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Organophotoredox/Copper Hybrid Catalysis for Regioselective Allylic Aminodecarboxylation of β,γ-Unsaturated Carboxylic Acids

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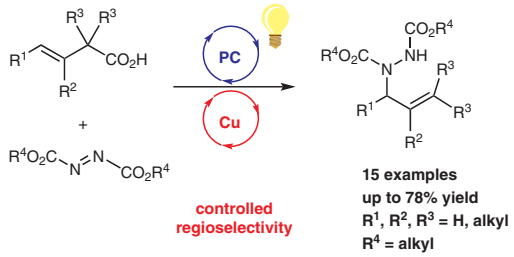

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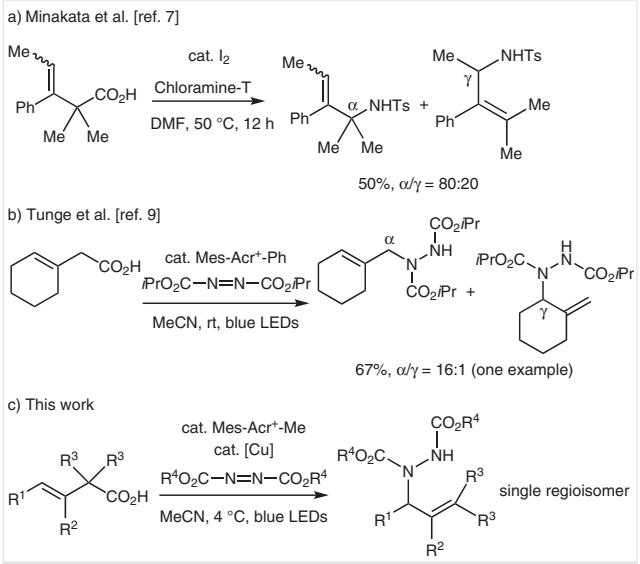
Abstract A new cooperative organophotoredox/copper catalysis allowing for the conversion of β,γ-unsaturated carboxylic acids into allylic hydrazides via radical regioselective allylic decarboxylative amination is reported. The coexistence of the copper catalyst is essential for the high yield and regioselectivity.

Key words photoredox catalysis, copper, decarboxylation, β,γ-unsaturated carboxylic acids, allylic hydrazides, dual catalysis

Carboxylic acids are abundant and relatively inexpensive, and thus widely used in organic synthesis in both laboratory and industrial scale chemistry.[1] The decarboxylative reaction of carboxylic acids represents in particular a powerful tool to form carbon–carbon and carbon–heteroatom bonds.[2] The difficulty of this method is based on the extrusion of CO_2 which generally requires harsh conditions or preactivation of the carboxylic acid.[3]

A decarboxylation process promoted by visible-light photoredox catalysis has recently attracted much attention.[4] This strategy involves radical precursors and proceeds under mild conditions compared with traditional radical decarboxylations. The formation of C–C and C–X bonds (X = heteroatom) via decarboxylative conjugate addition,[5a,b] alkynylation,[5c,d] alkenylation,[5e,f] arylation,[5g,h] alkylation,[5i] and allylation reactions[5j] has been investigated. Among these approaches, the photoredox aminodecarboxylation of carboxylic acids has emerged as a broadly applicable method to synthesize alkyl amines,[6] although it remains largely unexplored by organic chemists. For allylic aminodecarboxylation in particular, only a few examples have been reported to date (Scheme 1). Minakata and co-workers described the decarboxylative amidation of β,γ-unsaturated carboxylic acids catalyzed by iodine with chloramine salts via two-electron redox pathways (Scheme 1, a).[7] This protocol led to the generation of a mixture of regioisomers. Decarboxylation of this type of acid using hypervalent iodine has been reported, with uncontrolled regioselectivity.[8] Only one example of photocatalyzed aminodecarboxylation of β,γ-unsaturated carboxylic acids has been accomplished, by Tunge and co-workers (Scheme 1, b).[9] This reaction catalyzed by an organic photocatalyst was limited to 1-cyclohexene-1-acetic acid with one type of azodicarboxylate, leading to a mixture of regioisomers despite high selectivity. As represented by these precedents, controlling regioselectivity (α- vs γ-) in allylic aminodecarboxylation with broad substrate generality remains challenging.

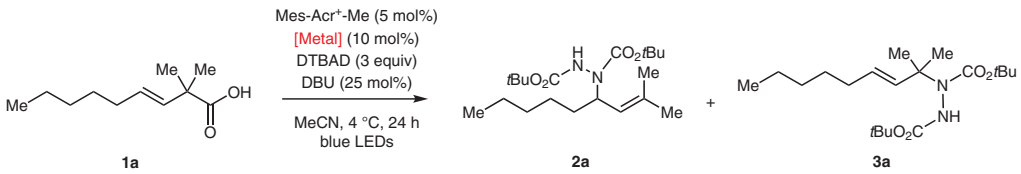


Scheme 1 Strategies for catalytic aminodecarboxylation of β,γ-unsaturated carboxylic acids

Inspired by these reported methodologies, we developed a new organophotoredox/copper hybrid catalysis for the generation of allylic hydrazides via regioselective aminodecarboxylation of β,γ-unsaturated carboxylic acids (Scheme 1, c).

Based on the rich literature on metallophotoredox-catalyzed transformations,[6e,f,10] and the background of copper-catalyzed allylation reactions in our laboratory,[11] we began our investigation into regioselective aminodecarboxylation of β,γ-unsaturated carboxylic acids by screening the metal source (Table 1). (*E*)-2,2-Dimethylnon-3-enoic acid (**1a**) and azodicarboxylate, respectively, were selected as the model substrate and electrophilic radical-trapping agent to form the C–N bond.[12,13] The reaction was performed in the presence of 9-mesityl-10-methylacridinium perchlorate photocatalyst (Mes-Acr$^+$-Me, 5 mol%),[14] di-*tert*-butyl azodicarboxylate (DTBAD, 3 equiv), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base (25 mol%) in MeCN at 4 °C under irradiation with blue LED lamps. In the absence of a metal source, a mixture of allylic hydrazides **2a** and **3a** in an 80:20 ratio was obtained in 57% yield (Table 1, entry 1). The regioselectivity of the reaction was influenced by the presence of CuOAc and (*R*,*R*)-Me-DuPHOS ((–)-1,2-bis[(2*R*,5*R*)-2,5-dimethylphospholano]benzene) as the ligand with the formation of single regioisomer **2a** in a very good yield without prefunctionalization of the acid (78%, entry 2). $Bi(OAc)_3$ afforded the same regioselectivity with a slightly lower yield (73%, entry 3). The use of indium, zinc, iron, and nickel sources also produced the single regioisomer **2a**, but the yield was substantially decreased (53%, 51%, 53%, and 36%, respectively; entries 4–7). Silver and boron sources gave similar results (entries 8 and 9), whereas $Co(OAc)_2$ led to a loss of regioselectivity (**2a**/**3a** = 90:10, entry 10). Ytterbium, titanium, and scandium sources usually promote the carbonyl allylation reaction as redox-inert Lewis acid catalysts.[15] Use of these metals, however, led to a significant

Table 1 Optimization of the Metal Source for Allylic Aminodecarboxylation of **1a**[a]

