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Report

Visible light, Cu(I)-catalyzed, Electron-deficient olefins, β-amino alcohols, *O*-benzoylhydroxylamines

CJC Chinese Journal of Chemistry 中国化学 - An International Journal

Visible Light Driven Copper(I) Catalyzed Oxyamination of Electron Deficient Alkenes

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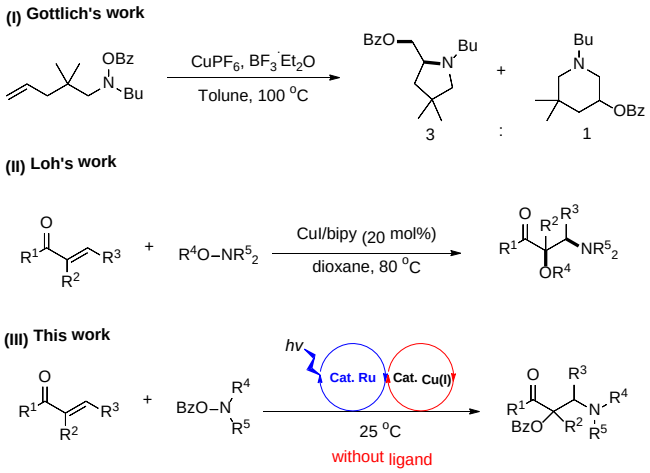
Summary of main observation and conclusion A visible light driven Cu(I)-catalyzed intermolecular oxyamination of electron-deficient olefins has been achieved by using *O*-benzoylhydroxylamines as donors both for amine and oxygen. The transformation properties afford mild conditions and a wide substrate scope, providing access to ester derivatives of β-amino alcohols with good yields and high regioselectivity.

Background and Originality Content

Ester derivatives of β-amino alcohols[1] are not only present in natural compounds and bioactive molecules but also have been utilized in modern organic synthesis as ligands or auxiliaries. Therefore, considerably more efforts have been made for the pursiut of new synthetic methods for the construction of β-amino alcohols derivatives. Electrophilic difunctionalization of olefins[2-5] has proven to be a useful integrated strategy toward synthesis of polyfunctionalized compounds. Particularly, the straightforward conversion of alkenes via an oxyamination process are efficient approaches to access β-amino alcohols derivatives with concomitant formation of C-O and C-N bonds. In 2002, Gottlich's group developed a Cu-catalyzed intramolecular oxyamination of alkenes, providing pyrrolidine and piperidine in a 3:1 regioselectivity (**Scheme 1**, I).[6] In 2007, Yoon and co-workers reported an impressive work on copper(II)-catalyzed regioselective addition of *N*-sulfonyl oxaziridine to styrenes and electron-rich olefins.[7] In 2016, Loh and co-workers disclosed a copper/bipy-catalyzed intermolecular oxyamination of electron-deficient olefins by using *N*-acyloxyamines as donors for amine and oxygen (**Scheme 1**, II)[8]. Although these available synthetic methods were shown as efficient and powerful strategies to introduce amino groups and hydroxyl groups in the same time, the methods often require high reaction temperature and suffer a significant challenge of controlling the regioselectivity. Therefore, the development of an atom-economical and environment-beneficial method for intermolecular alkene oxyamination would be important from either an academic or industrial development perspective.

Visible light driven photocatalysis is a powerful tool that can be integrated to solve useful organic transformations under economical and environmental benefits methods.[9] Through the tireless efforts of chemists, a good number of significant reactions, notably visible-light-driven difunctionalization of alkenes have been developed.[10] Nevertheless, significant progress has been made in the metal-catalyzed amination using *O*-benzoylhydroxylamines as an electrophilic amination reagent,[11] the initial electrophilic activation of alkenes with *O*-benzoylhydroxylamines in visible-light photoredox catalysis reaction has not been achieved. In addition, the application of *O*-benzoylhydroxylamines in a single transformation as well as amine and oxygen donors has been much less explored.[8, 11,12] Herein, we wish to exploit the visible light driven regioselective oxyamination of electron-deficient olefins with *O*-benzoylhydroxylamines (**Scheme 1**, III).

Scheme 1. Difunctionalization of alkenes for the synthesis of valuable ester derivatives of β-amino alcohols

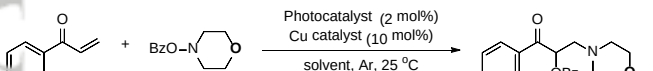


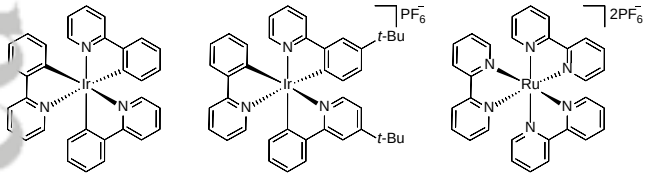
Results and Discussion

Our study began with the visible light-promoted copper(I)-catalyzed difunctionalization reaction of unsaturated ketone **1a** and *O*-benzoylhydroxylamine **2a** (Table 1). In DCM at 25 °C under an Ar atmosphere, a catalytic amount of CuI (10

mol%) and *fac*-Ir(ppy)$_3$ (2 mol%) as the cooperative catalysts delivered the desired product **3aa** in 64% yield under 40 h irradiated by a 3 W blue LED lamp (Table 1, entry 1). Further investigation of copper catalysts indicated that only copper halides such as CuCl, $CuCl_2$, CuBr, and $CuBr_2$ (Table 1, entry 2-5) showed catalytic activity for this reaction and the order in which the yield increased Cl < Br < I, indicating that halide counter ions significant effect this process.[13] To further confirmed the role of halides, numbers of coppers such as $Cu(CH_3CN)_4PF_6$, $Cu(CH_3CN)_4BF_4$, CuOAc, $Cu(OAc)_2$, and $Cu(OTf)_2$ were used as catalysts. Regretfully, all of them failed to give any product (Table 1, entries 6-10). $Ir(ppy)_2(dtbbpy)PF_6$ and $Ru(bpy)_3(PF_6)_2$ as the commonly photocatalysts were also tested (Table 1, entries 11-12). To our delight, the desired product **3aa** was obtained in 85% yield (Table 1, entry 12), while $Ru(bpy)_3(PF_6)_2$ was) was used as photocatalyst. The use of other solvents, such as DCE, 1,4-dioxane, Et_2O and THF, didn't give the best yields of **3aa** (Table 1, entries 13-16). In the absence of photocatalyst, copper catalysts or visible light could not give the product at room temperature (Table 1, entries 17-19). It was demonstrated that the cooperative catalysts and irradiation were the things of indispensability in this transformation.

