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Retention of chirality of 5-membered alicyclic α-amino acids bearing *N*-(2-phenyl)benzoyl group in photoinduced decarboxylative intermolecular radical addition to acrylonitrile

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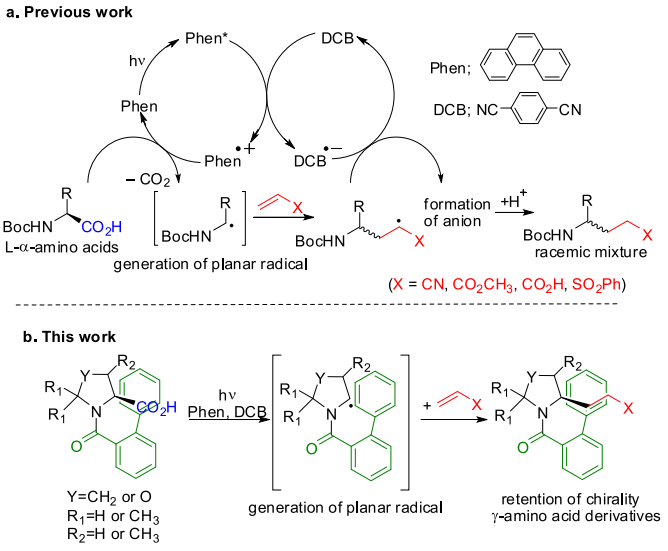
ABSTRACT

Photoinduced decarboxylative radical additions of 5-membered alicyclic α-amino acids bearing a (2-phenyl)benzoyl protective group to acrylonitrile under mild organic photoredox catalysis conditions furnished γ-amino acid derivatives with high retention of chirality via the memory of chirality (MOC) strategy. The retention of chirality in the photoinduced decarboxylation was strongly dependent on the structure of the alicyclic α-amino acids and alkenes. To the best of our knowledge, this is the first example of the decarboxylative intermolecular radical addition to alkenes with retention of chirality at the position of radical generation using the MOC strategy.

1. Introduction

Decarboxylative radical reactions of carboxylic acids in the presence of a photoredox catalyst have recently been identified as a powerful and environment-friendly tool in polymer chemistry [1] and synthetic organic chemistry [2,3]. This is because carboxylic acids exist widely in nature and are easy to handle, and decarboxylation releases the nonflammable and nontoxic product CO_2 under mild conditions (e.g., room temperature). The process is initiated by oxidation of the carboxylate ions via photoinduced electron transfer (PET) to form carboxy radicals. As per our previous report [3], the radical cation of phenanthrene (Phen) generated by PET between Phen and 1,4-dicyanobenzene (DCB) can oxidize the carboxylate ions to form carboxy radicals (Scheme 1a). The carboxy radicals undergo decarboxylation smoothly to generate the corresponding alkyl radicals, which can react with a variety of reagents to provide the corresponding products in high yields. However, the



Scheme 1. Loss and retention of chirality of *N*-Boc amino acids in photoinduced decarboxylative radical addition.