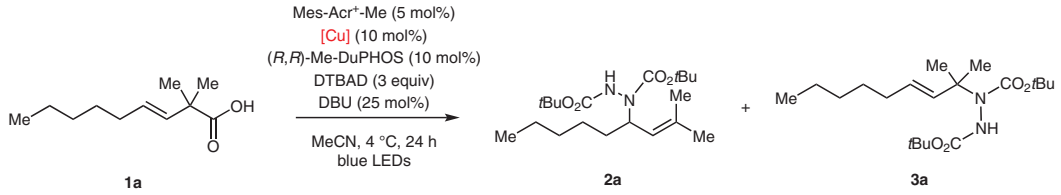


1a **2a** **3a**

Entry	[Metal]	Yield (%)[b]	Ratio **2a**/**3a**[c]
1	–	57	80:20[d]
2[e]	CuOAc	78	>99:1
3	$Bi(OAc)_3$	73	>99:1
4	$In(OH)_3$	53	>99:1
5[f]	$ZnEt_2$	51	>99:1
6	$Fe(OAc)_2$	53	>99:1
7[g]	$Ni(COD)_2$	36	>99:1
8	AgOAc	56	>99:1
9	$B(OH)_3$	49	>99:1
10	$Co(OAc)_2$	67	90:10
11	$Yb(CF_3SO_3)_3$	7	–
12	$Ti(OEt)_4$	6	–
13	$ScCl_3(H_2O)_6$	0	–
14	NaH	0	–
15	LiH	0	–
16	nBu_2Mg	0	–

[a] Reaction conditions: **1a** (0.2 mmol), [metal] (0.02 mmol), Mes-Acr$^+$-Me (0.01 mmol), DTBAD (0.6 mmol), DBU (0.05 mmol), MeCN (2 mL), 4 °C, blue LEDs, 24 h.
[b] Yields refer to isolated products.
[c] The product ratio was determined by ^{1}H NMR analysis of the crude mixture.
[d] Mixture of inseparable regioisomers (see Supporting Information).
[e] Addition of (*R*,*R*)-Me-DuPHOS (0.02 mmol).
[f] Addition of (*S*,*S*)-(–)-2,2′-isopropylidenebis(4-*tert*-butyl-2-oxazoline) (0.2 mmol), $ZnEt_2$ (1 equiv), substrate (2 equiv).
[g] Addition of 2,2′-bis[(4*S*)-4-benzyl-2-oxazoline] (0.02 mmol).

Table 2 Optimization of the Copper Source Using **1a**[a]



Entry	[Cu]	Yield (%)[b]	Ratio **2a**/**3a**[c]
1	Cu(I)OAc	78	>99:1
2	$Cu(I)PF_6(CH_3CN)_4$	77	>99:1
3	Cu(I)Mes	61	>99:1
4	Cu(I)CN	52	>99:1
5	Cu(I)Cl	0	>99:1
6	$Cu(II)(CF_3SO_3)_2$	64	>99:1
7	$Cu(II)(OMe)_2$	64	>99:1
8	$Cu(II)(OH)_2$	63	>99:1
9	$Cu(II)(OAc)_2$	56	>99:1
10	$Cu(II)Br_2$	45	>99:1

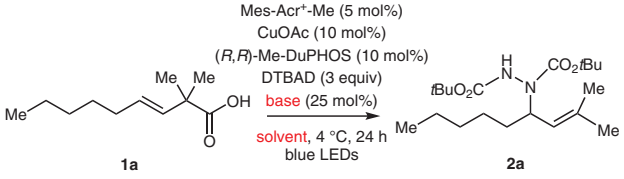
[a] Reaction conditions: **1a** (0.2 mmol), [Cu] (0.02 mmol), (*R*,*R*)-Me-DuPHOS (0.02 mmol), Mes-Acr$^+$-Me (0.01 mmol), DTBAD (0.6 mmol), DBU (0.05 mmol), MeCN (2 mL), 4 °C, blue LEDs, 24 h.
[b] Yields refer to isolated products.
[c] The product ratio was determined by ^{1}H NMR analysis of the crude mixture.

loss of the product yield (entries 11–13). Finally, the use of alkali and alkaline earth metals completely inhibited the reaction (entries 14–16).

This first set of experiments highlighted the potential of copper salts to promote the reaction in high yield and regioselectivity. A number of Cu(I) sources were therefore investigated (Table 2, entries 1–5). The use of weakly coordinating anions resulted in a similar yield as copper acetate (entry 2 vs 1), while a copper source bearing mesitylene as the ligand (CuMes), generating a copper carboxylate of the substrate through an acid–base reaction, decreased the yield (61%, entry 3). Replacing CuOAc with CuCN afforded less satisfactory results (52%, entry 4), while CuCl inhibited the reaction (entry 5). Cu(II) sources were also examined and afforded **2a** in a slightly lower yield compared with Cu(I)OAc (entries 6–10). Interestingly, all the reactions using copper as a metal complex catalyst proceeded with excellent regioselectivity.

Keeping acid **1a** as a model substrate (1 equiv), Mes-Acr$^+$-Me (5 mol%), CuOAc (10 mol%), (*R*,*R*)-Me-DuPHOS (10 mol%), and DBU (25 mol%), we next focused on the effects of the solvent on the reaction outcome (Table 3). Replacing MeCN with THF, CH_2Cl_2, or acetone drastically decreased the yield (20%, 18%, and 15%, respectively, vs 78%; entries 1–3 vs 5). The use of DMF led to complete recovery of the starting material (entry 4). The effect of the base was then examined, keeping MeCN as solvent. Organic bases such as

Table 3 Optimization of Solvent and Base Using **1a**[a]



Entry	Base	Solvent	Yield (%)[b]
1	DBU	THF	20
2	DBU	CH_2Cl_2	18
3	DBU	acetone	15
4	DBU	DMF	0
5	DBU	MeCN	78
6	DIPEA	MeCN	54
7	Et_3N	MeCN	19
8	pyridine	MeCN	12
9	Cs_2CO_3	MeCN	66

[a] Reaction conditions: **1a** (0.2 mmol), CuOAc (0.02 mmol), (*R*,*R*)-Me-DuPHOS (0.02 mmol), Mes-Acr$^+$-Me (0.01 mmol), DTBAD (0.6 mmol), base (0.05 mmol), solvent (2 mL), 4 °C, blue LEDs, 24 h.
[b] Yields refer to isolated products. All entries produced single regioisomer **2a**.

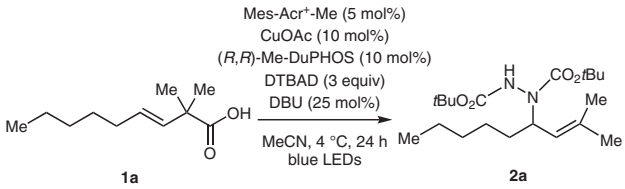
N,*N*-diisopropylethylamine (DIPEA), triethylamine, or pyridine (entries 6–8) and an inorganic base like Cs_2CO_3 (entry 9) gave less satisfactory results than DBU (entry 5).