Table 1. Optimization of reaction conditions[a]



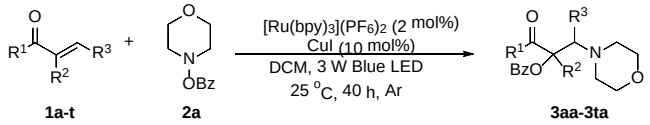


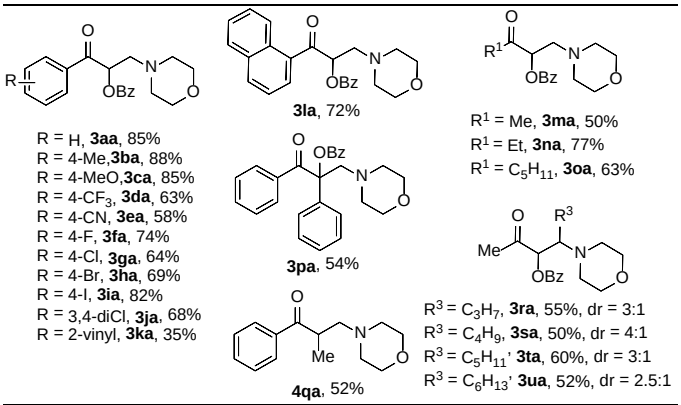
Entry	Photo-catalyst	Cu catalyst	Solven	Yield (%)[b]
1	**I**	CuI	DCM	64
2	**I**	CuCl	DCM	trace
3	**I**	CuBr	DCM	42
4	**I**	$CuCl_2$	DCM	trace
5	**I**	$CuBr_2$	DCM	55
6	**I**	$Cu(CH_3CN)_4PF_6$	DCM	NR
7	**I**	$Cu(CH_3CN)_4BF_4$	DCM	NR
8	**I**	CuOAc	DCM	NR
9	**I**	$Cu(OAc)_2$	DCM	NR
10	**I**	$Cu(OTf)_2$	DCM	NR
11	**II**	CuI	DCM	44
12	**III**	CuI	DCM	85
13	**III**	CuI	DCM	62
14	**III**	CuI	Et_2O	NR
15	**III**	CuI	1,4-dioxane	trace
16	**III**	CuI	THF	NR
17	**III**	--	DCM	NR
18	--	CuI	DCM	NR
19	**III**	CuI	DCM	NR

[a] Unless otherwise noted, reaction conditions are as follows: **1a** (0.1 mmol), **2a** (0.11 mmol), photocatalyst (0.002 mmol), Cu catalyst (0.01 mmol), solvent (1.5 mL), 3 W blue LED, 25 oC under an Ar atmosphere. [b] Isolated yield. c Reaction carried out in the dark

With the optimal conditions, we first tested the feasibility of substrate *α,β*-unsaturated ketones **1a-t** (Scheme 2). Generally, the difunctionalization reaction proceeded smoothly with *α,β*-unsaturated ketones **1a-j** bearing either electron donor or electron hogging aryl group (R1) at the ketone position. Only *α,β*-unsaturated ketone **1k** with an *ortho*-position olefin substituent on the aryl ring R^1 gave the corresponding **3ka** in a lower yield. When 1-(naphthalen-1-yl)prop-2-en-1-one **1l** was employed, the desired product **3la** was afforded in 72% yield. Furthermore, the reaction was also compatible with alkyl groups R^1 such as Me, Et, C_5H_{11}, and the corresponding ester derivatives product **3ma-3oa**

Scheme 2. Scope of *α,β*-unsaturated ketones in visible light driven copper(I)-catalyzed oxyamination reaction[a]

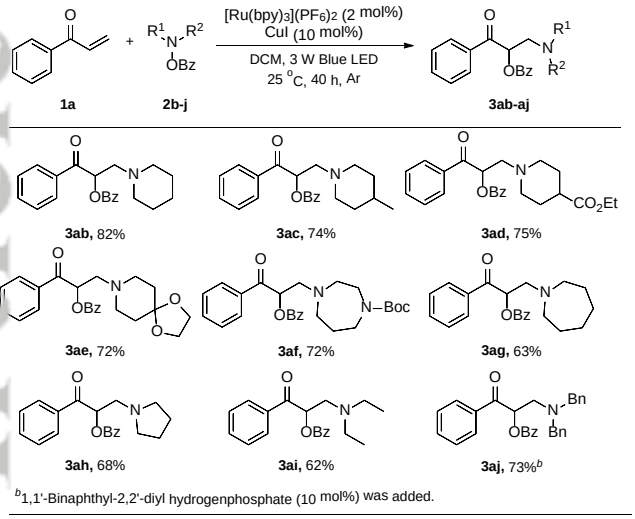




were obtained in 50-77% yield. The sterically bulkier substrates was also assessed in oxyamination process. For example, when *α,α*-disubstituted enone **1p** (R^2=Ph) was used, the corresponding product **3pa** gave in 54% yield. Unexpectedly, *α,α*-disubstituted enone **1q** (R^2 = Me) was used, only the amination product **4qa** was delivered in 52% yield. Additionally, we found the substrates of

α,*β*-substituted enone had good adaptability and easily provided the difunctionalized products **3ra-3ua** in 50-60% yield with 2.5:1-4:1 dr. It is worth mentioning that despite our efforts, the difunctionalization of 1,2-allenic ketones, acrylates or alkynone failed under the optimal conditions (see the ESI for details).