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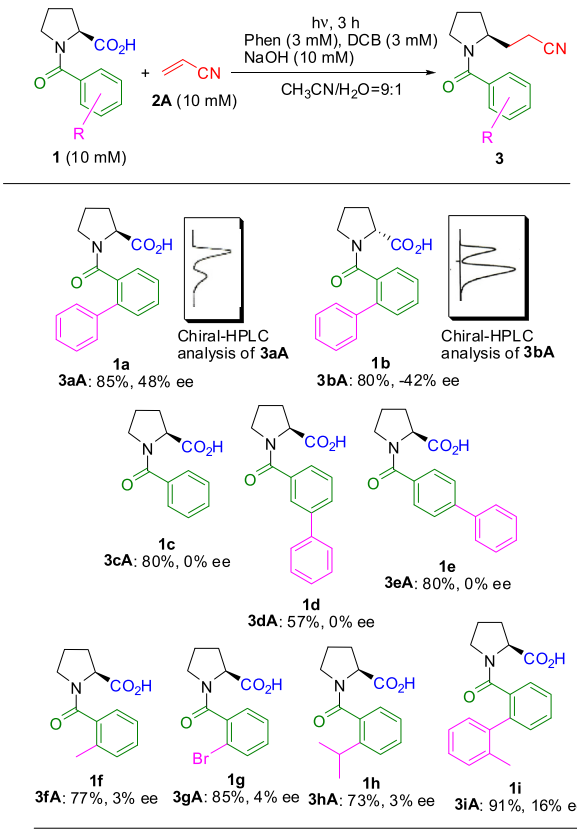
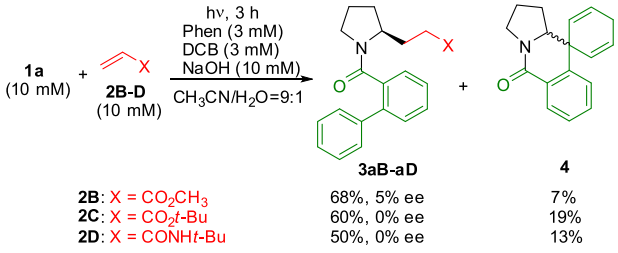
radical generated from chiral carboxylic acids such as *N*-Boc α-amino acids via a photoinduced decarboxylation lost the chirality at the radical-generated position to yield products as a racemic mixture due to the generation of the planar radical by a hyperconjugation (π-radical). In fact, photoinduced decarboxylative radical addition of *N*-Boc-L-α-amino acids to electron-deficient alkenes yielded racemic adducts [4]. There are only four reported examples in which the loss of chirality at the radical formed via decarboxylation is prevented [5]. MacMillan reported the enantioselective decarboxylative arylation of *N*-Boc α-amino acids using both Ir photoredox and chiral Ni catalysts [5c]. The other three examples[5a,b,d] pertain to intramolecular radical cyclization via decarboxylation using the memory of chirality [6] (MOC) strategy. The latter (MOC strategy) is not required to add another chiral source such as the chiral metal catalyst, and is employed by only substrate chirality. Thus, we attempted the intermolecular radical addition of α-amino acids bearing a highly hindered protective group such as *N*-(2-phenyl)benzoyl to alkenes via photoinduced decarboxylation using the MOC strategy for retention of chirality, because the resulting products are useful γ-amino acid derivatives [7] (Scheme 1b). Interestingly, photoinduced decarboxylative intermolecular radical reactions with MOC have not been reported till date.

2. Results and discussion

First, we chose *N*-(2-phenyl)benzoyl-L-proline **1a** as the substrate and acrylonitrile **2A** as an electron-deficient alkene for the photoinduced decarboxylative radical addition because alicyclic amino acids bearing the *N*-(2-phenyl)benzoyl group showed high retention of chirality via the generation of a carbenium ion by electrochemical oxidation [8]. Irradiation of an aqueous acetonitrile solution ($CH_3CN/H_2O = 9:1$) containing **1a** (10 mM), **2A** (10 mM), NaOH (10 mM), Phen (3 mM), and DCB (3 mM) by a 100 W high-pressure mercury lamp through a Pyrex filter (>280 nm) under argon atmosphere for 3 h at room temperature afforded adduct **3 aA** in high yield (85%) and with moderate enantiomeric excess (48% ee) (Table 1). Unfortunately, decreasing the temperature (0 °C) did not affect the retention of chirality under these conditions. The photoreaction of *N*-(2-phenyl)benzoyl-D-proline **1b** yielded adduct **3bA** in a similar yield (80%) but with a slight decrease of retention of chirality (−42%ee). In order to investigate effect of the *N*-benzoyl group on the retention of chirality, prolines **1c**–**i** with various *N*-benzoyl groups were subjected to the abovementioned photoreaction conditions. Photoinduced decarboxylative addition of *N*-benzoyl-L-proline **1c** to **2A** under the same conditions provided racemic product **3 cA** in a similar yield (80%). The photoreactions of *N*-(3-phenyl)benzoyl-L-proline **1d** and *N*-(4-phenyl)benzoyl-L-proline **1e** did not lead to retention of chirality, and gave decreased yield of **3 dA** (57%) along with the formation of side-reaction products in the case of **1d**. These results indicated that the retention of chirality of proline **1** in the photoinduced decarboxylation requires a substituent at the 2-position of the benzoyl group. The photoreactions of 2-substituted benzoyl prolines **1f**–**i** having methyl, bromo, *iso*-propyl, and 2′-methylphenyl groups resulted in a significantly low ee% and similar yields of **3 fA**–**iA**. In addition, the use of relatively bulky electron-deficient alkenes such as methyl acrylate **2B**, *t*-butyl acrylate **2C**, and *N*-*t*-butyl acrylamide **2D** instead of **2A** provided almost racemic adducts **3 aB**–**aD** in low yields, along with polymeric materials and spirodihydroisoquinolinone **4** via our previously reported *ipso*-radical cyclization [9] (Scheme 2). These results indicated that the poor electron accepting ability and high steric hindrance of the alkenes decreased the rate of intermolecular radical addition of **1a** to **2** without

Table 1
Effect of protective group in photoinduced decarboxylative radical addition of **1**–**2A** for retention of chirality.



