl chloride under slightly modified conditions, the desired product **46** was obtained in 69% yield. Afterward, oxygen-containing substrates were incorporated onto C–C double bond of alkenes, in moderate to good yields and with excellent regioselectivity under the optimized conditions (**47–49**). It is particularly noteworthy that our photochemical method was not limited to tertiary (3°) alkyl radicals. Indeed, the less stable secondary (2°) and primary (1°) alkyl radicals were likewise compatible with this dual catalysis. Based on these results, we wondered whether our protocol can be extended to unactivated C–H precursors other than ether motifs. Importantly, a wide range of alkanes with various groups were successfully employed as radical precursors, thus resulting in the corresponding ketone compounds in satisfactory yields with excellent regioselectivities (**50–54**). For instance, 2,3-dimethylbutane was selectively functionalized on the tertiary C–H bond (**52**). Cyclopentanone was exclusively functionalized at the β position in 57% yield (**53**). In addition, the reaction conducted with



Scheme 2 Synthetic applications.



yields through increasing the equivalents of alkenes and acyl chlorides.

To gain insight into the catalysis mode of action, several mechanistic experiments were performed (Scheme 4). The addition of TEMPO (1.0 equiv.) strongly inhibited the three-component coupling reaction, suggesting that this transformation involved a radical mechanism. Thus, a small amount of the TEMPO-adduct 2,2,6,6-tetramethylpiperidin-1-yl pentanoate could be observed by GC-MS (Scheme 4a). Then, a reaction of Ni(COD)₂ with benzoyl chloride in THF at room temperature afforded nickel(II) complex **61**. We have not observed the corresponding 1,4-diketone **7** when a stoichiometric reaction of nickel(II) complex **61** was performed with valeraldehyde (**1**) and ethyl acrylate (**2**) (Scheme 4b). This finding demonstrates that oxidative addition takes place after radical capture of the nickel complex. Furthermore, when the reaction was carried out with 10 mol% of nickel-complex **61** to replace Ni(dtbbpy)Br₂ as the catalyst under conditions of carbonylation, the expected product **7** was observed in 65% yield (Scheme 4c).

Based on our experimental results and previous findings,^{5a,10} we propose a plausible mechanism for the photoredox/nickel-catalyzed carbonylation, as outlined in Scheme 5. Upon visible light irradiation, NaDT is excited to generate photoexcited decatungstate **A**, which is capable of abstracting a hydrogen atom from a non-activated C–H bond of aldehydes/hydrocarbon resulting in carbon-centered radical intermediate **D** and [W]^{5−}H⁺ (**B**). The latter can be reduced to afford [W]^{6−}2H⁺ (**C**) in the presence of [W]^{4−}, while **C** is able to reduce Ni(I) catalyst to the corresponding Ni(0) species *via* successive single-electron transfer. The addition of **D** to alkenes gives an alkyl radical **E**, which can be captured by Ni(0) to form alkyl-Ni(I) intermediate **F**. Then oxidative addition of acyl chloride to alkyl-Ni(I) intermediate generates a nickel(III) species **G**, which performs reductive elimination to give the corresponding carbonyl compounds and nickel(I) species **H**.

Conclusions

In conclusion, we have successfully achieved three-component intermolecular carbonylation of alkenes by the synergy of nickel-photoredox catalysts. This robust strategy provided facile access to various complex ketones with excellent regioselectivities starting from a diverse class of inexpensive commercial chemicals. With the use of aldehydes and unactivated hydrocarbons, this methodology showed a broad scope and high functional group tolerance. Our strategy is expected to find broad applications in medical chemists as well as pharmaceutical and agricultural industries because it enables the facile construction of carbonyl compounds with high levels of complexity.

Data availability

All experimental data, procedures for data analysis and pertinent data sets are provided in the ESI.†

Author contributions

D. W. and L. A. conceived the project. D. W. conducted the experiments. D. W. and L. A. wrote the manuscript. All authors discussed the results.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Generous support by the DFG (Gottfried-Wilhelm-Leibniz award to L. A.) and the Alexander von Humboldt Foundation (fellowship to D. W.) is gratefully acknowledged.