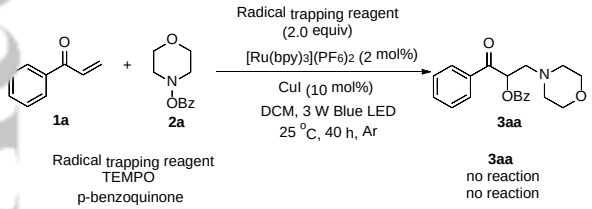
Scheme 3. Scope of *O*-benzoylhydroxylamine in visible light driven copper(I)-catalyzed oxyamination reaction [a]



[b]1,1'-Binaphthyl-2,2'-diyl hydrogenphosphate (10 mol%) was added.

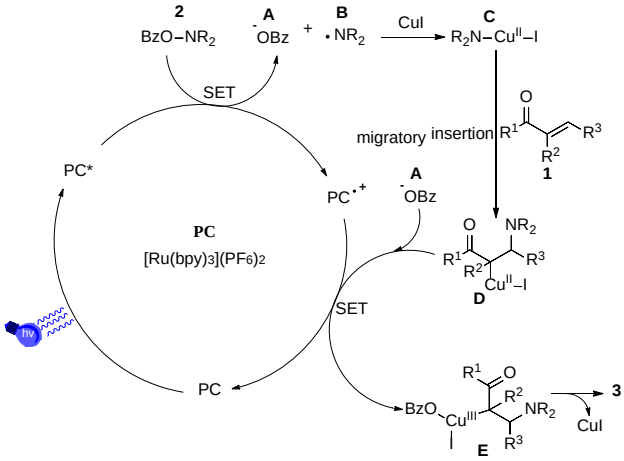
Next, the reaction generality and limitation of the *O*-benzoylhydroxylamine reagents were investigated. Primarily, we synthesized a series of *O*-benzoylhydroxylamine, then all of them were tested and the results are as follows (Scheme 3). Six-membered cyclic *O*-benzoylhydroxylamines such as **2b**, **2c**, **2d** and **2e** participated well in the amino oxygenation reaction, affording the desired **3ab-3ae** in 72-82% yield. Meanwhile, bigger cyclic *O*-benzoylhydroxylamines **2f** and **2g** also worked well, giving the corresponding ester derivatives **3af-3ag** in good yields. Five membered *O*-benzoylhydroxylpyrrolidine **3h** was also applied to this transformation, providing the difunctionalized product **3ah** in 68% yield. Moreover, *N*,*N*-diethylamine and *N*,*N*-dibenzylamine were both investigated as a contrast, derived from acyclic hydroxylamines constructed of **3ai** and **3aj** in 62% and 73% yield, respectively. In the case of *N*,*N*-dibenzylamine **2j**, 10 mol% of 1,1'-binaphthyl-2,2'-diyl hydrogenphosphate was needed to promote the reaction.

Scheme 4. Control experiment with radical trapping reagent



To learn more about the mechanism of this reaction, the possible formation of radical species was investigated. When 2.0 equivalents of TEMPO or *p*-benzoquinone respectively added to the system under the standard reaction conditions (**Scheme 4**), the reaction was completely inhibited, albeit no trapped intermediate detected. These results implied that the reaction forms a radical intermediate and is a radical process. Based on the present observations, we proposed a plausible mechanism for this visible light-driven Cu(I)-catalyzed direct intermolecular oxyamination reaction (**Scheme 5**). Firstly, under the irradiation of the 3W blue LED, the photocatalyst (PC) reached to its excited

Scheme 5 Proposed Mechanism



state (**PC***) and oxidized by complex **2** to generate the BzO^- species **A** and nitrogen-centered radical species **B**. Addition of the radical **B** and CuI forms an aminocopper intermediate **C**.[8] Afterwords, intermediate C undergoes a series of alkene complexation and migratory insertion to form alkyl-Cu(II) species **D**.[8,14] The key intermediate **D** further undergoes reaction with BzO^- species **A** and reduction, completing the photocatalytic cycle by affording the alkyl-Cu(III) species **E**. Finally, this key intermediate **E** further undergoes a selective reductive elimination and the desired product **3** was produced.

Conclusions

In summary, we have first developed a visible light-driven Cu(I)-catalyzed intermolecular oxyamination of electron-deficient olefins by using O-benzoylhydroxylamines as donors both for amine and oxygen along with two new bonds C-O and C-N were constructed. The reaction properties provide mild conditions and a wide substrate scope. Furthermore, a series of ester derivatives of β-amino alcohols were accessed under the mild reaction condition.

Experimental

General Procedure for the Preparation of 3.

In a 10 mL Schlenk flask were placed $Ir(ppy)_2(dtbbpy)PF_6$ (1.7

mg, 2 mol%), CuI (1.9 mg, 10 mol%), *α,β*-unsaturated ketone (**1**, 0.1 mmol, 1 equiv), *O*-benzoylhydroxylamine (**2**, 0.11 mmol, 1.1 equiv), and DCM (1.5 mL). At agon atmosphere, irradiation by a 3 W blue LED (λ = 450–455 nm) at 25 °C for 40 hours. After completion of the reaction, the reaction mixture was directly purified by silica gel chromatography using petroleum ether/EtOAc as the eluent to afford **3**

3-Morpholino-1-oxo-1-phenylpropan-2-yl benzoate (**3aa**) was obtained in 85% isolated yield (28.8 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12–8.05 (m, 2H), 8.04–7.98 (m, 2H), 7.64–7.55 (m, 2H), 7.53–7.41 (m, 4H), 6.32 (dd, *J* = 6.8, 4.1 Hz, 1H), 3.66–3.52 (m, 4H), 3.01 (qd, *J* = 13.9, 5.5 Hz, 2H), 2.70–2.60 (m, 2H), 2.57–2.46 (m, 2H); ^{13}C NMR δ 195.5, 165.8, 135.3, 133.4, 133.3, 129.8, 129.4, 128.7, 128.4, 128.3, 74.1, 66.9, 59.0, 53.8. HRMS (ESI): Calcd. for $C_{20}H_{22}NO_4$ $(M+H)^+$ 340.1543, found 340.1551.

