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Photosensitized intermolecular carboimination of alkenes through persistent radical effect

Tuhin Patra, Peter Bellotti, Felix Strieth-Kalthoff and Frank Glorius*

Dedicated to Prof. Goutam K. Lahiri on the occasion of his 60th birthday

Abstract: An intermolecular, two-component vicinal carboimination of alkenes has been accomplished *via* energy transfer catalysis. Oxime esters of alkyl carboxylic acids are used as bifunctional reagents to generate both alkyl and iminyl radicals. Subsequently, the addition of alkyl radical to alkenes generates a transient radical for selective radical-radical cross coupling with persistent iminyl radical. Furthermore, this protocol readily allows for direct access to aliphatic primary amines and *α*-amino acids through simple hydrolysis.

The 1,2-difunctionalization of olefins, which allows simultaneous construction of two new covalent bonds, is one of the most powerful and straightforward strategies for the rapid development of molecular complexity.[1] Given the ubiquity of C–C and C–N bonds in bioactive compounds, carboamination of alkenes represents an important subset of such reactions, resulting in concurrent installation of both carbon and nitrogen functionalities into the alkenyl framework.[2-4] Ideally, cleavage of a C–N bond, followed by the addition of two fragments into olefins, would be the most direct means of carboamination. However, the intrinsic inertness of C–N bonds, as well as the potential difficulties in C(sp^3)–N reductive elimination over facile *β*-hydride elimination, present a formidable challenge.[5] Overcoming these issues, pioneering work by Wolfe,[6] Rovis,[7] Liu,[8] Engle[9] and our group[10] have shown the prospect of transition metals in intermolecular carboamination reactions.

Alternatively, a radical approach *via* either an N- or C-centered initiation has also offered an attractive strategy to circumvent these problems.[11,12] Notwithstanding these significant breakthroughs, carboamination with general alkyl groups for easily accessible primary amines remains an unsolved problem. This can be mainly attributed to the difficulty in generating a broad range of C-centered radicals from alkylating reagents, such as alkyl halides.[13] Additionally, the obligation to protect, and later deprotect, the amine functionality and the requirement for a radical-polar crossover step emphasizes the retrosynthetic deficiencies of accessing primary amines through a C-centered initiation.[14] Similarly, N-centered initiation often requires excess use of alkene, since N-centered radicals exhibit higher reactivity and electrophilicity, which makes allylic H-atom abstraction a kinetically competing process.[15] To address this, Stephenson and co-workers have targeted alkenes for single-electron oxidation followed by nucleophilic trapping with an arylsulfonylacetamide. In this approach, arylsulfonylacetamides were elegantly used as a single, bifunctional reagent for diastereoselective, intermolecular carboamination of alkenes *via* linear *N*-addition (Figure 1A).[16]

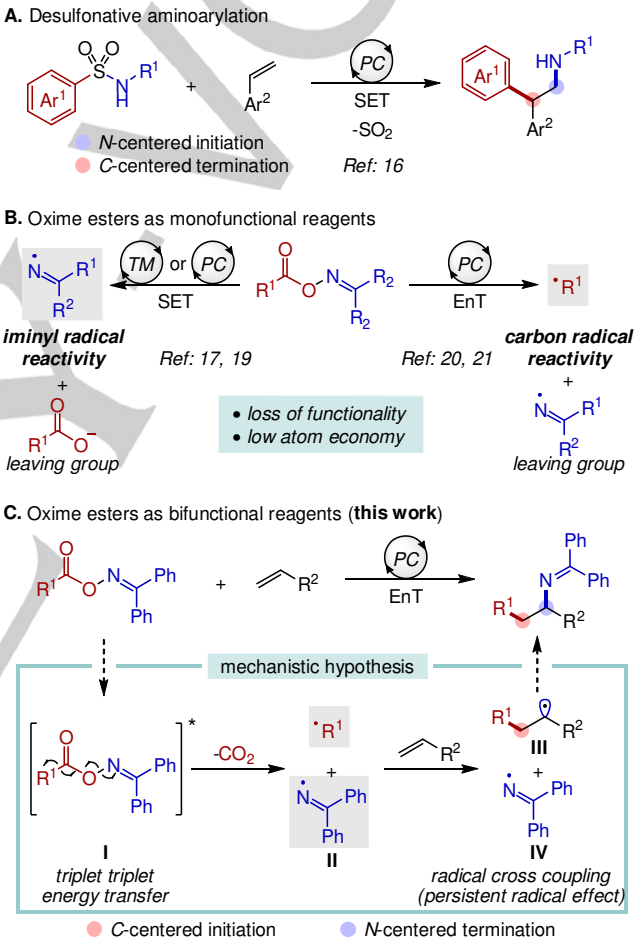

Figure 1. Bifunctional reagents as both *C*- and *N*- sources.