Notes and references

- (a) J. Derosa, O. Apolinar, T. Kang, V. T. Tran and K. M. Engle, *Chem. Sci.*, 2020, **11**, 4287–4296; (b) Z. Zhang, T. Roisnel, P. H. Dixneuf and J.-F. Soulé, *Angew. Chem., Int. Ed.*, 2020, **58**, 14110–14114; *Angew. Chem.*, 2019, **131**, 14248–14252; (c) R. K. Dhungana, S. Kc, P. Basnet and R. Giri, *Chem. Rec.*, 2018, **18**, 1314–1340; (d) J. S. Zhang, L. Liu, T. Chen and L. B. Han, *Chem.-Asian J.*, 2018, **13**, 2277–2291.
- (a) H. Tu, F. Wang, L. Huo, Y. Li, S. Zhu, X. Zhao, H. Li, F. Qing and L. Chu, *J. Am. Chem. Soc.*, 2020, **142**, 9604–9611; (b) L. Song, D.-M. Fu, L. Chen, Y.-X. Jiang, J.-H. Ye, L. Zhu, Y. Lan, Q. Fu and D.-G. Yu, *Angew. Chem., Int. Ed.*, 2020, **59**, 21121–21128; *Angew. Chem.*, 2020, **132**, 14248–14252; (c) X. Wu and C. Zhu, *Acc. Chem. Res.*, 2020, **53**, 1620–1636; (d) Z. Li, G. Fang, Q. Gu and X. Liu, *Chem. Soc. Rev.*, 2020, **49**, 32–48; (e) P. Fan, Y. Lan, C. Zhang and C. Wang, *J. Am. Chem. Soc.*, 2020, **142**, 2180–2186; (f) H. Jiang and A. Studer, *Chem. Soc. Rev.*, 2020, **49**, 1790–1811; (g) Z. Li, M. Wang and Z. Shi, *Angew. Chem., Int. Ed.*, 2020, **60**, 186–190; *Angew. Chem.*, 2020, **133**, 188–192; (h) X. Wang, X. Lu, S. He and Y. Fu, *Chem. Sci.*, 2020, **11**, 7950–7956; (i) D. Anthony, Q. Lin, J. Baudet and T. Diao, *Angew. Chem., Int. Ed.*, 2019, **58**, 3198–3202; *Angew. Chem.*, 2019, **131**, 3230–3234; (j) D. Wang, B. Dong, Y. Wang, J. Qian, J. Zhu, Y. Zhao and Z. Shi, *Nat. Commun.*, 2019, **10**, 3539–3548; (k) Q. Fu, Z.-Y. Bo, J.-H. Ye, T. Ju, H. Huang, L.-L. Liao and D.-G. Yu, *Nat. Commun.*, 2019, **10**, 3592–3600; (l) M. Zhang, J. Xie and C. Zhu, *Nat. Commun.*, 2018, **9**, 3517–3526; (m) F. Wang, P. Chen and G. Liu, *Acc. Chem. Res.*, 2018, **51**, 2036–2046; (n) M. Yan, J. C. Lo, J. T. Edwards and P. S. Baran, *J. Am. Chem. Soc.*, 2016, **138**, 12692–12714.
- (a) T. Xiong and Q. Zhang, *Chem. Soc. Rev.*, 2021, **50**, 8857–8873; (b) S. Sharma, J. Singh and A. Sharma, *Adv. Synth. Catal.*, 2021, **363**, 3146–3169; (c) L. Pitzer, J. L. Schwarz and F. Glorius, *Chem. Sci.*, 2019, **10**, 8285–8291; (d) Y. Jin and C. Wang, *Chem. Sci.*, 2019, **10**, 1780–1785; (e) Z. Zhang, L. Gong, X.-Y. Zhou, S.-S. Yan, J. Li and D.-G. Yu, *Acta Chim. Sin.*, 2019, **77**, 783–793; (f) T. Koike and M. Akita,