3-Morpholino-1-oxo-1-(p- tolyl)propan-2-yl benzoate (**3ba**) was obtained in 88% isolated yield (31.1 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dt, *J* = 8.4, 1.5 Hz, 2H), 8.00–7.88 (m, 2H), 7.63–7.52 (m, 1H), 7.48–7.39 (m, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 6.30 (dd, *J* = 6.9, 4.0 Hz, 1H), 3.68–3.51 (m, 4H), 3.00 (qd, *J* = 13.9, 5.5 Hz, 2H), 2.64 (dt, *J* = 9.3, 4.6 Hz, 2H), 2.58–2.50 (m, 2H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.9, 165.8, 144.4, 133.3, 132.6, 129.8, 129.5, 129.4, 128.5, 128.4, 74.0, 66.9, 59.0, 53.8, 21.7. HRMS (ESI): Calcd. for $C_{21}H_{24}NO_4$ $(M+H)^+$ 354.1700, found 354.1707.

1-(4-Methoxyphenyl)-3-morpholino-1-oxopropan-2-yl benzoate (**3ca**) was obtained in 85% isolated yield (31.5 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.3, 1.2 Hz, 2H), 8.05–7.98 (m, 2H), 7.62–7.54 (m, 1H), 7.45 (dd, *J* = 10.9, 4.7 Hz, 2H), 7.02–6.93 (m, 2H), 6.29 (dd, *J* = 6.8, 4.2 Hz, 1H), 3.87 (s, 3H), 3.67–3.56 (m, 4H), 3.06–2.94 (m, 2H), 2.64 (dt, *J* = 9.2, 4.5 Hz, 2H), 2.58–2.51 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.7, 165.8, 163.8, 133.3, 130.8, 129.8, 129.5, 128.4, 128.0, 114.0, 73.7, 66.9, 59.2, 55.5, 53.8. HRMS (ESI): Calcd. for $C_{21}H_{24}NO_5$ $(M+H)^+$ 370.1649, found 370.1655.

3-Morpholino-1-oxo-1-(4-(trifluoromethyl)phenyl)propan-2-yl benzoate (**3da**) was obtained in 63% isolated yield (25.6 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.1 Hz, 2H), 8.07 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.60 (td, *J* = 7.7, 1.1 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 6.33–6.20 (m, 1H), 3.66–3.51 (m, 4H), 3.10–2.90 (m, 2H), 2.63 (dd, *J* = 10.6, 4.1 Hz, 2H), 2.57–2.46 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.2 (s), 165.9 (s), 138.5 (s), 134.6 (q, *J* = 32.7 Hz), 133.6 (s), 129.8 (s), 129.1 (s), 128.6 (d, *J* = 13.7 Hz), 125.8 ((d, *J* = 3.7 Hz), 124. 6 (s), 122.4 (s), 74.2 (s), 66.8 (s), 58.8 (s), 53.8 (s). HRMS (ESI): Calcd. for $C_{21}H_{21}F_3NO_4$ $(M+H)^+$ 408.1417, found 408.1425.

1-(4-Cyanophenyl)-3-morpholino-1-oxopropan-2-yl benzoate (**3ea**) was obtained in 58% isolated yield (21.0 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14–8.07 (m, 2H), 8.07–8.02 (m, 2H), 7.85–7.77 (m, 2H), 7.65–7.57 (m, 1H), 7.47 (dt, *J* = 7.5, 3.2 Hz, 2H), 6.19 (dd, *J* = 6.4, 4.7 Hz, 1H), 3.61–3.50 (m, 4H), 3.02 (qd, *J* = 13.8, 5.5 Hz, 2H), 2.65–2.57 (m, 2H), 2.53–2.46 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.1, 165.8, 139.0, 133.7, 132.5, 129.8, 128.9, 128.7, 128.6, 117.8, 116.5, 74.1, 66.8, 58.8, 53.8. HRMS (ESI): Calcd. for $C_{21}H_{21}N_2O_4$ $(M+H)^+$ 365.1496, found 365.1503.

1-(4-Fluorophenyl)-3-morpholino-1-oxopropan-2-yl benzoate (**3fa**) was obtained in 74% isolated yield (26.6 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14–8.00 (m, 4H), 7.63–7.54 (m, 1H), 7.50–7.41 (m, 2H), 7.23–7.11 (m, 2H), 6.24 (dd, *J* = 6.7, 4.3 Hz, 1H), 3.66–3.52 (m, 4H), 3.00 (qd, *J* = 13.9, 5.5 Hz, 2H), 2.69–2.59 (m, 2H), 2.58–2.45 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.1 (s), 165.9 (t, *J* = 127.8 Hz), 133.4 (s), 131.8 (d, *J* = 3.1 Hz), 131.1 (d, *J* = 9.3 Hz), 129.8 (s), 129.2 (s), 128.5 (s), 116.0 (s), 115.8 (s), 73.9 (s), 66.9 (s), 59.0 (s), 53.8 (s). HRMS (ESI): Calcd. for $C_{20}H_{21}FNO_4$ $(M+H)^+$ 358.1449, found 358.1458.

1-(4-Chlorophenyl)-3-morpholino-1-oxopropan-2-yl benzoate (**3ga**) was obtained in 64% isolated yield (23.8 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14–8.03 (m, 2H), 8.00–7.91 (m, 2H), 7.63–7.55 (m, 1H), 7.50–7.39 (m, 4H), 6.22 (dd, *J* = 6.7, 4.3 Hz, 1H), 3.67–3.48 (m, 4H), 3.00 (qd, *J* = 13.9, 5.5 Hz, 2H), 2.66–2.57 (m, 2H), 2.50 (dt, *J* = 56.3, 28.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 165.8, 139.9, 133.7, 133.5, 129.8, 129.8, 129.2, 129.1, 128.5, 74.0, 66.8, 58.9, 53.8. HRMS (ESI): Calcd. for $C_{20}H_{21}ClNO_4$ $(M+H)^+$ 374.1154, found 374.1163.