Unlike carboamination reactions, the carboimination of alkenes is still in its infancy and is limited mainly to intramolecular annulation reactions generating five or six membered *N*-heterocycles.[17] Additionally, their high reactivity has been utilized in a plethora of 1,5-hydrogen atom transfer (HAT) reactions.[18,19] In all these cases, iminyl radicals are first generated from oxime esters through a single electron transfer (SET) event (Figure 1B, left).[19] Alternatively, oxime esters have also been employed successfully in the photosensitized generation of iminyl radicals through N–O bond homolysis.[20] Recently, we have utilized this distinctive energy transfer (EnT) pathway to develop a general

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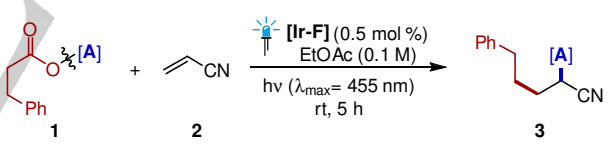
radical decarboxylation process applicable to both aromatic and aliphatic carboxylic acids (Figure 1B, right).[21] Nevertheless, all of these approaches are plagued by poor atom-economy, since either the carboxylate unit or the iminyl unit always become part of the waste stream. The advantageous generation of two different radicals from N–O bond homolysis, coupled with our continuous interest in EnT catalysis[22] prompted us to investigate whether both C-centered and N-centered radicals could effectively leverage the vicinal carboimination of alkenes (Figure 1C). During our previous investigation concerning the decarboxylation of oxime esters,[21] we realized relatively long lifetimes of the benzophenone iminyl radicals through the observation of iminyl byproducts. Considering the triplet energies of the oxime esters of aliphatic carboxylic acids (E_T = 45.4 kcal mol^{-1}, SI section 2.1), we envisioned that a triplet-triplet energy transfer (TTEnT) from the excited photosensitizer (with E_T > 46 kcal mol^{-1}) should be thermodynamically favored. This excited oxime ester **I** would participate in a concerted decarboxylation/fragmentation process to generate a C-centered alkyl radical and an N-centered diphenyliminyl radical pair **II**.[21, 23] Long lifetime of the diphenyliminyl radical **IV** should allow the transient alkyl radical to escape the solvent cage and add to the terminal position of the alkene to generate a stabilized radical **III**. Lastly, a highly selective radical-radical cross coupling between **III** and **IV** would be kinetically feasible based on the persistent radical effect (PRE).[24] However, such radical-radical cross-coupling approach possesses numerous challenges connected to potentially unproductive pathways outperforming the desired reaction.

Herein we report an unprecedented intermolecular radical carboimination of alkenes involving benzophenone oxime carboxylates as a bifunctional source of both N- and C-centered radicals with excellent regioselectivity for linear C-radical addition. In the majority of the reported protocols, N-centered radicals are known to be highly reactive species favoring linear N-radical additions.[11] In our study, the use of benzophenone oxime esters is key to the generation of a persistent iminyl radical in order to achieve the inverted selectivity. Benzophenone imines are synthetic equivalents to ammonia and have been used in a variety of transition metal-catalyzed coupling reactions.[25] The diarylmethylene protecting group can be easily removed by hydrolysis or transamination to release primary amines or can be converted to a wide range of valuable amine building blocks.[26,27] Importantly, the use of benzophenone-based oxime esters is also crucial to shut down unwanted SET reduction pathways, owing to their high reduction potential (E_{irr}^{red} = -2.05 V, SI section 2.2), which is inaccessible by commonly used photo(redox) catalysts. The use of an EnT pathway is also inimitable for two reasons: (1) concurrent generation of two different radicals in equal rates from the N–O bond homolysis of the oxime ester and (2) overall decarboxylation/fragmentation and carboamination steps should be independent of the intrinsic regeneration/turnover of the catalyst in the absence of any redox event. Expediently, this method uses highly abundant and stable aliphatic carboxylic acids (*via* their oxime ester derivative) in a highly atom economic fashion, generating carbon dioxide as the sole byproduct.[28]