- Chem.*, 2018, **4**, 409–437; (g) G. S. Sauer and S. Lin, *ACS Catal.*, 2018, **8**, 5175–5187; (h) K. Wang, Z. Ding, Z. Zhou and W. Kong, *J. Am. Chem. Soc.*, 2018, **140**, 12364–12368.
- 4 (a) X. Wei, W. Shu, A. García-Domínguez, E. Merino and C. Nevado, *J. Am. Chem. Soc.*, 2020, **142**, 13515–13522; (b) W. Shu, A. García-Domínguez, M. T. Quirls, R. Mondal, D. J. Cordenas and C. Nevado, *J. Am. Chem. Soc.*, 2019, **141**, 13812–13821; (c) A. García-Domínguez, R. Mondal and C. Nevado, *Angew. Chem., Int. Ed.*, 2019, **58**, 12286–12290; *Angew. Chem.*, 2019, **131**, 12414–12418; (d) A. García-Domínguez, Z. Li and C. Nevado, *J. Am. Chem. Soc.*, 2017, **139**, 6835–6838; (e) E. Merino and C. Nevado, *Chem. Soc. Rev.*, 2014, **43**, 6598–6608.
- 5 (a) M. W. Campbell, M. Yuan, V. C. Polites, O. Gutierrez and G. A. Molander, *J. Am. Chem. Soc.*, 2021, **143**, 3901–3910; (b) A. Lipp, S. O. Badir and G. A. Molander, *Angew. Chem., Int. Ed.*, 2021, **60**, 1714–1726; *Angew. Chem.*, 2021, **133**, 1738–1750; (c) S. O. Badir and G. A. Molander, *Chem.*, 2020, **6**, 1327–1339; (d) M. W. Campbell, J. S. Compton, C. B. Kelly and G. A. Molander, *J. Am. Chem. Soc.*, 2019, **141**, 20069–20078.
- 6 R. S. Mega, V. K. Duong, A. Noble and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2020, **59**, 4375–4379; *Angew. Chem.*, 2020, **132**, 4405–4409.
- 7 (a) B. Maity, C. Zhu, H. Yue, L. Huang, M. Harb, Y. Minenkov, M. Rueping and L. Cavallo, *J. Am. Chem. Soc.*, 2020, **142**, 16942–16952; (b) L. Huang, T. Ji and M. Rueping, *J. Am. Chem. Soc.*, 2020, **142**, 3532–3539; (c) A. Dewanji, P. E. Krach and M. Rueping, *Angew. Chem., Int. Ed.*, 2019, **58**, 3566–3570; *Angew. Chem.*, 2019, **131**, 3604–3608; (d) L. Huang and M. Rueping, *Angew. Chem., Int. Ed.*, 2018, **57**, 10333–10337; *Angew. Chem.*, 2018, **130**, 10490–10494; (e) H. Yue, C. Zhu and M. Rueping, *Angew. Chem., Int. Ed.*, 2017, **57**, 1371–1375; *Angew. Chem.*, 2017, **130**, 1385–1389.
- 8 S. Sun, Y. Duan, R. S. Mega, R. J. Somerville and R. Martin, *Angew. Chem., Int. Ed.*, 2020, **59**, 4370–4374; *Angew. Chem.*, 2020, **132**, 4400–4404.