1-(4-Bromophenyl)-3-morpholino-1-oxopropan-2-yl benzoate (**3ha**) was obtained in 69% isolated yield (28.7 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11–8.02 (m, 2H), 7.94–7.84 (m, 2H), 7.65–7.61 (m, 2H), 7.61–7.57 (m, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 6.21 (dd, *J* = 6.6, 4.3 Hz, 1H), 3.68–3.51 (m, 4H), 3.00 (qd, *J* = 13.9, 5.5 Hz, 2H), 2.67–2.58 (m, 2H), 2.54–2.48 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.8, 165.8, 134.1, 133.5, 132.0, 129.8, 129.8, 129.2, 128.6, 128.5, 74.0, 66.8, 58.9, 53.8. HRMS (ESI): Calcd. for $C_{20}H_{21}BrNO_4$ $(M+H)^+$ 418.0648, found 418.0660.

1-(4-Iodophenyl)-3-morpholino-1-oxopropan-2-yl benzoate (**3ia**) was obtained in 82% isolated yield (38.1 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13–8.01 (m, 2H), 7.89–7.79 (m, 2H), 7.77–7.68 (m, 2H), 7.65–7.53 (m, 1H), 7.45 (dd, *J* = 10.8, 4.8 Hz, 2H), 6.21 (dd, *J* = 6.7, 4.3 Hz, 1H), 3.75–3.48 (m, 4H), 2.99 (qd, *J* = 13.9, 5.5 Hz, 2H), 2.66–2.57 (m, 2H), 2.56–2.46 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.0, 165.8, 138.0, 134.7, 133.5, 129.8, 129.7, 129.2, 128.5, 101.4, 74.0, 66.8, 58.9, 53.8. HRMS (ESI): Calcd. for $C_{20}H_{21}INO_4$ $(M+H)^+$ 466.0510, found 466.0518.

1-(3,4-dichlorophenyl)-3-morpholino-1-oxopropan-2-yl benzoate (**3ja**) was obtained in 68% isolated yield (27.6 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 2.0 Hz, 1H), 8.12–8.03 (m, 2H), 7.85 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.65–7.55 (m, 2H), 7.56–7.44 (m, 2H), 6.14 (dd, *J* = 6.3, 4.6 Hz, 1H), 3.68–3.55 (m, 4H), 3.02 (qd, *J* = 13.9, 5.5 Hz, 2H), 2.71–2.59 (m, 2H), 2.59–2.50 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.9, 165.8, 138.0, 135.1, 133.6, 133.4, 130.8, 130.5, 129.8, 129.0, 128.5, 127.3, 74.1, 66.8, 58.9, 53.9. HRMS (ESI): Calcd. for $C_{20}H_{20}Cl_2NO_4$ $(M+H)^+$ 408.0764, found 408.0775.

3-Morpholino-1-oxo-1-(2-vinylphenyl)propan-2-yl benzoate (**3ka**) was obtained in 35% isolated yield (12.8 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.3 Hz, 2H), 7.81 (d, *J* = 7.4 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 6.9 Hz, 1H), 7.47 (d, *J* = 5.5 Hz, 3H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.19 (dd, *J* = 17.3, 11.1 Hz, 1H), 6.18 (s, 1H), 5.73 (d, *J* = 17.5 Hz, 1H), 5.36 (d, *J* = 10.9 Hz, 1H), 3.55 (s, 4H), 3.10–2.85 (m, 2H), 2.62 (s, 2H), 2.36 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.3, 165.9, 137.4, 136.2, 134.9, 133.4, 131.4, 129.8, 129.4, 128.5, 127.8, 127.3, 126.7, 116.6, 76.4, 66.7, 58.6, 53.9. HRMS (ESI): Calcd. for $C_{22}H_{24}NO_4$ $(M+H)^+$ 366.1700, found 366.1709.

3-Morpholino-1-(naphthalen-1-yl)-1-oxopropan-2-yl benzoate (**3la**) **was** obtained in 72% isolated yield (28.0 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.4 Hz, 1H), 8.12 (d, *J* = 7.4 Hz, 2H), 8.09 (d, *J* = 7.2 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.64–7.52 (m, 4H), 7.49 (t, *J* = 7.8 Hz, 2H), 6.33 (dd, *J* = 6.1, 4.1 Hz, 1H), 3.50–3.41 (m, 2H), 3.39 (d, *J* = 4.8 Hz, 2H), 3.04 (dd, *J* = 13.8, 6.2 Hz, 1H), 2.96 (dd, *J* = 13.7, 4.0 Hz, 1H), 2.61 (s, 2H), 2.37–2.27 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0, 166.0, 134.9, 133.8, 133.4, 132.4, 130.2, 129.8, 129.4, 128.5, 128.3, 127.6, 126.8, 126.6, 125.9, 124.3, 76.6, 66.6, 58.8, 53.8. HRMS (ESI): Calcd. for $C_{24}H_{24}NO_4$ $(M+H)^+$ 390.1700, found 390.1707.

Morpholino-3-oxobutan-2-yl benzoate (**3ma**) was obtained in 50% isolated yield (13.8 mg) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14–7.99 (m, 2H), 7.68–7.55 (m, 1H), 7.53–7.40 (m, 2H), 5.43 (dd, *J* = 6.5, 3.8 Hz, 1H), 3.77–3.52 (m, 4H), 2.99 (dd, *J* = 13.9, 6.5 Hz, 1H), 2.88 (dd, *J* = 13.9, 3.8 Hz, 1H), 2.66 (dt, *J* = 9.4, 4.5 Hz, 2H), 2.57–2.49 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.2, 165.8, 133.5, 129.8, 129.3, 128.6, 77.7, 66.9, 58.6, 54.0, 27.1. HRMS (ESI): Calcd. for $C_{15}H_{20}NO_4$ $(M+H)^+$ 278.1387, found 278.1392.