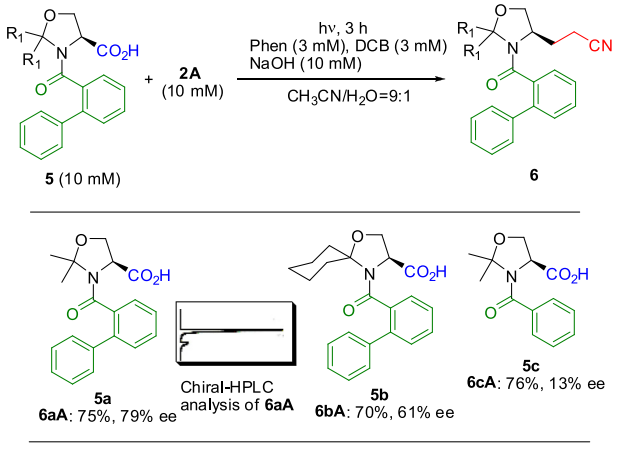


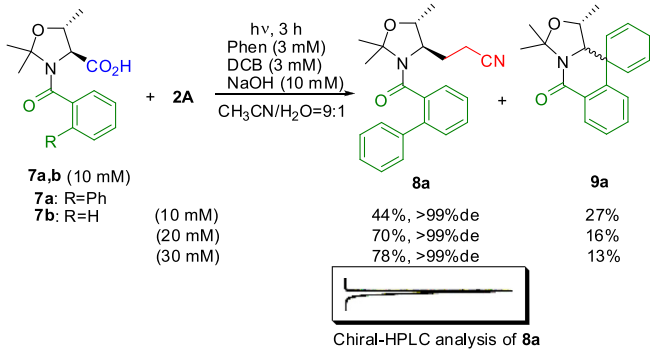
Scheme 2. Effect of alkenes **2B**–**D** in photoinduced decarboxylative radical addition of **1a**.

retention of chirality, and promoted radical cyclization at the *ipso*-position. Thus, for the retention of chirality of proline **1** via the photoinduced decarboxylative radical addition, an *N*-(2-phenyl) benzoyl protective group and acrylonitrile **2A** as an alkene are required.

Next, the substrate scope of alicyclic amino acids for the retention of chirality was explored, and five-membered alicyclic amino acids **5** and **7** derived from serine and threonine bearing *N*-benzoyl group were subjected to the above reaction conditions (Table 2 and Scheme 3). The more hindered cyclic amino acids **5a**, which is prepared from *N*-(2-phenyl)benzoyl-L-serine methyl ester in two steps [9], was excited under the same conditions to lead the similar yield of **6 aA** (75%) and the improved retention of chirality (79% ee). The photoreaction of **5b** having cyclohexyl part in the place of dimethyl part provided the similar yield of **6bA** (70%) and the moderate retention (61% ee). Interestingly, *N*-benzoyl alicyclic

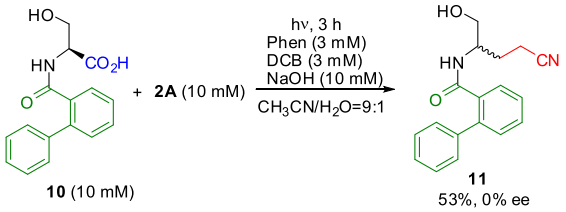
Table 2
Retention of chirality in photoinduced decarboxylative radical addition of **5** to **2A**.





Scheme 3. Retention of chirality in photoinduced decarboxylative radical addition of **7** to **2A**.