To elucidate the critical parameters in this transformation, various control experiments were conducted. In the absence of light, no desired product was observed, revealing that visible light is essential for the reaction (Table 4, entry 1 vs 2). Moreover, no reaction occurred in the absence of the base, indicating that a catalytic amount of the base also plays an important role in initiating the reaction (entry 3). In addition, both copper and ligand proved to be essential for the reaction to proceed smoothly, as the absence of this combination led to decreased yield and regioselectivity (entries 4 and 5). Unfortunately, chiral ligands did not affect the enantioselectivity of the reaction (see Supporting Information for details).

With the optimized conditions in hand, the scope of azodicarboxylates was examined using **1a** as a partner (Scheme 2). Allylic hydrazides **2a**, **4a**, and **5a** from dialkyl azodicarboxylates were produced in good yields with controlled regioselectivity (78%, 68%, and 52% yield, respectively). Ether functional groups were tolerated, leading to the formation of the product **6a** (60% yield). It is noteworthy that dibenzyl azodicarboxylate completely inhibited the reaction. Replacing CuOAc/DuPHOS ligand with $Bi(OAc)_3$, however, produced **7a** in moderate yield (38%).

Next, the transformation of various β,γ-unsaturated carboxylic acids was envisioned with our optimized conditions (Table 5). The reaction proved to easily tolerate acyclic and cyclic (including heterocyclic) substituents at the α-position. The desired products **2a**, **2b**, **2c**, and **2d** were isolated in good to excellent yields (78%, 68%, 75%, and 76%, respectively; entries 1–4). The substrates **1e**, with no substituents at the γ-position (terminal alkene), and **1f**, bearing an aryl-

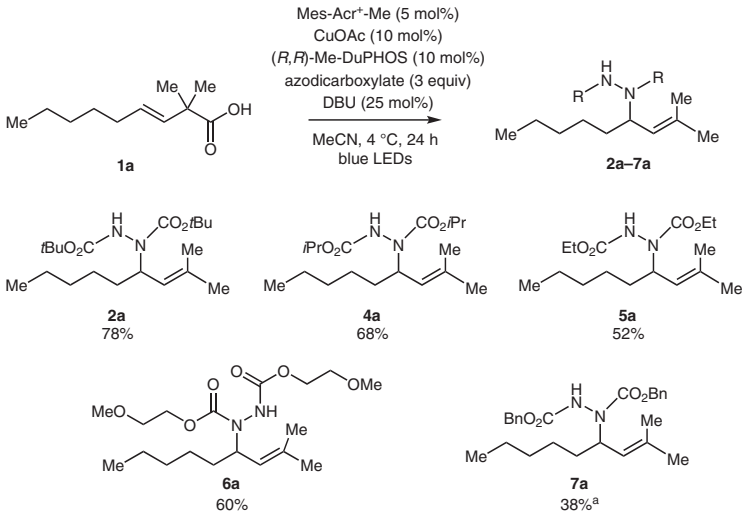
Table 4 Effects of Reaction Parameters[a]



Entry	Variation from the 'standard' reaction conditions	Yield (%)[b]
1	none	78
2	absence of LED irradiation	0
3	absence of DBU	0
4	absence of DuPHOS ligand	70[c]
5	absence of CuOAc	36[c]

[a] Standard reaction conditions: **1a** (0.2 mmol), CuOAc (0.02 mmol), (*R*,*R*)-Me-DuPHOS (0.02 mmol), Mes-Acr$^+$-Me (0.01 mmol), DTBAD (0.6 mmol), DBU (0.05 mmol), MeCN (2 mL), 4 °C, blue LEDs, 24 h.
[b] Yields refer to isolated products.
[c] Traces of regioisomer **3a**.

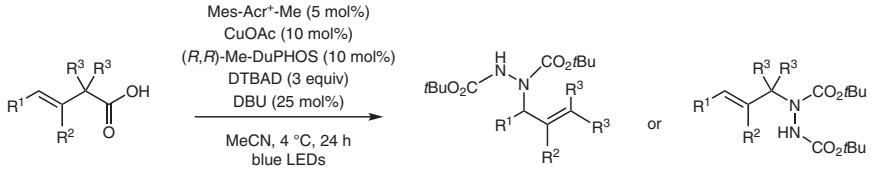
alkyl substituent at the γ-position, were submitted to the optimized conditions, leading to the isolation of regioisomers **2e** and **2f** in moderate yields (44% and 58%, entries 5 and 6). Interestingly, the reaction proceeded with excellent regioselectivity using acid **1e** compared with the copper-free conditions (85:15 ratio of inseparable regioisomers, see Supporting Information). The use of an α-unsubstituted substrate, (*E*)-non-3-enoic acid (**1g**), resulted in a lower yield (29%, entry 7) and the γ-regioselectivity was surprisingly observed. In this example, it is important to emphasize that the absence of copper and ligand induced a better yield of **2g**. The regioselectivity, however, was drastically decreased (49% yield, 7:3 ratio of regioisomers; see Sup-



Scheme 2 Scope of azodicarboxylates. [a] CuOAc-DuPHOS was replaced with $Bi(OAc)_3$.

porting Information). Using 1,2-β,γ-disubstituted substrate 1-cyclohexene-1-acetic acid (**1h**), the reaction proceeded smoothly to produce allylic hydrazide **2h** in good yield and high α-selectivity with the formation of stable cyclic alkene (56%, entry 8). Notably, with the copper-free conditions described by Tunge and co-workers,[9] no desired product was obtained. Substrates bearing alkyl substituents at the β- or γ-position provided the α-selective compounds **2i** and **2j** with moderate to good yields (60% and 51%, respectively; entries 9 and 10). The α-selectivity was favored in these cases with the formation of a more substituted double bond. Finally, the reaction was extended to α-amino acid **1k** to give the desired product **2k** in excellent yield (72%, entry 11). The α-selectivity was also observed by stabilizing the carbon-centered radical with the carbamate group at the α-position.

Table 5 Scope of β,γ-Unsaturated Carboxylic Acids[a]



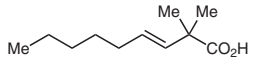
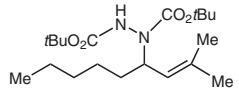
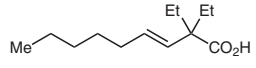
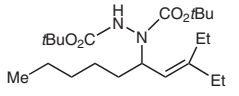
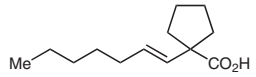
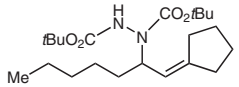
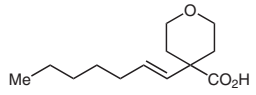
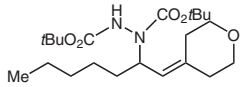
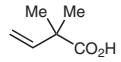
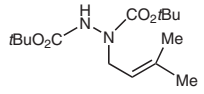
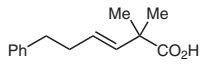
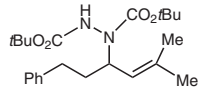
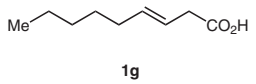
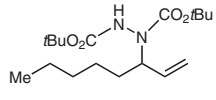
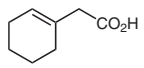
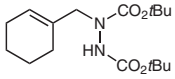
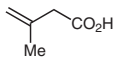
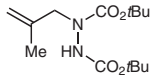
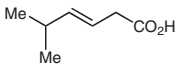
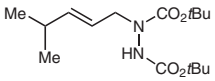
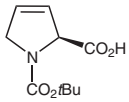
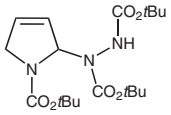
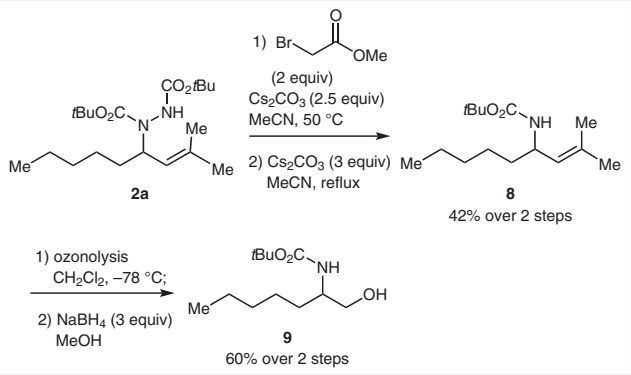
Entry	Acid	Product	Yield (%)[b]
1	 **1a**	 **2a**	78
2	 **1b**	 **2b**	68
3	 **1c**	 **2c**	75
4	 **1d**	 **2d**	76
5	 **1e**	 **2e**	44
6	 **1f**	 **2f**	58
7	 **1g**	 **2g**	29