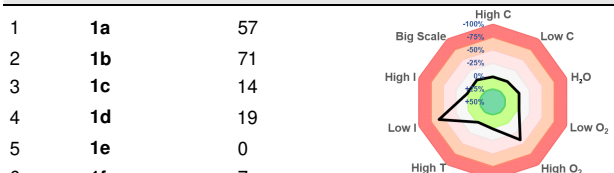
Upon exploring the various reaction parameters in line with our previous experience with oxime esters,[21] we found that the oxime ester **1a** provided the desired carboimination product with acrylonitrile (**2**) when [Ir(dF(CF_3)ppy)$_2$(dtbbpy)](PF_6) (**[Ir-F]**, dF-(CF_3)ppy=2-(2,4-difluorophenyl)-5-trifluoromethylpyridine, dtbbpy=4,4'-di-*tert*-butyl-2,2'-bipyridine) was used as the photosensitizer under irradiation with blue LEDs. The desired carboimination product was afforded in 57% yield (^{1}H NMR) with complete regioselectivity for the linear C-radical addition (Table 1, entry 1). Encouraged by this, we evaluated a series of oxime esters with varying steric and electronic properties (entries 2-6). Pleasingly, simple benzophenone oxime ester **1b** was identified as the optimal choice in terms of reaction efficiency, affording the desired product **3a** in 71% NMR yield. Control experiments with respect to the photosensitizer as well as light irradiation further demonstrated the necessity of each component. Additionally, to further identify the crucial parameters for our reaction, a systematic reaction parameters-based sensitivity screening was performed (Table 1, radar diagram).[29] Notably, the reaction was found to be sensitive towards low light intensity and high oxygen concentration, but robust in respect of water content and temperature fluctuations (SI section 3.2).

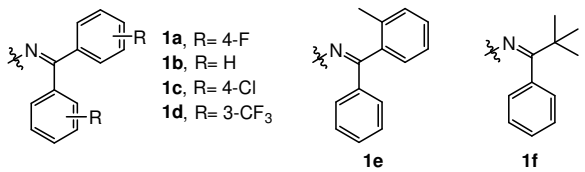
Notably, a critical distinction between an EnT and a hypothetical SET pathway is that the EnT-induced reactivity should also be accessible via direct excitation with high energy light sources in absence of any photocatalyst or any electron source. Indeed, the desired carboiminated product **33** was observed upon direct photoirradiation with 365 nm LED source, albeit in reduced yield (SI, section 2.3). Additionally, use of different photocatalysts revealed a direct correlation of the product yield with the triplet energies of the photocatalysts (SI section 2.4). All these observations further substantiate the involvement of an EnT-mediated carboimination process.

Table 1. Effect of activators and sensitivity assessment.[a]



entry	activator ([**A**])	yield (%)	sensitivity assessment
1	**1a**	57	
2	**1b**	71	
3	**1c**	14	
4	**1d**	19	
5	**1e**	0	
6	**1f**	7	





[a] Reaction conditions: **1** (0.15 mmol), **2** (0.1 mmol), **[Ir-F]** (0.5 mol %) in ethyl acetate (1 mL), irradiating with 30 W blue LEDs (λ_{max}= 455 nm) under an argon atmosphere at room temperature for 5 h. Yields were determined by ^{1}H NMR.

Next, with these optimized conditions, the generality of the carboimination reaction was evaluated by exploring different substrates. First, we explored a range of alkenes with different