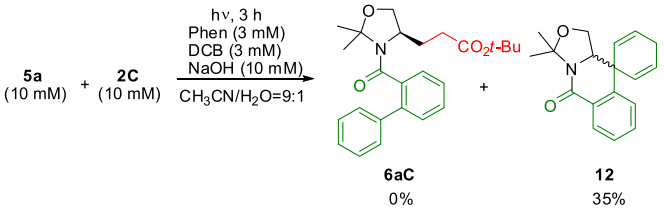
amino acid **5c** in the absence of 2-phenyl group led to the low retention of chirality (13% ee) in **6 cA** even though the corresponding proline **1c** yielded racemic mixture of **3 cA** (Table 1). Thus, the more bulky alicyclic amino acid **5a** than **1a** is proven to improve the retention of chirality, but **5b** bearing cyclohexyl part than **5a** decreased ee%. The photoreaction of **7a**, which is also prepared from *N*-(2-phenyl)benzoyl-L-threonine methyl ester [9], under the same conditions yielded the single diastereomer of adduct **8a** (44%) and cyclized product **9a** (27%) (Scheme 3). Increase of the concentration of **2A** (20 and 30 mM) caused an increase of the yield of the single diastereomer **8a** (70 and 78%) and a decrease of the yield of **9a** (16 and 13%), indicating that the additional methyl part disturbed intermolecular radical addition to **2A** to require the high concentration of the alkene for the formation of **8a**. In addition, this situation also promoted the radical cyclization at *ipso*-position and restricted the formation of another diastereomer to lead to the high retention of chirality. To exclude the possibility that the diastereoselectivity arises from the methyl group adjacent to the radical center, the photoreaction of threonine derivative bearing benzoyl group **7b** was examined. Unfortunately, the similar photoreaction of **7b** provided complex mixture. As reported previously [7], the photoreaction of the corresponding *N*-Boc threonine derivative with methyl acrylate using Ir photocatalyst gave the diastereomer mixture (65:35) of adduct, indicating that *N*-(2-phenyl)benzoyl group in **7a** promoted the retention of chirality by MOC. On the other hand, the photoreaction of open serine derivative **10** provided the racemic adduct **11** in a 53% yield (Scheme 4). Similar



Scheme 4. Loss of chirality in photoinduced decarboxylative radical addition of **10** to **2A**.

photoreaction of **5a** with **2C** did not lead to the formation of adduct **6 aC** and yielded only the cyclized product **12** (Scheme 5). Thus, the high retention of chirality of α-amino acid via the photoinduced decarboxylation requires both the suitable hindrance of alicyclic α-amino acid bearing *N*-(2-phenyl)benzoyl group as a substrate and the low hindrance of alkene.

To gain further information about the retention of chirality using the MOC strategy in the photoreaction of alicyclic amino acids, molecular orbital calculations were carried out by using the HF/3-21G basis set (Fig. 1). For this purpose, two conformers (**open** and **closed**) arising from rotation about the CO (carbonyl)–C (phenyl)



Scheme 5. Photoreaction of **5a** to **2C**.

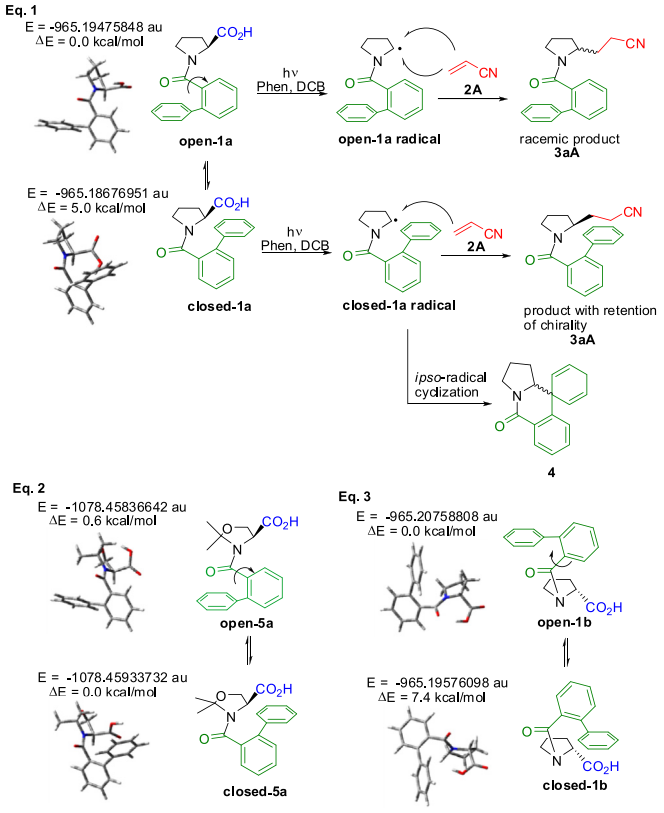


Fig. 1. Proposed mechanism and molecular orbital calculations for retention of chirality of **1a**, **5a**, and **1b**.