- 9 H. Jiang, X. Yu, C. G. Daniliuc and A. Studer, *Angew. Chem., Int. Ed.*, 2021, **60**, 14399–14404; *Angew. Chem.*, 2021, **133**, 14520–14525.
- 10 T. Yang, X. Chen, W. Rao and M. Koh, *Chem.*, 2020, **6**, 738–751.
- 11 For reported elegant examples see: (a) C. A. Vasilopoulos, S. W. Krska and S. S. Stahl, *Science*, 2021, **372**, 398–403; (b) L. Zhang, S. Chen, H. He, W. Li, C. Zhu and J. Xie, *Chem. Commun.*, 2021, **57**, 9064–9067; (c) B. Maity, C. Zhu, M. Rueping and L. Cavallo, *ACS Catal.*, 2021, **11**, 13973–13982; (d) C. Zhu, H. Yue, L. Chu and M. Rueping, *Chem. Sci.*, 2020, **11**, 4051–4064; (e) P. Fan, Y. Lan, C. Zhang and C. Wang, *J. Am. Chem. Soc.*, 2020, **142**, 2180–2186; (f) D. X. Shu, L. Huan, Q. Huang and H. Huo, *J. Am. Chem. Soc.*, 2020, **45**, 19058–19064; (g) L. Guo, H. Tu, S. Zhu and L. Chu, *Org. Lett.*, 2019, **21**, 4771–4776.
- 12 For selected reviews, see: (a) A. Y. Chan, I. B. Perry, N. B. Bissonnette, B. F. Buksh, G. A. Edwards, L. I. Frye, O. L. Garry, M. N. Lavagnino, B. X. Li, Y. Liang, E. Mao, A. Millet, J. V. Oakley, N. L. Reed, H. A. Sakai, C. P. Seath and D. W. C. MacMillan, *Chem. Rev.*, 2022, **122**, 1485–1542; (b) B. N. Holmberg-Douglas and D. A. Nicewicz, *Chem. Rev.*, 2022, **122**, 1925–2016; (c) L. Yi, T. Ji, K.-Q. Chen, X.-Y. Chen and M. Rueping, *CCS Chem.*, 2022, **4**, 9–30; (d) F.-D. Lu, G.-F. He, L.-Q. Lu and W.-J. Xiao, *Green Chem.*, 2021, **23**, 5379–5393; (e) F.-D. Lu, J. Chen, X. Jiang, J.-R. Chen, L.-Q. Lu and W.-J. Xiao, *Chem. Soc. Rev.*, 2021, **50**, 12808–12827; (f) S. K. Kariofillis and A. G. Doyle, *Acc. Chem. Res.*, 2021, **54**, 988–1000; (g) C. Zhu, H. Yue, L. Chu and M. Rueping, *Chem. Sci.*, 2020, **11**, 4051–4064; (h) H. Cao, X. Tang, H. Tang, Y. Yuan and J. Wu, *Chem. Catal.*, 2021, **1**, 523–598; (i) L. Guillemard and J. Wencel-Delord, *Beilstein J. Org. Chem.*, 2020, **16**, 1754–1804; (j) W.-J. Zhou, Y.-H. Zhang, Y.-Y. Gui, L. Sun and D.-G. Yu, *Synthesis*, 2018, **50**, 3359–3378; (k) J. Twilton, C. Le, P. Zhang, M. H. Shaw, R. W. Evans and D. W. C. MacMillan, *Nat. Rev. Chem.*, 2017, **1**, 52–69; (l) K. Skubi, T. V. Blum and T. P. Yoon, *Chem. Rev.*, 2016, **116**, 10035–10074; (m) Y.-Y. Gui, L. Sun, Z.-P. Lua and D.-G. Yu, *Org. Chem. Front.*, 2016, **3**, 522–526.