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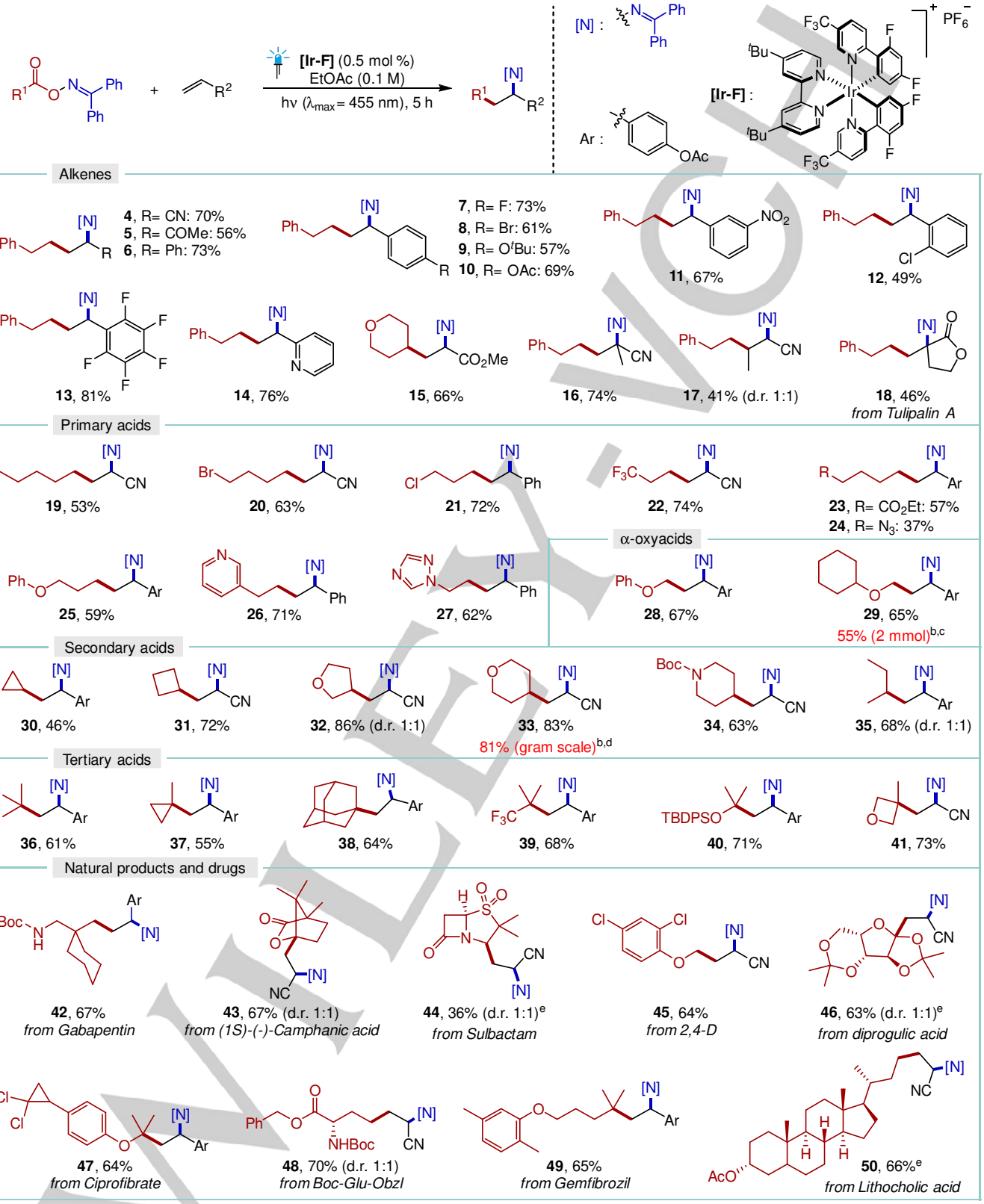
Table 2. Scope for decarboxylative intermolecular carboimination of alkenes.[a]



[a] Reaction conditions: alkene (0.3 mmol), oxime ester (0.45 mmol), [Ir-F] (0.5 mol %) in ethyl acetate under an argon atmosphere, irradiating with 30 W blue LEDs (λ_{max}= 455 nm) at room temperature for 5 h. Isolated yields. [b] Reaction time 16 h. [c] 1.25 equiv. of oxime ester was used. [d] 1.1 equiv. of oxime ester was used. [e] 1.0 equiv. of oxime ester was used.

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electronic and steric properties (Table 2, entries **4**-**18**). Electron deficient alkenes such as acrylonitrile (**4**), vinyl ketone (**5**) and acrylate (**15**) reacted smoothly providing the desired carboimination products. While styrenes bearing *meta*- and *para*-substitutions worked efficiently, *ortho*-substituted styrenes returned diminished yields (**7**-**12**). Delightfully, electron-poor nitrostyrene (**11**), pentafluorostyrene (**13**) as well as heterocyclic 2-vinylpyridine (**14**) effectively delivered the desired products in good yields. Substituents at either the *α*- or the *β*-positions on the alkene could be accommodated (**16**-**18**) despite their greater steric demand and lower electrophilicity, with a 1:1 diastereoselectivity for **17**. Naturally occurring Tulipalin A was successfully utilized to generate sterically congested imine **18** in moderate yield. However, cyclic alkenes and alkynes proved to be incompatible with our conditions.