Table 5 (continued)

Entry	Acid	Product	Yield (%)[b]
8	 **1h**	 **2h**	56
9	 **1i**	 **2i**	60
10	 **1j**	 **2j**	51
11	 **1k**	 **2k**	72

[a] Reaction conditions: β,γ-unsaturated carboxylic acid **1** (0.2 mmol), CuOAc (0.02 mmol), (*R*,*R*)-Me-DuPHOS (0.02 mmol), Mes-Acr$^+$-Me (0.01 mmol), DTBAD (0.6 mmol), DBU (0.05 mmol), MeCN (2 mL), 4 °C, blue LEDs, 24 h.
[b] Yields refer to isolated products.

Postfunctionalizations of the hydrazide derivative **2a** were examined (Scheme 3). The N–N bond could be easily cleaved using the Magnus protocol to give the corresponding carbamate **8** in 42% yield in two steps.[16] Derivative **8** under ozonolysis conditions, followed by treatment with $NaBH_4$, led to the formation of the corresponding 1,2-amino alcohol **9** as a potentially useful building block in 60% yield in only two steps.[17]



Scheme 3 Postfunctionalization of the product **2a**

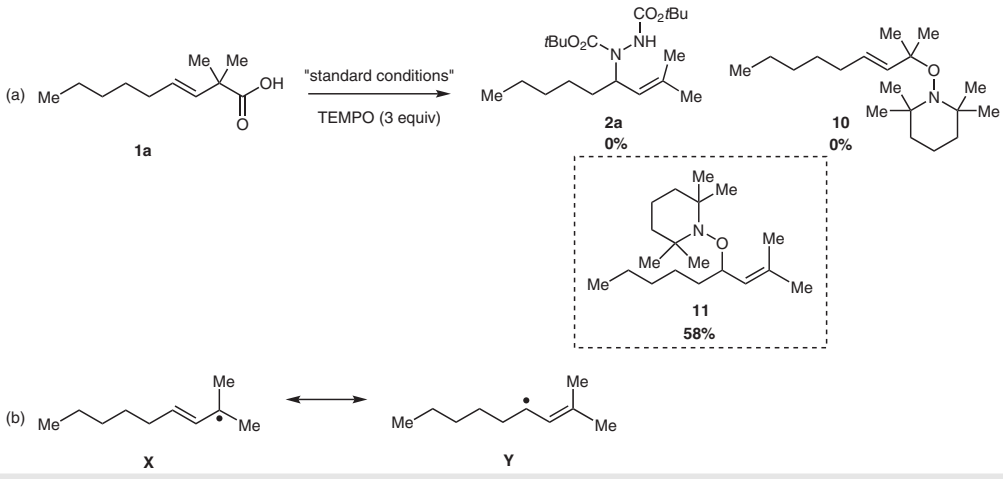
Next, to gain insight into the mechanism of decarboxylative allylation of β,γ-unsaturated carboxylic acids catalyzed by the copper/organophotoredox system, a radical-trapping experiment was carried out (Scheme 4, a). The reaction was completely inhibited in the presence of the radical scavenger TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl) under the standard conditions. Only the radical-trapping product **11** was formed and isolated in 58% yield. This result demonstrated that the allylic radical **X** (and the resonance form **Y**) was generated by the loss of CO_2 via single-electron oxidation by photoredox catalysis (Scheme 4, b).

On the basis of the above-described investigations and previous reports, a presumable mechanism is proposed (Scheme 5).[9,14a,18] The reaction is initiated by oxidation of carboxylate by photoexcited Mes-Acr$^+$-Me*, resulting in the allylic radical (**C**) after CO_2 extrusion.[19] The generated tertiary radical may be intercepted directly by the azodicarboxylate, providing the minor regioisomer (**3**) due to the steric hindrance of the radical. Otherwise, radical addition of the resonance form (**D**), which is expected to be stabilized by the substituted alkene, to DTBAD may occur to give the nitrogen-centered radical intermediate (**E**). The allylation step could be accelerated in the presence of the copper catalyst, possibly acting as a Lewis acid.[10a,20] Moreover, regioselectivity was improved in the presence of the copper catalyst, likely due to the enhanced steric hindrance of DTBAD by coordination to the copper complex. The copper(I) catalyst might not trap the carbon-centered radical (**C**) or (**D**), presumably because the electron-rich copper complex would preferentially combine with more electron-deficient radicals.[21] As a result, no enantioinduction was observed when using chiral ligands. The observations that

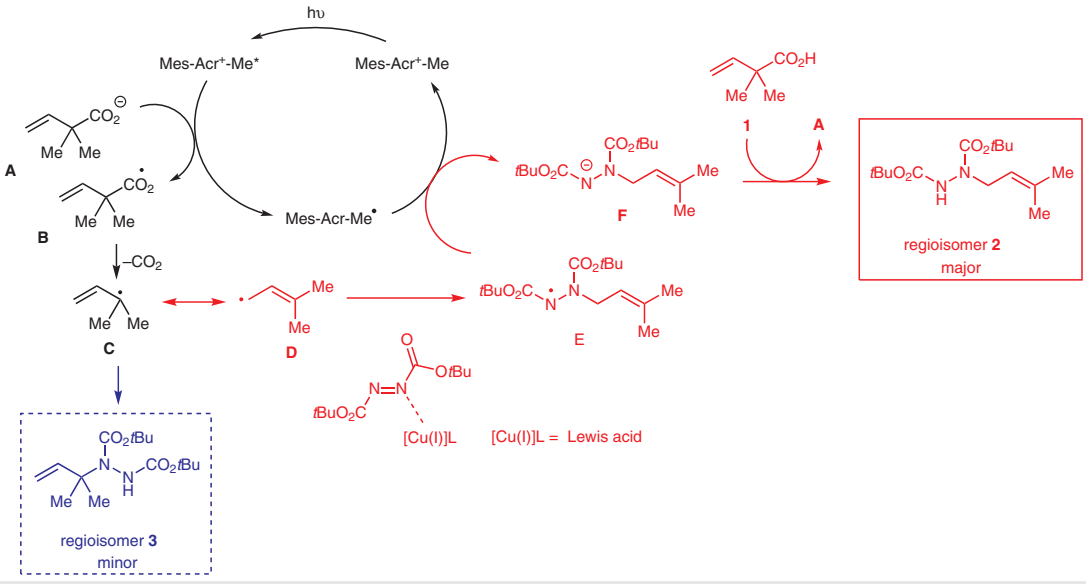
redox-innocent $Bi(OAc)_3$ afforded comparable and improved results to CuOAc for **1a** (Table 1, entries 2 and 3) and for formation of **7a** (Scheme 2), respectively, would support the hypothetical Lewis acid role of the catalytic CuOAc.[22] Finally, regeneration of the photocatalyst Mes-Acr$^+$-Me takes place with formation of the amide anion (**F**), which could deprotonate the acid substrate, leading to the carboxylate (**A**) and the predominant regioisomer (**2**).