- 13 S. Xu, H. Chen, Z. Zhou and W. Kong, *Angew. Chem., Int. Ed.*, 2021, **60**, 7405–7411; *Angew. Chem.*, 2021, **133**, 7481–7487.
- 14 (a) R. L. Sutar, S. Sen, O. Eivgi, G. Segalovich, I. Schapiro, O. Reany and N. G. Lemcoff, *Chem. Sci.*, 2018, **9**, 1368–1374; (b) J. Li, M. Kong, B. Qiao, R. Lee, X. Zhao and Z. Jiang, *Nat. Commun.*, 2018, **9**, 2445–2453; (c) J. T. Edwards, R. R. Merchant, K. S. McClymont, K. W. Knouse, T. Qin, L. R. Malins, B. Vokits, S. A. Shaw, D.-H. Bao, F.-L. Wei, T. Zhou, M. D. Eastgate and P. S. Baran, *Nature*, 2017, **545**, 213–219; (d) L. Lin, X. Bai, X. Ye, X. Zhao, C.-H. Tan and Z. Jiang, *Angew. Chem., Int. Ed.*, 2017, **56**, 13842–13846; *Angew. Chem.*, 2017, **129**, 14030–14034; (e) H. Renata, Q. H. Zhou, G. Dunstl, J. Felding, R. R. Merchant, C. H. Yeh and P. S. Baran, *J. Am. Chem. Soc.*, 2015, **137**, 1330–1340; (f) A. Démolis, N. Essayem and F. Rataboul, *ACS Sustainable Chem. Eng.*, 2014, **2**, 1338–1352; (g) F. Alois and N. Takashi, *J. Am. Chem. Soc.*, 2007, **129**, 1906–1907.
- 15 (a) Y. Yamamoto, H. Maekawa, S. Goda and I. Nishiguchi, *Org. Lett.*, 2003, **5**, 2755–2758; (b) Y. Liu and Y. Zhang, *Tetrahedron*, 2003, **59**, 8429–8437; (c) N.-S. Li, S. Yu and G. W. Kabalka, *Organometallics*, 1998, **17**, 3815–3817.
- 16 T. H. Meyer, L. H. Finger, P. Gandeepan and L. Ackermann, *Trends Chem.*, 2019, **1**, 63–76.
- 17 (a) Y. Matsuki, N. Ohnishi, Y. Kakeno, S. Takemoto, T. Ishii, K. Nagao and H. Ohmiya, *Nat. Commun.*, 2021, **12**, 3848–3855; (b) Q. Zhang, Y. Huang, L. W. Zhan, W. Y. Tang, J. Hou and B. D. Li, *Org. Lett.*, 2020, **22**, 7460–7464; (c) H. Zhang, Q. Xiao, X.-K. Qi, X.-W. Gao, Q.-X. Tong and J.-J. Zhong, *Chem. Commun.*, 2020, **56**, 12530–12533; (d) T. Morack, C. Mck-Lichtenfeld and R. Gilmour, *Angew. Chem., Int. Ed.*, 2019, **58**, 1208–1212; *Angew. Chem.*, 2019, **131**, 1221–1225; (e) G. Goti, B. Bieszczad, A. Vega-Peñalozza and P. Melchiorre, *Angew. Chem., Int. Ed.*, 2019, **58**, 1213–1217; *Angew. Chem.*, 2019, **131**, 1226–1230; (f) C. M. Wang, D. Song, P. J. Xia, J. Wang, H. Y. Xiang and H. Yang, *Chem.-Asian J.*, 2018, **13**, 271–274; (g) M. D. Vu, M. Das and