Subsequently, we explored the carboxylic acid scope including two large scale demonstrations. A plethora of carboxylic acids featuring primary, secondary and tertiary carbon centers were found effective for carboimination reaction. Simple halides (**20** and **21**), trifluoromethyl (**22**), ester (**23**), azide (**24**) or ether (**25**) containing primary carboxylic acids were employed without any problem. Similarly, primary carboxylic acids comprising heterocycles such as pyridine (**26**) and 1,2,4-triazole (**27**) were tolerated under the optimized conditions. Both aliphatic (**28**) and aromatic *α*-oxyacids (**29**) could be applied successfully to form *γ*-amino ethers. Different cyclic (**30** and **31**) and heterocyclic secondary carboxylic acids (**32**, **33** and **34**) with varying ring sizes could be easily accommodated. Tertiary carboxylic acids starting from simple pivalic acid (**36**) to adamantane (**38**) or heterocyclic 3-methyloxetane (**41**) derivatives reacted smoothly to generate quaternary carbon centers. Pleasingly, comparable reactivity was also observed in the case of sterically demanding acids (**37**-**40**). Unfortunately, carboimination with oxime esters of aromatic carboxylic acids and phenyl acetic acids were unsuccessful.

We next probed the range of densely functionalized substrates amenable to our reaction condition. Pharmaceuticals and agrochemicals like gabapentin, sulbactam, ciprofibrate, gemfibrozil and 2,4-D afforded the desired carboiminated products (**42**, **44**, **45**, **47** and **49**) in synthetically useful yields. Naturally occurring carboxylic acids such as diprogulic acid, lithocholic acid, chiral auxiliary (*1S*)-(-)-camphanic acid and natural amino acid derived Boc-Glu-Obzl also reacted smoothly (**43**, **46**, **48** and **50**).

Finally, after developing a convenient method for alkene carboimination, we sought to explore their reactivity and synthetic utility (Figure 2A). Simple hydrolysis of the carboimination product **33** with 1.5 equiv. of HCl in wet MeOH delivered the corresponding primary ammonium chloride salt in 89% isolated yield (Figure 2A, entry **51**).[25b] Similarly, concomitant hydrolysis of both the nitrile and iminyl functionality produced the valuable *α*-amino acid **52** in racemic fashion. Furthermore, the biologically relevant diarylmethylamine class[27] of compounds could be easily generated from simple reduction of the iminyl moiety (**53**). Most interestingly, direct radical-radical cross coupled iminyl products were isolated in the absence of an alkene acceptor (Figure 2B, entries **54** and **55**). Remarkably, expensive iridium-based photosensitizers could be replaced by simple organic sensitizers, albeit with diminished efficiency (Figure 2C). As a result, a metal-free, intermolecular carboimination process can be developed based on this study.

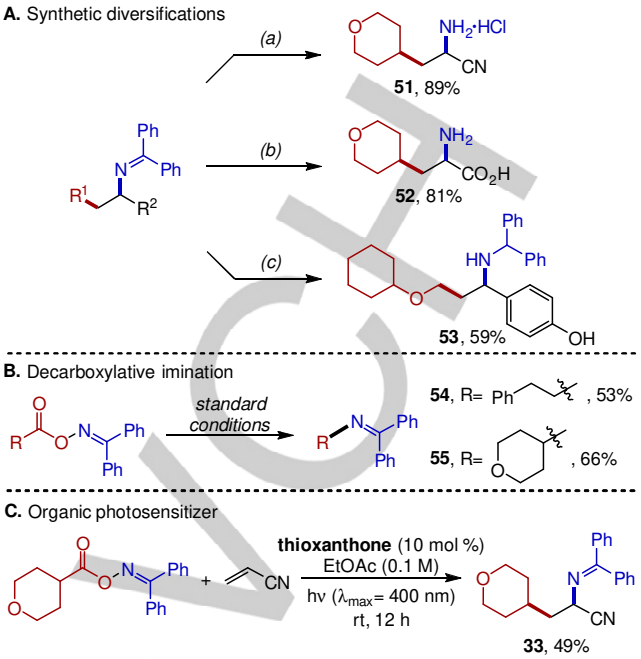

Figure 2. Synthetic utilities and ramifications. (a) 1N HCl (1.5 equiv.) in MeOH. (b) 6N HCl. (c) $NaBH_4$ (3 equiv.) in MeOH/CH_2Cl_2.