Morpholino-3-oxopentan-2-yl benzoate (**3na**) was obtained in 72% isolated yield (22.4 mg) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11–8.00 (m, 2H), 7.68–7.55 (m, 1H), 7.52–7.39 (m, 2H), 5.45 (dd, *J* = 6.6, 3.9 Hz, 1H), 3.74–3.56 (m, 4H), 2.97 (dd, *J* = 13.8, 6.7 Hz, 1H), 2.86 (dd, *J* = 13.8, 3.9 Hz, 1H), 2.69–2.53 (m, 4H), 2.53–2.47 (m, 2H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.0, 165.8, 133.4, 129.7, 129.4, 128.5, 67.0, 58.8, 54.0, 32.9, 7.2. HRMS (ESI): Calcd. for $C_{16}H_{22}NO_4$ $(M+H)^+$ 292.1543, found 292.1552.

Morpholino-3-oxooctan-2-yl benzoate (**3oa**) was obtained in 63% isolated yield (20.9 mg) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18–7.98 (m, 2H), 7.65–7.55 (m, 1H), 7.52–7.39 (m, 2H), 5.44 (dd, *J* = 6.6, 3.8 Hz, 1H), 3.74–3.55 (m, 4H), 2.98 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.86 (dd, *J* = 13.8, 3.8 Hz, 1H), 2.69–2.62 (m, 2H), 2.61–2.48 (m, 4H), 1.68–1.59 (m, 2H), 1.35–1.27 (m, 4H) 0.98–0.82 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.3, 165.78, 133.4, 129.7, 129.4, 128.5, 77.3, 66.9, 58.7, 54.0, 39.5, 31.3, 22.7, 22.4, 13. 9. HRMS (ESI): Calcd. for $C_{19}H_{28}NO_4$ $(M+H)^+$ 334.2013, found 334.2019.

3-Morpholino-1-oxo-1,2-diphenylpropan-2-yl benzoate (**3pa**) was obtained in 54% isolated yield (22.3 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.79 (dd, *J* = 8.4, 1.1 Hz, 2H), 7.73 (d, *J* = 7.4 Hz, 2H), 7.63–7.57 (m, 1H), 7.46 (dt, *J* = 17.1, 8.0 Hz, 4H), 7.38–7.33 (m, 1H), 7.32–7.27 (m, 1H), 7.18 (dd, *J* = 10.8, 4.8 Hz, 2H), 3.83 (d, *J* = 14.5 Hz, 1H), 3.34 (dd, *J* = 9.3, 4.6 Hz, 4H), 2.32–2.24 (m, 2H), 2.21–2.14 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.8, 165.0, 138.2, 135.1, 133.4, 132.2, 130.1, 129.6, 129.0, 128.7, 128.6, 128.1, 128.0, 125.1, 88.1, 67.1, 63.5, 54.5. HRMS (ESI): Calcd. for $C_{26}H_{26}NO_4$ $(M+H)^+$ 416.1856, found 416.1869.

2-methyl-3-morpholino-1-phenylpropan-1-one (**4qa**) was obtained in 52% isolated yield (12.2 mg) as colorless oli. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 5.2, 3.4 Hz, 1H), 7.63 – 7.36 (m, 3H), 3.84 – 3.67 (m, 2H), 3.61 (dd, *J* = 6.6, 2.6 Hz, 4H), 2.86 (dd, *J* = 12.5, 7.8 Hz, 1H), 2.51 – 2.40 (m, 4H), 1.20 (d, *J* = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.7, 132.9, 128.6, 128.2, 127.1, 66.9, 61.9, 53.9, 38.4, 16.5.

4-Morpholino-2-oxoheptan-3-yl benzoate (**3ra**) was obtained in 55% isolated yield, 3:1 dr (17.6 mg) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09–8.03 (m, 2H), 7.65–7.58 (m, 1H), 7.54–7.45 (m, 2H), 5.45 (m, 4.1 Hz, 1H), 3.74–3.54 (m, 4H), 3.20 (m, 4.5 Hz, 1H), 2.99–2.69 (m, 2H), 2.65–2.49 (m, 2H), 2.23 (d, *J* = 4.7 Hz, 3H), 1.97–1.79 (m, 1H), 1.74–1.61 (m, 1H), 1.59–1.48 (m, 1H), 1.48–1.34 (m, 2H), 0.94 (dt, *J* = 10.4, 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.7, 165.9, 133.6, 129.8, 129.4, 128.6, 81.3, 67.4, 64.7, 49.6, 28.9, 27.2, 20.2, 14.0. HRMS (ESI): Calcd. for $C_{18}H_{26}NO_4$ $(M+H)^+$ 320.1856, found 320.1849.

4-Morpholino-2-oxooctan-3-yl benzoate (**3sa**) was obtained in 50% isolated yield, 4:1 dr (16.7 mg) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (m, 1.2 Hz, 2H), 7.61 (m, 1.3 Hz, 1H), 7.48 (m, 3.0 Hz, 2H), 5.44 (dd, *J* = 13.1, 4.2 Hz, 1H), 3.72–3.56 (m, 4H), 3.18 (m, 4.4 Hz, 1H), 2.97–2.71 (m, 2H), 2.60–2.51 (m, 2H), 2.23 (d, *J* = 6.7 Hz, 3H), 1.93–1.82 (m, 1H), 1.71–1.60 (m, 1H), 1.53–1.39 (m, 2H), 1.39–1.24 (m, 4H), 0.96–0.83 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.7, 165.7, 133.6, 129.8, 129.4, 128.6, 78.1, 67.4, 65.0, 49.6, 29.3, 27.3, 26.7, 22.7, 13.9. HRMS (ESI): Calcd. for $C_{19}H_{28}NO_4$ $(M+H)^+$ 334.2013, found 334.2021.