- X. W. Liu, *Chem.–Eur. J.*, 2017, **23**, 15899–15902; (h) J. A. Walker, K. L. Vickerman, J. N. Humke and L. M. Stanley, *J. Am. Chem. Soc.*, 2017, **139**, 10228–10231; (i) M. M. D. Wilde and M. Gravel, *Angew. Chem., Int. Ed.*, 2013, **52**, 12651–12654; (j) Q. Liu, S. Perreault and T. Rovis, *J. Am. Chem. Soc.*, 2008, **130**, 14066–14067; (k) M. Ischay and T. P. Yoon, *Eur. J. Org. Chem.*, 2012, 3359–3372; (l) M. C. Myers, A. R. Bharadwaj, B. C. Milgram and K. A. Scheidt, *J. Am. Chem. Soc.*, 2005, **127**, 14675–14680; (m) A. E. Mattson, A. R. Bharadwaj and K. A. Scheidt, *J. Am. Chem. Soc.*, 2004, **126**, 2314–2315.
- 18 (a) S. Dong, G. Wu, X. Yuan, C. Zou and J. Ye, *Org. Chem. Front.*, 2017, **4**, 2230–2234; (b) G. Bergonzini, C. Cassani, H. Lorimer-Olsson, J. Horberg and C.-J. Wallentin, *Chem.–Eur. J.*, 2016, **22**, 3292–3295; (c) G.-Z. Wang, R. Shang, W.-M. Cheng and Y. Fu, *Org. Lett.*, 2015, **17**, 4830–4833; (d) G. Bergonzini, C. Cassani and C.-J. Wallentin, *Angew. Chem., Int. Ed.*, 2015, **54**, 14066–14069; (e) I. Ryu, A. Tani, T. Fukuyama, D. Ravelli, M. Fagnoni and A. Albinì, *Angew. Chem., Int. Ed.*, 2011, **50**, 1869–1872; *Angew. Chem.*, 2011, **123**, 1909–1912; (f) M. T. Wentzel, V. J. Reddy, T. K. Hyster and C. J. Douglas, *Angew. Chem., Int. Ed.*, 2009, **48**, 6121–6123.
- 19 For reported elegant examples see: (a) S. Jin, X. Sui, G. C. Haug, V. D. Nguyen, H. T. Dang, H. D. Arman and O. V. Larionov, *ACS Catal.*, 2022, **12**, 285–294; (b) Y.-Y. Cheng, J.-X. Yu, T. Lei, H.-Y. Hou, B. Chen, C.-H. Tung and L.-Z. Wu, *Angew. Chem., Int. Ed.*, 2021, **60**, 26822–26828; *Angew. Chem.*, 2021, **133**, 27026–27032; (c) K. Liu and A. Studer, *J. Am. Chem. Soc.*, 2021, **143**, 4903–4909; (d) Z. Li, M. Huang, X. Zhang, J. Chen and Y. Huang, *ACS Catal.*, 2021, **11**, 10123–10130; (e) M. Kusakabe, K. Nagao and H. Ohmiya, *Org. Lett.*, 2021, **23**, 7242–7247; (f) Y. Gao, Y. Quan, Z. Li, L. Gao, Z. Zhang, X. Zou, R. Yan, Y. Qu and K. Guo, *Org. Lett.*, 2021, **23**, 183–189; (g) C. Zhu, J. Dong, X. Liu, L. Gao, Y. Zhao, J. Xie, S. Li and C. Zhu, *Angew. Chem., Int. Ed.*, 2020, **59**, 12817–12821; *Angew. Chem.*, 2020, **132**, 12917–12921; (h) L. Chen, S. Jin, J. Gao, T. Liu, Y. Shao, J. Feng, K. Wang, T. Lu and D. Du, *Org. Lett.*, 2021, **23**, 394–399; (i) Q.-Y. Meng, N. Dçben and A. Studer, *Angew. Chem., Int. Ed.*, 2020, **59**, 19956–19960; *Angew. Chem.*, 2020, **132**, 20129–20134; (j) J.-L. Li, Y.-Q. Liu, W.-L. Zou, R. Zeng, X. Zhang, Y. Liu, B. Han, Y. He, H.-J. Leng and Q.-Z. Li, *Angew. Chem., Int. Ed.*, 2020, **59**, 1863–1870; *Angew. Chem.*, 2020, **132**, 1879–1886; (k) Y. Yuan, F.-P. Wu, J.-X. Xu and X.-F. Wu, *Angew. Chem., Int. Ed.*, 2020, **59**, 17055–17061; *Angew. Chem.*, 2020, **132**, 17203–17209; (l) H.-B. Yang, Z.-H. Wang, J.-M. Li and C. Wu, *Chem. Commun.*, 2020, **56**, 3801–3804; (m) L. Wang and C. Wang, *Org. Lett.*, 2020, **22**, 8829–8835; (n) X. Zhao, B. Li and W. Xia, *Org. Lett.*, 2020, **22**, 1056–1061; (o) B. Zhang, Q. Peng, D. Guo and J. Wang, *Org. Lett.