In summary, using oxime esters of readily available alkyl carboxylic acids as bifunctional reagent an intermolecular, two-component carboimination of olefins was developed. A photosensitized energy transfer strategy was used for effective generation of both C- and N-centered radicals in a highly atom-economic fashion. The persistency of iminyl radical underpins their exquisite regioselectivity. In addition, the mild reaction conditions, operational simplicity and a broad scope provide an easy gateway towards unprotected alkyl amines.

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Keywords: photocatalysis • amination • cross coupling • carboxylic acids • energy transfer

[1] a) S. R. Chemler, P. H. Fuller, *Chem. Soc. Rev.* **2007**, *36*, 1153-1160; b) T. E. Muller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.* **2008**, *108*, 3795-3892; c) X.-W. Lan, N.-X. Wang, Y. Xing, *Eur. J. Org. Chem.* **2017**, *2017*, 5821-5851; d) R. Giri, S. Kc, *J. Org. Chem.* **2018**, *83*, 3013-3022.

[2] For selected examples of alkenes carboamination with intramolecular carbon source, see: a) Y.-M. Li, X.-H. Wei, X.-A. Li, S.-D. Yang, *Chem. Commun.* **2013**, *49*, 11701-11703; b) K. Matcha, R. Narayan, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2013**, *52*, 7985-7989; c) Z. Wu, R. Ren, C. Zhu, *Angew. Chem. Int. Ed.* **2016**, *55*, 10821-10824.

[3] For selected examples of alkenes carboamination with intramolecular nitrogen source, see: a) C. F. Rosewall, P. A. Sibbald, D. V. Liskin, F. E.

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Michael, *J. Am. Chem. Soc.* **2009**, *131*, 9488-9489; b) B. Sunsdahl, A. R. Smith, T. Livinghouse, *Angew. Chem. Int. Ed.* **2014**, *53*, 14352-14356; c) G. J. Choi, R. R. Knowles, *J. Am. Chem. Soc.* **2015**, *137*, 9226-9229.

[4] For selected examples of alkenes carboamination with both intramolecular carbon and nitrogen sources, see: a) K.-T. Yip, M. Yang, K.-L. Law, N.-Y. Zhu, D. Yang, *J. Am. Chem. Soc.* **2006**, *128*, 3130-3131; b) W. Zeng, S. R. Chemler, *J. Am. Chem. Soc.* **2007**, *129*, 12948-12949; c) W. Du, Q. Gu, Y. Li, Z. Lin, D. Yang, *Org. Lett.* **2017**, *19*, 316-319.

[5] R. I. McDonald, G. S. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981-3019.

[6] a) J. S. Nakhla, J. W. Kampf, J. P. Wolfe, *J. Am. Chem. Soc.* **2006**, *128*, 2893-2901; b) D. N. Mai, J. P. Wolfe, *J. Am. Chem. Soc.* **2010**, *132*, 12157-12159; c) D. M. Schultz, J. P. Wolfe, *Synthesis* **2012**, *44*, 351-361; d) D. R. White, J. T. Hutt, J. P. Wolfe, *J. Am. Chem. Soc.* **2015**, *137*, 11246-11249.

[7] T. Piou, T. Rovis, *Nature* **2015**, *527*, 86.

[8] a) F. Wang, X. Qi, Z. Liang, P. Chen, G. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 1881-1886; b) J. Cheng, X. Qi, M. Li, P. Chen, G. Liu, *J. Am. Chem. Soc.* **2015**, *137*, 2480-2483; c) D. Wang, L. Wu, F. Wang, X. Wan, P. Chen, Z. Lin, G. Liu, *J. Am. Chem. Soc.* **2017**, *139*, 6811-6814; d) W. Zhang, P. Chen, G. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 5336-5340.

[9] Z. Liu, Y. Wang, Z. Wang, T. Zeng, P. Liu, K. M. Engle, *J. Am. Chem. Soc.* **2017**, *139*, 11261-11270.