In summary, regioselective allylic aminodecarboxylation of β,γ-unsaturated carboxylic acids involving a dual organophotoredox/copper catalysis was developed. The mild and efficient reaction conditions provided access to allylic hydrazides with total control of the regioselectivity and high yields. Simple postfunctionalizations of the synthesized allylic hydrazides could provide highly valuable building units.

All reagents were purchased from chemical suppliers and used without further purification. Reactions were performed using dried MeCN, THF, CH_2Cl_2, DMF, and acetone purchased from chemical suppliers. Allylic aminodecarboxylation reactions were carried out in dried and degassed solvents under argon atmosphere. Analytical TLC was performed on commercial silica gel $60F_{254}$ plates. Flash column chromatography was performed on silica gel 60 (40–63 μm, purchased from Kanto Chemical Co., Inc.) or by using a Biotage® Isolera™ One 3.0 system with a prepacked Biotage® SNAP Ultra column. NMR spectra were recorded on JEOL ECX500 (500 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR) and JEOL ECS400 (400 MHz for ^{1}H NMR, 100 MHz



Scheme 4 Mechanistic study of the reaction



Scheme 5 Proposed mechanism

for ^{13}C NMR) spectrometers. Chemical shifts are reported in ppm on the δ scale relative to residual $CHCl_3$ (δ = 7.26 for ^1H NMR, δ = 77.16 for ^{13}C NMR) as an internal reference. Coupling constants (*J*) are reported in hertz units (Hz); multiplicities are described using standard abbreviations. ESI-mass spectra were measured on a Shimadzu LCMS-2020 spectrometer (for LRMS) and a JEOL JMS-T100LC AccuTOF spectrometer (for HRMS). IR spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. The syntheses of substrates **1a–1d**, **1f**, **1i**, and **1j** are described in the Supporting Information.

Allylic Aminodecarboxylation of β,γ-Unsaturated Carboxylic Acids; General Procedure

A β,γ-unsaturated carboxylic acid **1** (1 equiv) in degassed MeCN (concn = 0.1 M) was added into a 4-mL vial equipped with a Teflon-coated magnetic stirring bar. The vial was sealed with a septum cap and the internal atmosphere was exchanged with argon via three repeated cycles of vacuum–refill. Then, 9-mesityl-10-methylacridinium perchlorate (5 mol%) was added, followed by CuOAc (10 mol%), (*R*,*R*)-Me-DuPHOS (10 mol%), the azodicarboxylate (3 equiv), and DBU (25 mol%). The vial was irradiated with blue LEDs (Aldrich® micro photochemical reactor, 100–240 V, 435–445 nm) under vigorous stirring at 4 °C (cold room). After 24 h, the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (pentane/EtOAc, 9:1 to 8:2) which provided the desired product.

Di-*tert*-butyl 1-(2-Methylnon-2-en-4-yl)hydrazine-1,2-dicarboxylate (2a)

Prepared from (*E*)-2,2-dimethylnon-3-enoic acid (**1a**) and di-*tert*-butyl azodicarboxylate.

Colorless oil; yield: 61 mg (78%).

R_f = 0.42 (pentane/EtOAc, 9:1).

IR (KBr): 3267, 2930, 1699, 1456, 1366, 1244, 1160, 1049, 865, 730 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.22–5.89 (br s, 1 H, NH), 5.06 (d, *J* = 8.5 Hz, 1 H), 4.89–4.60 (br m, 1 H), 1.76–1.58 (m, 6 H), 1.45 (s, 18 H), 1.39–1.14 (br m, 8 H), 0.87 (t, *J* = 5.6 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.9, 123.9, 80.7, 55.5, 33.3, 31.8, 28.4, 28.2, 25.7, 25.6, 22.6, 18.5, 14.0.

LRMS (ESI): *m*/*z* = 393 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{38}N_2O_4Na$: 393.2729; found: 393.2728.

Di-*tert*-butyl 1-(3-Ethyldec-3-en-5-yl)hydrazine-1,2-dicarboxylate (2b)

Prepared from (*E*)-2,2-diethylnon-3-enoic acid (**1b**) and di-*tert*-butyl azodicarboxylate.

Colorless foam; yield: 72 mg (68%).

R_f = 0.38 (pentane/EtOAc, 9:1).

IR (KBr): 2966, 1702, 1366, 1162, 1022, 755 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.07–5.69 (br s, 1 H, NH), 5.03 (d, *J* = 9.0 Hz, 1 H), 4.87–4.73 (br m, 1 H), 2.10 (q, *J* = 7.5 Hz, 2 H), 2.03 (q, *J* = 7.0 Hz, 2 H), 1.70–1.22 (m, 8 H), 1.46 (s, 18 H), 0.99 (t, *J* = 7.5 Hz, 3 H), 0.97 (t, *J* = 7.5 Hz, 3 H), 0.88 (t, *J* = 6.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.9, 121.7, 80.9, 54.8, 33.6, 31.9, 29.1, 28.5, 28.4, 25.9, 24.1, 22.7, 14.1, 13.4, 12.9.

LRMS (ESI): *m*/*z* = 421 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{42}N_2O_4Na$: 421.3042; found: 421.3021.

Di-*tert*-butyl 1-(1-Cyclopentylideneheptan-2-yl)hydrazine-1,2-dicarboxylate (2c)

Prepared from (*E*)-1-(hept-1-en-1-yl)cyclopentane-1-carboxylic acid (**1c**) and di-*tert*-butyl azodicarboxylate.

Colorless foam; yield: 40 mg (75%).

R_f = 0.37 (pentane/EtOAc, 9:1).

IR (KBr): 3266, 2957, 1701, 1455, 1366, 1253, 1162, 1048, 1020, 864, 758 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.08–5.93 (br s, 1 H, NH), 5.19 (d, *J* = 8.5 Hz, 1 H), 4.72–4.54 (br m, 1 H), 2.42–2.08 (br m, 4 H), 1.72–1.51 (m, 5 H), 1.45 (s, 18 H), 1.35–1.06 (br m, 7 H), 0.87 (t, *J* = 5.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.1, 130.6, 119.1, 80.8, 56.9, 33.8, 33.3, 31.9, 29.4, 28.5, 28.4, 26.5, 26.3, 25.9, 22.8, 14.1.

LRMS (ESI): *m*/*z* = 419 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{40}N_2O_4Na$: 419.2886; found: 419.2898.