*, 2020, **22**, 443–447; (p) T. Ishii, K. Ota, K. Nagao and H. Ohmiya, *J. Am. Chem. Soc.*, 2019, **141**, 14073–14077; (q) T. Ishii, Y. Kakeno, K. Nagao and H. Ohmiya, *J. Am. Chem. Soc.*, 2019, **141**, 3854–3858; (r) H. Wang, Y. Wang, X. Chen, C. Mou, S. Yu, H. Chai, Z. Jin and Y. R. Chi, *Org. Lett.*, 2019, **21**, 7440–7444; (s) X. Zhao, H.-Y. Tu, L. Guo, S. Zhu, F.-L. Qing and L. Chu, *Nat. Commun.*, 2018, **9**, 3488–3492; (t) Z.-Y. Song, K.-Q. Chen, X.-Y. Chen and S. Ye, *J. Org. Chem.*, 2018, **83**, 2966–2970.
- 20 For reported elegant examples see: (a) X. Wu, Y. Zhang, Y. Wang, J. Ke, M. Jeret, R. N. Reddi, S. Yang, B.-A. Song and Y. R. Chi, *Angew. Chem., Int. Ed.*, 2017, **56**, 2942–2946; *Angew. Chem.*, 2017, **129**, 2988–2992; (b) Y. Huang, K. B. Smith and M. Brown, *Angew. Chem., Int. Ed.*, 2017, **56**, 13314–13318; *Angew. Chem.*, 2017, **129**, 13499–13503; (c) Y. Wang, Y. Du, X. Huang, X. Wu, Y. Zhang, S. Yang and Y. R. Chi, *Org. Lett.*, 2017, **19**, 632–635; (d) X.-Y. Chen, K.-Q. Chen, D.-Q. Sun and S. Ye, *Chem. Sci.*, 2017, **8**, 1936–1941; (e) W. Yang, W. Hu, X. Dong, X. Li and J. Sun, *Angew. Chem., Int. Ed.*, 2016, **55**, 15783–15786; *Angew. Chem.*, 2016, **128**, 16015–16018; (f) B.-S. Li, Y. Wang, R. S. J. Proctor, Y. Zhang, R. D. Webster, S. Yang, B. Song and Y. R. Chi, *Nat. Commun.*, 2016, **7**, 12933–12940; (g) N. A. White and T. Rovis, *J. Am. Chem. Soc.*, 2015, **137**, 10112–10115; (h) Y. Zhang, Y. Du, Z. Huang, J. Xu, X. Wu, Y. Wang, M. Wang, S. Yang, R. D. Webster and Y. R. Chi, *J. Am. Chem. Soc.*, 2015, **137**, 2416–2419; (i) N. A. White and T. Rovis, *J. Am. Chem. Soc.*, 2014, **136**, 14674–14677; (j) Y. Du, Y. Wang, X. Li, Y. Shao, G. Li, R. D. Webster and Y. R. Chi, *Org. Lett.*, 2014, **16**, 5678–5681; (k) K. Takaki, A. Ohno, M. Hino, T. Shitaoka, K. Komeyama and H. Yoshida, *Chem. Commun.*, 2014, **50**, 12285–12288; (l) J. Guin, S. D. Sarkar, S. Grimme and A. Studer, *Angew. Chem., Int. Ed.*, 2008, **47**, 8727–8730; *Angew. Chem.*, 2008, **120**, 8855–8858.
- 21 (a) D. Mazzarella, A. Pulcinella, L. Bovy, R. Broersma and T. Noël, *Angew. Chem., Int. Ed.*, 2021, **60**, 21277–21282; *Angew. Chem.*, 2020, **133**, 21447–21452; (b) G. Laudadio, Y. Deng, K. van der Wal, D. Ravelli, M. Nuño, M. Fagnoni, D. Guthrie, Y. Sun and T. Noël, *Science*, 2020, **369**, 92–96; (c) L. K. G. Ackerman, J. I. Martínez Alvarado and A. G. Doyle, *J. Am. Chem. Soc.*, 2018, **140**, 14059–14063.
- 22 (a) A. Ghosh, K. F. Johnson, K. L. Vickerman, J. A. Walker and L. M. Stanley, *Org. Chem. Front.*, 2016, **3**, 639–644; (b) S. K. Murphy and V. M. Dong, *Chem. Commun.*, 2014, **50**, 13645–13649; (c) M. C. Willis, *Chem. Rev.*, 2010, **110**, 725–748; (d) M. Christmann, *Angew. Chem., Int. Ed.*, 2005, **44**, 2632–2634.
- 23 J. D. Earley, A. Zieleniewska, H. H. Ripberger, N. Y. Shin, M. S. Lazorski, Z. J. Mast, H. J. Sayre, J. K. McCusker, G. D. Scholes, R. R. Knowles, O. G. Reid and G. Rumbles, *Nat. Chem.*, 2022, DOI: [10.1038/s41557-022-00911-6](https://doi.org/10.1038/s41557-022-00911-6).