[10] A. Lerchen, T. Knecht, C. G. Daniliuc, F. Glorius, *Angew. Chem. Int. Ed.* **2016**, *55*, 15166-15170.

[11] For examples of intermolecular carboamination with *N*-radical initiation, see: a) H. Zhang, W. Pu, T. Xiong, Y. Li, X. Zhou, K. Sun, Q. Liu, Q. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 2529-2533; b) Y. Zhang, H. Liu, L. Tang, H.-J. Tang, L. Wang, C. Zhu, C. Feng, *J. Am. Chem. Soc.* **2018**, *140*, 10695-10699; c) H. Jiang, G. Seidler, A. Studer, *Angew. Chem. Int. Ed.* **2019**, *58*, 16528-16532.

[12] For examples of intermolecular carboamination with *C*-radical initiation, see: a) G. Fumagalli, S. Boyd, M. F. Greaney, *Org. Lett.* **2013**, *15*, 4398-4401; b) Y. Yasu, T. Koike, M. Akita, *Org. Lett.* **2013**, *15*, 2136-2139; c) D. Prasad Hari, T. Hering, B. König, *Angew. Chem. Int. Ed.* **2014**, *53*, 725-728; d) Y.-Y. Liu, X.-H. Yang, R.-J. Song, S. Luo, J.-H. Li, *Nat. Commun.* **2017**, *8*, 14720; e) B. Qian, S. Chen, T. Wang, X. Zhang, H. Bao, *J. Am. Chem. Soc.* **2017**, *139*, 13076-13082.

[13] S. N. Gockel, T. L. Buchanan, K. L. Hull, *J. Am. Chem. Soc.* **2018**, *140*, 58-61.

[14] L. Legnani, G. Prina-Cerai, T. Delcaillau, S. Willems, B. Morandi, *Science* **2018**, *362*, 434.

[15] S. Z. Zard, *Chem. Soc. Rev.* **2008**, *37*, 1603-1618.

[16] T. M. Monos, R. C. McAtee, C. R. J. Stephenson, *Science* **2018**, *361*, 1369.

[17] a) S.-H. Cai, J.-H. Xie, S. Song, L. Ye, C. Feng, T.-P. Loh, *ACS Catal.* **2016**, *6*, 5571-5574; b) J. Davies, N. S. Sheikh, D. Leonori, *Angew. Chem. Int. Ed.* **2017**, *56*, 13361-13365; c) H. Jiang, A. Studer, *Angew. Chem. Int. Ed.* **2017**, *56*, 12273-12276.

[18] Z. Mirjafary, M. Abdoli, H. Saeidian, S. Boroon, A. Kakanejadifard, *RSC Adv.* **2015**, *5*, 79361-79384.

[19] a) J. Davies, S. P. Morcillo, J. J. Douglas, D. Leonori, *Chem. Eur. J.* **2018**, *24*, 12154-12163; b) B. Zhao, H. Tan, C. Chen, N. Jiao, Z. Shi, *Chin. J. Chem.* **2018**, *36*, 995-999.

[20] a) M. Hasebe, K. Kogawa, T. Tsuchiya, *Tetrahedron Lett.* **1984**, *25*, 3887-3890; b) R. T. McBurney, J. C. Walton, *J. Am. Chem. Soc.* **2013**, *135*, 7349-7354.

[21] T. Patra, S. Mukherjee, J. Ma, F. Strieth-Kalthoff, F. Glorius, *Angew. Chem. Int. Ed.* **2019**, *58*, 10514-10520.

[22] a) F. Strieth-Kalthoff, M. J. James, M. Teders, L. Pitzer, F. Glorius, *Chem. Soc. Rev.* **2018**, *47*, 7190-7202; b) M. Teders, C. Henkel, L. Anhäuser, F. Strieth-Kalthoff, A. Gómez-Suárez, R. Kleinmans, A. Kahnt, A. Rentmeister, D. Guldi, F. Glorius, *Nat. Chem.* **2018**, *10*, 981-988.

[23] V. K. Soni, S. Lee, J. Kang, Y. K. Moon, H. S. Hwang, Y. You, E. J. Cho, *ACS Catal.* **2019**, *9*, 10454-10463.

[24] a) H. Fischer, *Chem. Rev.* **2001**, *101*, 3581-3610; b) D. Leifert, A. Studer, *Angew. Chem. Int. Ed.* **2019**, 10.1002/anie.201903726.