Di-*tert*-butyl 1-(1-(Tetrahydro-4*H*-pyran-4-ylidene)heptan-2-yl)hydrazine-1,2-dicarboxylate (2d)

Prepared from (*E*)-4-(hept-1-en-1-yl)tetrahydro-2*H*-pyran-4-carboxylic acid (**1d**) and di-*tert*-butyl azodicarboxylate.

White foam; yield: 47 mg (76%).

R_f = 0.24 (pentane/EtOAc, 9:1).

IR (KBr): 3313, 2977, 2857, 1801, 1746, 1456, 1367, 1251, 1049, 854, 759 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.05–5.93 (br s, 1 H, NH), 5.15 (d, *J* = 8.5 Hz, 1 H), 4.85–4.74 (br m, 1 H), 3.89–3.57 (br m, 4 H), 2.48–2.26 (br m, 2 H), 2.25–2.15 (br m, 2 H), 1.56–1.48 (br m, 4 H), 1.47 (s, 9 H), 1.46 (s, 9 H), 1.33–1.23 (br m, 4 H), 0.88 (t, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.8, 122.3, 83.7, 81.1, 69.6, 68.9, 54.2, 37.1, 33.2, 31.8, 30.8, 28.4, 28.3, 28.1, 25.9, 22.7, 14.1.

LRMS (ESI): *m*/*z* = 435 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{40}N_2O_5Na$: 435.2835; found: 435.2811.

Di-*tert*-butyl 1-(3-Methylbut-2-en-1-yl)hydrazine-1,2-dicarboxylate (2e)

Prepared from 2,2-dimethylbut-3-enoic acid (**1e**) and di-*tert*-butyl azodicarboxylate.

White foam; yield: 35 mg (44%).

R_f = 0.41 (pentane/EtOAc, 9:1).

IR (KBr): 3319, 2977, 1705, 1455, 1366, 1254, 1157 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$, 50 °C): δ = 6.10–5.75 (br m, 1 H, NH), 4.97 (t, *J* = 7.0 Hz, 1 H), 3.79 (d, *J* = 6.0 Hz, 2 H), 1.47 (s, 3 H), 1.40 (s, 3 H), 1.21 (s, 9 H), 1.21 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$, 50 °C): δ = 155.5, 136.7, 119.4, 81.2, 47.4, 28.4, 25.8, 17.9.

LRMS (ESI): *m*/*z* = 323.0 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{28}N_2O_4Na$: 323.1947; found: 323.1938.

Data are in accordance with the literature.[23]

Di-*tert*-butyl 1-(5-Methyl-1-phenylhex-4-en-3-yl)hydrazine-1,2-dicarboxylate (2f)

Prepared from (*E*)-2,2-dimethyl-6-phenylhex-3-enoic acid (**1f**) and di-*tert*-butyl azodicarboxylate.

Pale foam; yield: 39 mg (58%).

R_f = 0.40 (pentane/EtOAc, 9:1).

IR (KBr): 3267, 2977, 2930, 1703, 1455, 1392, 1366, 1250, 1160, 699, 654 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$, 50 °C): δ = 7.32–7.23 (m, 2 H), 7.23–7.12 (m, 3 H), 6.05–5.80 (br m, 1 H), 5.13 (d, *J* = 9.0 Hz, 1 H), 4.89–4.69 (br m, 1 H), 2.86–2.56 (br m, 2 H), 2.09–1.91 (br m, 1 H), 1.72 (s, 3 H), 1.64 (s, 3 H), 1.71–1.59 (br m, 1 H), 1.47 (s, 9 H), 1.46 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$, 50 °C): δ = 155.9, 155.0, 142.5, 135.9, 128.6, 128.4, 125.8, 123.5, 81.1, 55.4, 35.1, 32.6, 28.4, 28.4, 25.8, 18.7.

LRMS (ESI): *m*/*z* = 427.1 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{36}N_2O_4Na$: 427.2573; found: 427.2566.

Di-*tert*-butyl 1-(Oct-1-en-3-yl)hydrazine-1,2-dicarboxylate (2g)

Prepared from (*E*)-non-3-enoic acid (**1g**) and di-*tert*-butyl azodicarboxylate.

Colorless oil; yield: 19 mg (29%).

R_f = 0.35 (pentane/EtOAc, 9:1).

IR (KBr): 3303, 2929, 1705, 1456, 1392, 1157, 601 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.10–5.88 (br s, 1 H, NH), 5.88–5.73 (m, 1 H), 5.19–5.08 (br m, 2 H), 4.59–4.44 (br m, 1 H), 1.74–1.59 (br m, 1 H), 1.46 (s, 18 H), 1.40–1.22 (br m, 7 H), 0.88 (br m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.1, 137.1, 116.4, 81.3, 60.4, 31.8, 31.5, 28.4, 28.4, 25.9, 22.7, 14.1.

LRMS (ESI): *m*/*z* = 365 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{34}N_2O_4Na$: 365.2416; found: 365.2419.

Di-*tert*-butyl 1-(Cyclohex-1-en-1-ylmethyl)hydrazine-1,2-dicarboxylate (2h)

Prepared from 1-cyclohexene-1-acetic acid (**1h**) and di-*tert*-butyl azodicarboxylate.

Colorless foam; yield: 23 mg (56%).

R_f = 0.34 (pentane/EtOAc, 9:1).

IR (KBr): 2930, 1699, 1366, 1156, 759 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.32–5.86 (br s, 1 H, NH), 5.60–5.45 (br m, 1 H), 4.06–3.73 (br m, 2 H), 2.09–1.97 (br m, 2 H), 1.96–1.83 (br m, 2 H), 1.68–1.52 (br m, 4 H), 1.46 (s, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7, 133.4, 125.1, 81.2, 56.2, 28.4, 26.6, 25.3, 22.8, 22.5.

LRMS (ESI): *m*/*z* = 349 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{30}N_2O_4Na$: 349.2103; found: 349.2105.

Di-*tert*-butyl 1-(2-Methylallyl)hydrazine-1,2-dicarboxylate (2i)

Prepared from 3-methylbut-3-enoic acid (**1i**) and di-*tert*-butyl azodicarboxylate.

Colorless foam; yield: 37 mg (60%).

R_f = 0.31 (pentane/EtOAc, 9:1).

IR (KBr): 3585, 2278, 1702, 1069, 667 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.36–6.07 (br s, 1 H, NH), 4.87 (s, 1 H), 4.81 (s, 1 H), 4.07–3.87 (br m, 2 H), 1.73 (s, 3 H), 1.47 (s, 9 H), 1.47 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 140.9, 112.9, 81.4, 81.3, 53.5, 29.9, 28.4, 20.3.

LRMS (ESI): *m*/*z* = 309 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{26}N_2O_4Na$: 309.1790; found: 309.1799.

Di-*tert*-butyl 1-((*E*)-4-Methylpent-2-en-1-yl)hydrazine-1,2-dicarboxylate (2j)

Prepared from (*E*)-5-methylhex-3-enoic acid (**1j**) and di-*tert*-butyl azodicarboxylate.

Colorless foam; yield: 31 mg (51%).

R_f = 0.33 (pentane/EtOAc, 9:1).