4-Morpholino-2-oxononan-3-yl benzoate (**3ta**) was obtained in 60% isolated yield, 2.5:1 dr. (20.7 mg) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10–8.01 (m, 2H), 7.64–7.57 (m, 1H), 7.53–7.45 (m, 2H), 5.44 (dd, *J* = 12.4, 4.2 Hz, 1H), 3.70–3.56 (m, 4H), 3.18 (m, 4.5 Hz, 1H), 2.98–2.70 (m, 2H), 2.61–2.50 (m, 2H), 2.23 (d, *J* = 6.1 Hz, 3H), 1.93–1.81 (m, 1H), 1.64 (m, 6.2 Hz, 1H), 1.58–1.48 (m, 1H), 1.48–1.35 (m, 2H), 1.35–1.24 (m, 5H), 0.87 (dt, *J* = 12.0, 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.7, 165.7, 133.5, 129.7, 129.4, 128.6, 78.2, 67.4, 65.0, 49.6, 31.8, 27.3, 26.8, 23.5, 22.6, 14.0. HRMS (ESI): Calcd. for $C_{20}H_{30}NO_4$ $(M+H)^+$ 348.2169, found 348.2178.

4-Morpholino-2-oxodecan-3-yl benzoate (**3ua**) was obtained in 52% isolated yield, 2.5:1 dr (18.9 mg) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (m, 2H), 7.61 (m, 1H), 7.49 (m, 2H), 5.44 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.69–3.56 (m, 4H), 3.29–3.07 (m, 1H), 2.97–2.70 (m, 2H), 2.62–2.51 (m, 2H), 2.23 (d, *J* = 6.5 Hz, 3H), 1.88 (m, 1H), 1.73–1.60 (m, 1H), 1.46 (m, 1H), 1.39–1.22 (m, 6H), 0.95–0.79 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.7, 165.7, 133.5, 129.8, 129.4, 128.6, 78.1, 67.4, 65.0, 49.6, 31.7, 29.7, 27.3, 26.8, 23.5, 22.6, 14.0. HRMS (ESI): Calcd. for $C_{21}H_{32}NO_4$ $(M+H)^+$ 362.2326, found 362.2333.

1-Oxo-1-phenyl-3-(piperidin-1-yl)propan-2-yl benzoate (**3ab**) was obtained in 82% isolated yield (27.8 mg) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0 Hz, 2H), 8.04 (d, *J* = 7.9 Hz, 2H), 7.58 (td, *J* = 7.1, 0.9 Hz, 2H), 7.53–7.43 (m, 4H), 6.33–6.26 (m, 1H), 3.09–2.93 (m, 2H), 2.62–2.44 (m, 4H), 1.54–1.43 (m, 4H), 1.41–1.33 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 166.0, 135.3, 133.3, 133.2, 129.8, 129.5, 128.6, 128.4, 128.4, 74.4, 59.3, 54.7, 25.9, 23.9. HRMS (ESI): Calcd. for $C_{21}H_{23}NNaO_3$ $(M+Na)^+$ 360.1570, found 360.1572.

3-(4-Methylpiperidin-1-yl)-1-oxo-1-phenylpropan-2-yl benzoate (**3ac**) was obtained in 74% isolated yield (26.0 mg) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.6 Hz, 2H), 8.03 (d, *J* = 7.7 Hz, 2H), 7.59 (dd, *J* = 7.8, 5.8 Hz, 2H), 7.47 (dt, *J* = 15.2, 7.7 Hz, 4H), 6.29 (dd, *J* = 6.2, 4.7 Hz, 1H), 3.07–3.00 (m, 2H), 2.96 (d, *J* = 12.2 Hz, 1H), 2.89 (d, *J* = 11.0 Hz, 1H), 2.19 (td, *J* = 11.3,

2.2 Hz, 2H), 1.55 (d, *J* = 12.8 Hz, 2H), 1.39–1.23 (m, 2H), 1.21–1.02 (m, 2H), 0.87 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 166.0, 135.3, 133.3, 133.2, 129.9, 129.5, 128.7, 128.5, 128.4, 74.6, 59.0, 54.1, 34.3, 30.4, 21.8. HRMS (ESI): Calcd. for $C_{22}H_{26}NO_3$ $(M+H)^+$ 352.1907, found 352.1909.

Ethyl 1-(2-(benzoyloxy)-3-oxo-3-phenylpropyl)piperidine-4-carboxylate (**3ad**) was obtained in 75% isolated yield (30.8 mg) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.6 Hz, 2H), 8.04 (d, *J* = 7.6 Hz, 2H), 7.61 (dd, *J* = 7.8, 6.2 Hz, 2H), 7.49 (dt, *J* = 15.2, 7.7 Hz, 4H), 6.37–6.25 (m, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.11–2.97 (m, 3H), 2.90 (d, *J* = 11.2 Hz, 1H), 2.35–2.19 (m, 3H), 1.89–1.80 (m, 2H), 1.73 – 1.56 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8, 175.0, 165.9, 135.3, 133.4, 133.3, 129.8, 129.4, 128.7, 128.4, 128.4, 74.3, 60.3, 58.8, 53.2, 53.1, 40.7, 28.2, 28.1, 14.2. HRMS (ESI): Calcd. for $C_{24}H_{28}NO_5$ $(M+H)^+$ 410.1962, found 410.1974.