[25] a) J. P. Wolfe, J. Åhman, J. P. Sadighi, R. A. Singer, S. L. Buchwald, *Tetrahedron Lett.* **1997**, *38*, 6367-6370; b) D. M. Peacock, C. B. Roos, J. F. Hartwig, *ACS Cent. Sci.* **2016**, *2*, 647-652; c) R. Mao, J. Balon, X. Hu, *Angew. Chem. Int. Ed.* **2018**, *57*, 9501-9504.

[26] a) D. Kong, M. Li, G. Zi, G. Hou, Y. He, *J. Org. Chem.* **2016**, *81*, 6640-6648; b) R. Sakamoto, T. Inada, S. Sakurai, K. Maruoka, *Org. Lett.* **2016**, *18*, 6252-6255; c) E. Kumarasamy, S. K. Kandappa, R. Raghunathan, S. Jockusch, J. Sivaguru, *Angew. Chem. Int. Ed.* **2017**, *56*, 7056-7061; d) R. Wang, M. Ma, X. Gong, X. Fan, P. J. Walsh, *Org. Lett.* **2019**, *21*, 27-31.

[27] a) G. A. M. Giardina, L. F. Raveglia, M. Grugni, H. M. Sarau, C. Farina, A. D. Medhurst, D. Graziani, D. B. Schmidt, R. Rigolio, M. Luttmann, S. Cavagnera, J. J. Foley, V. Vecchietti, D. W. P. Hay, *J. Med. Chem.* **1999**, *42*, 1053-1065; b) Q. Cai, H. Sun, Y. Peng, J. Lu, Z. Nikolovska-Coleska, D. McEachern, L. Liu, S. Qiu, C.-Y. Yang, R. Miller, H. Yi, T. Zhang, D. Sun, S. Kang, M. Guo, L. Leopold, D. Yang, S. Wang, *J. Med. Chem.* **2011**, *54*, 2714-2726; c) S. He, J. Xiao, A. E. Dulcey, B. Lin, A. Rolt, Z. Hu, X. Hu, A. Q. Wang, X. Xu, N. Southall, M. Ferrer, W. Zheng, T. J. Liang, J. J. Marugan, *J. Med. Chem.* **2016**, *59*, 841-853.

[28] a) N. Rodriguez, L. J. Goossen, *Chem. Soc. Rev.* **2011**, *40*, 5030-5048; b) C. P. Johnston, R. T. Smith, S. Allmendinger, D. W. C. MacMillan, *Nature* **2016**, *536*, 322-325; c) T. Qin, J. Cornella, C. Li, L. R. Malins, J. T. Edwards, S. Kawamura, B. D. Maxwell, M. D. Eastgate, P. S. Baran, *Science* **2016**, *352*, 801-805; d) T. Patra, D. Maiti, *Chem. Eur. J.* **2017**, *23*, 7382-7401; e) W. Zhao, R. P. Wurz, J. C. Peters, G. C. Fu, *J. Am. Chem. Soc.* **2017**, *139*, 12153-12156; f) S. Murarka, *Adv. Synth. Catal.* **2018**, *360*, 1735-1753; g) J. Schwarz, B. König, *Green Chem.* **2018**, *20*, 323-361; h) V. R. Yatham, P. Bellotti, B. König, *Chem. Commun.* **2019**, *55*, 3489-3492.

[29] L. Pitzer, F. Schäfers, F. Glorius, *Angew. Chem. Int. Ed.* **2019**, *58*, 8572-8576.

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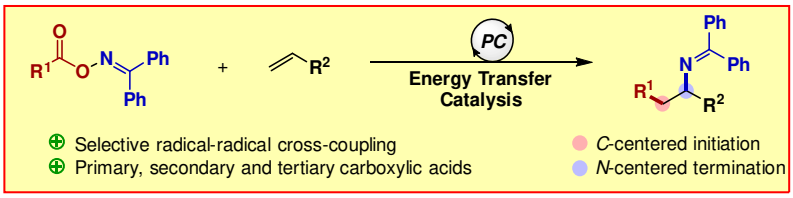

Two birds, one stone: Oxime esters of aliphatic carboxylic acids is used as a bifunctional source of both C- and N-radicals. Persistency of N-radicals enables intermolecular radical carboamination of alkenes in a highly selective fashion.

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Photosensitized intermolecular carboimination of alkenes through persistent radical effect

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