IR (KBr): 3326, 2977, 1707, 1652, 1541, 1365, 1152 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.39–6.11 (br s, 1 H, NH), 5.56 (dd, *J* = 6.5, 15.5 Hz, 1 H), 5.40 (dtd, *J* = 1.0, 6.5, 15.5 Hz, 1 H), 4.05–3.91 (br m, 2 H), 2.35–2.23 (m, 1 H), 1.47 (s, 9 H), 1.46 (s, 9 H), 0.98 (d, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.4, 141.9, 121.5, 81.2, 53.1, 51.5, 30.9, 28.3, 22.4.

LRMS (ESI): *m*/*z* = 337 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{30}N_2O_4Na$: 337.2103; found: 337.2106.

Di-*tert*-butyl 1-(1-(*tert*-Butoxycarbonyl)-2,5-dihydro-1*H*-pyrrol-2-yl)hydrazine-1,2-dicarboxylate (2k)

Prepared from 1-(*tert*-butoxycarbonyl)-2,5-dihydro-1*H*-pyrrole-2-carboxylic acid (**1k**) and di-*tert*-butyl azodicarboxylate.

Yellow foam; yield: 76 mg (72%).

R_f = 0.35 (pentane/EtOAc, 8:2).

IR (KBr): 3314, 2978, 1707, 1478, 1418, 1391, 1327, 1244, 1164, 896, 635 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$, 50 °C): δ = 6.73–6.53 (br m, 1 H), 6.21–5.89 (br m, 2 H), 5.84–5.59 (br m, 1 H), 4.21–3.95 (br m, 2 H), 1.47 (s, 18 H), 1.44 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$, 50 °C): δ = 155.9, 120.2, 111.9, 83.7, 81.6, 52.8, 28.4, 28.2.

LRMS (ESI): *m*/*z* = 422.1 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{33}N_3O_6Na$: 422.2267; found: 422.2265.

Diisopropyl 1-(2-Methylnon-2-en-4-yl)hydrazine-1,2-dicarboxylate (4a)

Prepared from (*E*)-2,2-dimethylnon-3-enoic acid (**1a**) and diisopropyl azodicarboxylate.

Colorless foam; yield: 25 mg (68%).

R_f = 0.35 (pentane/EtOAc, 9:1).

IR (KBr): 2927, 2359, 1715, 1385, 1109, 762 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.17–6.02 (br s, 1 H, NH), 5.06 (d, *J* = 8.0 Hz, 1 H), 5.01–4.88 (br m, 2 H), 4.87–4.69 (m, 1 H), 1.70 (s, 3 H), 1.67 (s, 3 H), 1.49–1.02 (m, 20 H), 0.87 (t, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.4, 155.6, 136.1, 123.4, 69.9, 69.5, 55.6, 33.2, 31.8, 25.8, 22.8, 22.2, 22.2, 22.1, 18.7, 14.2.

LRMS (ESI): *m*/*z* = 365 [M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{34}N_2O_4Na$: 365.2416; found: 365.2438.

Diethyl 1-(2-Methylnon-2-en-4-yl)hydrazine-1,2-dicarboxylate (5a)

Prepared from (*E*)-2,2-dimethylnon-3-enoic acid (**1a**) and diethyl azodicarboxylate.

Colorless foam; yield: 24 mg (52%).

R_f = 0.31 (pentane/EtOAc, 9:1).

IR (KBr): 2932, 1708, 1412, 1222, 1061, 667 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.26–6.00 (br s, 1 H, NH), 5.06 (d, *J* = 9.0 Hz, 1 H), 4.85–4.71 (br m, 1 H), 4.18 (q, *J* = 7.0 Hz, 4 H), 1.70 (s, 3 H), 1.68 (s, 3 H), 1.47–1.16 (m, 14 H), 0.87 (t, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.8, 156.0, 136.2, 123.1, 62.4, 62.0, 55.9, 33.1, 31.8, 25.8, 22.7, 18.7, 14.6, 14.6, 14.2.

LRMS (ESI): *m*/*z* = 337 [M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{30}N_2O_4Na$: 337.2103; found: 337.2090.

Bis(2-methoxyethyl) 1-(2-Methylnon-2-en-4-yl)hydrazine-1,2-dicarboxylate (6a)

Prepared from (*E*)-2,2-dimethylnon-3-enoic acid (**1a**) and bis(2-methoxyethyl) azodicarboxylate.

Colorless foam; yield: 21 mg (60%).

R_f = 0.28 (pentane/EtOAc, 1:1).

IR (KBr): 3284, 2927, 1757, 1714, 1519, 1455, 1245, 1128, 1067, 850, 759 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.59–6.29 (br s, 1 H, NH), 5.05 (d, *J* = 8.8 Hz, 1 H), 4.92–4.67 (br m, 1 H), 4.39–4.14 (br m, 4 H), 3.68–3.50 (br m, 4 H), 3.39 (s, 3 H), 3.36 (s, 3 H), 1.70 (s, 3 H), 1.68 (s, 3 H), 1.44–1.17 (m, 8 H), 0.87 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.5, 135.4, 122.9, 70.8, 65.4, 64.9, 59.1, 59.0, 33.1, 31.8, 25.8, 25.7, 22.7, 14.2.

LRMS (ESI): *m*/*z* = 397 [M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{34}N_2O_6Na$: 397.2765; found: 397.2747.

Dibenzyl 1-(2-Methylnon-2-en-4-yl)hydrazine-1,2-dicarboxylate (7a)

Prepared from (*E*)-2,2-dimethylnon-3-enoic acid (**1a**) and dibenzyl azodicarboxylate; reaction conditions: $Bi(OAc)_3$ utilized instead of CuOAc/DuPHOS ligand.

Colorless foam; yield: 18 mg (38%).

R_f = 0.21 (pentane/EtOAc, 9:1).

IR (KBr): 2926, 2361, 1709, 1407, 1217, 1049, 600 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48–7.17 (br m, 10 H), 6.48–6.25 (br s, 1 H, NH), 5.28–5.08 (br m, 4 H), 5.05 (d, *J* = 6.5 Hz, 1 H), 4.90–4.68 (br m, 1 H), 1.74–1.01 (br m, 14 H), 0.92–0.73 (br m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.8, 136.2, 135.9, 128.7, 128.6, 128.5, 128.3, 128.3, 128.1, 122.9, 68.1, 67.8, 56.0, 33.2, 31.8, 25.8, 22.7, 18.7, 14.2.

LRMS (ESI): *m*/*z* = 461 [M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{34}N_2O_4Na$: 461.2416; found: 461.2433.

Di-*tert*-butyl (*E*)-1-(2-Methylnon-3-en-2-yl)hydrazine-1,2-dicarboxylate (3a)

Prepared from (*E*)-2,2-dimethylnon-3-enoic acid (**1a**) and di-*tert*-butyl azodicarboxylate under standard conditions, in the absence of CuOAc and DuPHOS ligand.

Mixture of inseparable regioisomers **2a** and **3a** (ratio **2a**/**3a** = 80:20).

^{1}H NMR (400 MHz, $CDCl_3$, 50 °C): δ = 6.28–5.89 (br m, 0.8 H, NH, **2a**), 5.86–5.75 (br m, 0.2 H, NH, **3a**), 5.66 (d, *J* = 14.8 Hz, 0.2 H, **3a**), 5.43 (dt, *J* = 6.4, 16.0 Hz, 0.2 H, **3a**), 5.06 (d, *J* = 8.8 Hz, 0.8 H, **2a**), 4.94–4.57 (br m, 0.8 H, **2a**), 2.00 (q, *J* = 7.2 Hz, 0.4 H, **3a**), 1.79–1.58 (m, 6 H, **2a**, **3a**), 1.54–1.03 (m, 25.6 H, **2a**, **3a**), 0.93–0.80 (m, 3 H, **2a**, **3a**).