1-Oxo-1-phenyl-3-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)propan-2-yl benzoate (**3ae**) was obtained in 72% isolated yield (28.4 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12–8.05 (m, 2H), 8.05–7.99 (m, 2H), 7.61–7.55 (m, 2H), 7.52–7.41 (m, 4H), 6.37–6.18 (m, 1H), 3.92 (d, *J* = 3.9 Hz, 4H), 3.13–2.97 (m, 2H), 2.77–2.59 (m, 4H), 1.63 (d, *J* = 3.6 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 165.9, 135.4, 133.4, 133.3, 129.9, 129.5, 128.7, 128.4, 128.4, 106.8, 74.4, 64.2, 58.2, 51.6, 34.8. HRMS (ESI): Calcd. for $C_{23}H_{26}NO_5$ $(M+H)^+$ 396.1805, found 396.1814.

tert-Butyl 4-(2-(benzoyloxy)-3-oxo-3-phenylpropyl)-1,4-diazepane-1-carboxylate (**3af**) was obtained in 72% isolated yield (32.8 mg) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.7 Hz, 2H), 8.01 (d, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 6.7 Hz, 2H), 7.47 (dt, *J* = 15.2, 7.7 Hz, 4H), 6.26 (dd, *J* = 8.1, 5.4 Hz, 1H), 3.42–3.25 (m, 4H), 3.19 (d, *J* = 5.5 Hz, 2H), 2.89–2.65 (m, 4H), 1.78–1.62 (m, 2H), 1.42 (d, *J* = 4.3 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 155.9, 155.5, 155.3, 135.5, 133.4, 133.3, 129.8, 129.4, 128.8, 128.4 128.3, 79.3, 74.8, 74.6, 58.1, 57.9, 56.5, 56.2, 55.2, 55.0, 47.0, 46.6, 45.9, 45.0, 28.4, 27.7, 27.6. HRMS (ESI): Calcd. for $C_{26}H_{33}N_2O_5$ $(M+H)^+$ 453.2384, found 453.2387.

3-(Azepan-1-yl)-1-oxo-1-phenylpropan-2-yl benzoate (**3ag**) was obtained in 63% isolated yield (20.8 mg) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12–8.08 (m, 2H), 8.06–8.02 (m, 2H), 7.62–7.55 (m, 2H), 7.47 (dt, *J* = 15.3, 7.7 Hz, 4H), 6.27 (t, *J* = 5.6 Hz, 1H), 3.26–3.15 (m, 2H), 2.88–2.68 (m, 4H), 1.60–1.45 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 166.0, 135.6, 133.3, 133.2, 129.9, 129.6, 128.7, 128.4, 128.4, 75.1, 58.7, 55.7, 28.4, 27.0. HRMS (ESI): Calcd. for $C_{22}H_{26}NO_3$ $(M+H)^+$ 352.1907, found 352.1907.

1-Oxo-1-phenyl-3-(pyrrolidin-1-yl)propan-2-yl benzoate (**3ah**) was obtained in 68% isolated yield (22.0 mg) as colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (dt, *J* = 8.4, 1.5 Hz, 2H), 8.02 (dt, *J* = 8.5, 1.6 Hz, 2H), 7.60–7.54 (m, 2H), 7.50–7.42 (m, 4H), 6.28 (dd, *J* = 6.7, 3.9 Hz, 1H), 3.19–3.03 (m, 2H), 2.73–2.54 (m, 4H), 1.82–1.64 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.4, 166.0, 135.0, 133.4 133.2, 129.9, 129.5, 128.7, 128.4, 128.4, 76.0, 56.2, 54.7, 23.7. HRMS (ESI): Calcd. for $C_{20}H_{22}NO_3$ $(M+H)^+$ 324.1594, found 324.1594.

3-(Diethylamino)-1-oxo-1-phenylpropan-2-yl benzoate (**3ai**) was obtained in 62% isolated yield (20.1 mg) as colorless oli. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.7 Hz, 2H), 8.04 (d, *J* = 7.7 Hz, 2H), 7.58 (dd, *J* = 12.6, 7.1 Hz, 2H), 7.47 (dt, *J* = 15.4, 7.7 Hz, 4H), 6.26 (dd, *J* = 6.8, 4.5 Hz, 1H), 3.15–3.02 (m, 2H), 2.65 (q, *J* = 7.1 Hz, 4H), 0.99 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 166.0, 135.4, 133.4, 133.2, 129.9, 129.5, 128.7, 128.5, 128.4, 74.9, 53.4, 47.5, 11.8. HRMS (ESI): Calcd. for $C_{20}H_{24}NO_3$ $(M+H)^+$ 326.1751, found 326.1755.

3-(Dibenzylamino)-1-oxo-1-phenylpropan-2-yl benzoate (**3aj**) was obtained in 73% isolated yield (32.7 mg) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 2H), 7.71 (d, *J* = 7.9 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.29 – 7.21 (m, 10H), 6.29 (dd, *J* = 8.1, 3.1 Hz, 1H), 3.81 (d, *J* = 13.5 Hz, 2H), 3.68 (d, *J* = 13.5 Hz, 2H), 3.25–3.07 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.1, 166.0, 138.8, 134.7, 133.4, 133.3, 129.9, 129.4, 128.9, 128.7, 128.4, 128.3, 128.3, 127.1, 75.3, 59.0, 54.0. HRMS (ESI): Calcd. for $C_{30}H_{28}NO_3$ $(M+H)^+$ 450.2064, found 450.2059.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2018xxxxx.

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Entry for the Table of Contents

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Visible Light Driven Copper(I) Catalyzed Oxyamination of Electron Deficient Alkenes

anliang Li,[a] Qiaoyu Chen,[a] Wenbo Li,[b] Guanxin Gu,*[,c] and Junliang Zhang*[,a]

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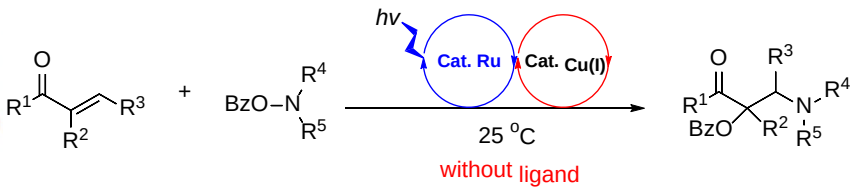

A visible light driven Cu(I)-catalyzed intermolecular oxyamination of electron-deficient olefins has been achieved by using *O*-benzoylhydroxylamines as donors both for amine and oxygen. The transformation properties afford mild conditions and a wide substrate scope, providing access to ester derivatives of *β*-amino alcohols with good yields and high regioselectivity.

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