Di-*tert*-butyl 1-(2-Methylbut-3-en-2-yl)hydrazine-1,2-dicarboxylate (3e)

Prepared from 2,2-dimethylbut-3-enoic acid (**1e**) and di-*tert*-butyl azodicarboxylate under standard conditions, in the absence of CuOAc and DuPHOS ligand.

Mixture of inseparable regioisomers **2e** and **3e** (ratio **2e**/**3e** = 85:15).

^{1}H NMR (500 MHz, $CDCl_3$, 50 °C): δ = 6.49–6.08 (br m, 1.7 H, NH, **2e**), 6.01–5.91 (br m, 0.3 H, NH, **3e**), 5.21 (t, *J* = 7.0 Hz, 1.3 H, **2e**), 5.11–5.00 (m, 0.4 H, **3e**), 4.99–4.93 (m, 0.2 H, **3e**), 1.73 (s, 3 H, **2e**, **3e**), 1.65 (s, 3 H, **2e**, **3e**), 1.46 (s, 18 H, **2e**, **3e**).

Di-*tert*-butyl (*E*)-1-(Oct-2-en-1-yl)hydrazine-1,2-dicarboxylate (3g)

Prepared from (*E*)-non-3-enoic acid (**1g**) and di-*tert*-butyl azodicarboxylate under standard conditions, in the absence of CuOAc and DuPHOS ligand.

Mixture of separable regioisomers **2g** and **3g** (ratio **2g**/**3g** = 7:3).

Colorless oil; yield: 29 mg (49%).

R_f = 0.35 (pentane/EtOAc, 9:1).

IR (KBr): 3321, 2925, 1716, 1456, 1393, 1367, 1254, 1155, 629 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.36–5.93 (br s, 1 H, NH), 5.64–5.53 (br m, 1 H), 5.49–5.37 (br m, 1 H), 4.11–3.86 (br m, 2 H), 2.02 (q, *J* = 7.2 Hz, 2 H), 1.46 (s, 18 H), 1.38–1.26 (br m, 6 H), 0.88 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.4, 135.2, 124.5, 81.3, 61.5, 32.4, 31.5, 29.9, 29.0, 28.4, 22.6, 14.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{34}N_2O_4Na$: 365.2416; found: 365.2407.

***tert*-Butyl (2-Methylnon-2-en-4-yl)carbamate (8)**

In a round-bottom flask were placed di-*tert*-butyl 1-(2-methylnon-2-en-4-yl)hydrazine-1,2-dicarboxylate (**2a**, 1.0 equiv) and Cs_2CO_3 (2.5 equiv) in MeCN (concn = 0.175 M) under argon. At r.t., methyl bromoacetate (2.0 equiv) was added. The mixture was heated at 50 °C for 18 h. The reaction was quenched with aq NH_4Cl and the resulting mixture was extracted with EtOAc (3 ×). The combined organic phases were dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The crude was placed in a round-bottom flask in MeCN (concn = 0.18 M). Then, Cs_2CO_3 (3 equiv) was added at r.t. The mixture was heated at reflux for 16 h. The reaction was quenched with aq NH_4Cl and the resulting mixture was extracted with EtOAc (3 ×). The combined organic phases were dried over Na_2SO_4, filtered,

and the solvent was removed under reduced pressure. The crude residue was purified by silica gel flash chromatography (pentane/EtOAc, 98:2 to 95:5).

White foam; yield: 21 mg (42% over 2 steps).

R_f = 0.51 (pentane/EtOAc, 9:1).

IR (KBr): 3419, 2284, 1055, 782, 601 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.93 (d, *J* = 8.5 Hz, 1 H), 4.44–4.28 (br m, 1 H), 4.28–4.15 (br m, 1 H), 1.69 (s, 3 H), 1.68 (s, 3 H), 1.43 (s, 9 H), 1.39–1.19 (br m, 8 H), 0.87 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.5, 134.6, 126.5, 79.1, 49.4, 36.7, 31.9, 28.6, 25.7, 25.5, 22.8, 18.5, 14.1.

LRMS (ESI): *m*/*z* = 278 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{29}NO_2Na$: 278.2096; found: 278.2077.

tert-Butyl (1-Hydroxyheptan-2-yl)carbamate (9)

A solution of *tert*-butyl (2-methylnon-2-en-4-yl)carbamate (**8**; 20 mg, 0.08 mmol, 1 equiv) in CH_2Cl_2 (1 mL) was cooled to –78 °C, which was followed by bubbling of ozone (converted from oxygen by an ozone generator) for 5 min with stirring. After the reaction color changed to blue, oxygen was bubbled through the solution to remove ozone. MeOH (0.5 mL) and $NaBH_4$ (3 equiv) were added to the mixture at –78 °C. Then, the reaction mixture was allowed to warm to r.t. for 1 h. The solvents were removed in vacuo and the residue was purified by silica gel flash chromatography (pentane/EtOAc, 6:4).

White foam; yield: 10 mg (60% over 2 steps).

R_f = 0.18 (pentane/EtOAc, 9:1).

IR (KBr): 3853, 3585, 3346, 2929, 2359, 1684, 1508, 1457, 1365, 1251, 1061, 670 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.62–4.42 (br s, 1 H, NH), 3.70–3.52 (br m, 2 H), 3.57–3.51 (br m, 1 H), 2.15–1.89 (br m, 1 H), 1.46 (s, 9 H), 1.43–1.24 (br m, 8 H), 0.90 (t, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.7, 79.8, 66.3, 53.3, 31.9, 31.8, 28.6, 25.8, 22.7, 14.0.

LRMS (ESI): *m*/*z* = 232 $[M + H]^+$, 254 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{25}NO_3Na$: 254.1732; found: 254.1716.

2,2,6,6-Tetramethyl-1-((2-methylnon-2-en-4-yl)oxy)piperidine (11)

Using the general procedure, prepared from (*E*)-2,2-dimethylnon-3-enoic acid (**1a**) and di-*tert*-butyl azodicarboxylate, with the addition of TEMPO (3 equiv).

Orange foam; yield: 22 mg (58%).

R_f = 0.63 (pentane/EtOAc, 95:5).

IR (KBr): 2871, 1774, 1459, 1375, 1248, 1154, 1048, 957, 865 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 5.11–5.03 (m, 1 H), 4.33 (td, *J* = 4.0, 8.5 Hz, 1 H), 1.63 (s, 3 H), 1.62 (s, 3 H), 1.44–1.35 (m, 4 H), 1.35–1.17 (m, 10 H), 1.15 (s, 6 H), 1.08 (s, 6 H), 0.87 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 132.5, 129.1, 80.6, 60.3, 40.6, 39.5, 35.1, 32.3, 31.7, 27.9, 25.9, 25.2, 22.8, 20.7, 18.7, 17.6, 17.2, 14.1.

LRMS (ESI): *m*/*z* = 296 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{38}NO$: 296.2875; found: 296.2890.

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Supporting Information

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