bond (green bond in Fig. 1) were subjected to geometry optimization. Other rotamers including s-*cis* conformer of the amide bond were not observed for minimization of energy by this calculation. The photochemical process is much faster than rotation in the ground state, and the ratio of the retention of chirality in adducts is directly determined by the ratio of the conformers in the ground state [10]. Thus, the axial chirality of CO (carbonyl)–C (phenyl) bond in the ground state could lead to the enantio- and diastereoselectivity of radical adducts. Molecular orbital calculations showed that the relative energy difference (ΔE) between the two conformers of **open** and **closed-1a** is 5.0 kcal/mol (Eq. (1)), because of which the ratio of **closed-1a** was smaller. The similar trend in the carboxylate ion of **1a** is observed by this calculation. Addition of a dimethyl unit to an alicyclic amino acid such as **5a** caused an inversion of the energy difference (−0.6 kcal/mol) between **open** and **closed-5a** by restricting the bond rotation due to the steric hindrance in the dimethyl region (Eq. (2)). This in turn led to a high ratio of **closed-5a** and high retention of chirality in **6 aA**. Furthermore, the additional methyl unit in the alicyclic amino acid, for example, threonine derivative **7a**, prevented the one direction of radical addition of **2A** through the **closed-7a radical** (not shown, similar **closed-5a radical**) to yield only a single diastereomer **8a**. The slightly larger energy difference (7.4 kcal/mol) in D-proline **1b** than in L-proline **1a** decreased the retention of chirality (Eq. (3)). The high steric hindrance in alkenes such as **2B**–**D** rendered the addition to **closed-1a** and **5a radical** (Eqs. (1) and (2)) difficult. Consequently, cyclized products **4** and **12** were formed via **closed-1a** and **5a radical** and poor retention of chirality was observed.

3. Conclusion

High retention of chirality in the photoinduced decarboxylative radical addition of 5-membered alicyclic amino acids bearing an *N*-(2-phenyl)benzoyl group to alkenes was achieved using the suitable steric hindrance of both substrate and alkene with the MOC strategy, despite the formation of a planar radical from the α-amino acid. In particular, threonine derivative **7a** exclusively provided a single diastereomer. Further investigation is being carried out on the retention of chirality of non-alicyclic α-amino acids (simple α-amino acids such as valine and phenylalanine) using new protective groups in this photoinduced decarboxylative radical addition.

4. Experimental section

4.1. General information

All reagents and solvents were used as received from commercial suppliers. IR spectra were recorded on an FT-IR spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 containing tetramethylsilane as an internal standard, and were acquired on either a 300 or 500 MHz spectrometers. $^{13}C\{^1H\}$ NMR spectra were acquired on a 125 MHz spectrometer. High-resolution mass spectra were obtained using double-focusing magnetic sector mass spectrometer coupled with FAB. The light source was a high-pressure (100 W) mercury arc. Column chromatography was performed on Wakogel C-300, particle size 45–75 μm. Theoretical calculations using the HF/3-21G basis set were performed by with the Gaussian 09 software package.

4.2. Procedure for the synthesis of N-benzoyl prolines 1a–i and N-(2-phenyl)benzoyl serine 10

Oxaly chloride (12 mmol, 0.87 mL) was added to the mixture of toluene (10 mL), THF (10 mL), and DMF (0.2 mL) solution containing benzoic acids (10 mmol, benzoic acid: 1.22g, 2-phenylbenzoic acid: 1.98g, 3-phenylbenzoic acid: 1.98g, 4-phenylbenzoic acid: 1.98g, 2-methylbenzoic acid: 1.36 g, 2-bromobenzoic acid: 2.00 g, 2-*iso*-propylbenzoic acid: 1.64 g, 2-(2′-methyl)phenylbenzoic acid: 2.12g), and stirred for 4 h. The organic solvent was concentrated *in vacuo* to give the corresponding benzoyl chlorides. To ice-cooled solution of NaOH (20 mmol, 0.800 g) in H_2O (20 mL) was added proline (10 mmol, 1.15 g) at 0 °C, and then THF (10 mL) solution of the corresponding benzoyl chloride (10 mmol) was slowly added. The mixture was stirred overnight at rt and then THF was evaporated. The aqueous layer was acidified (1 M HCl) to a pH 1–2 and then extracted with EtOAc and washed with brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography using hexane/EtOAc = 3:1 as the eluent, and the obtained product was recrystallized by hexane/EtOAc = 1:2 to yield the corresponding prolines **1a**–**i**. Similar procedure from L-serine provided *N*-(2-phenyl)benzoyl-L-serine **10**. Compounds **1a**–**g** and **10** have been previously reported.

4.2.1. N-(2-Phenyl)benzoyl-L-proline (**1a**)[8b,9]

1.91 g, 65%, white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.38 (m, 9H), 4.47 (m, 1H), 2.88 (m, 2H), 2.30–2.23 (m, 1H), 1.71–1.62 (m, 2H), 1.36 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.05, 172.07, 139.40, 135.71, 134.50, 130.47, 129.71, 128.83, 128.62, 128.50, 128.20, 127.97, 127.55, 60.12, 48.80, 45.83, 30.22, 27.53, 24.30, 22.42.

4.2.2. N-(2-Phenyl)benzoyl-D-proline (**1b**)[9]

0.89 g, 30%, white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.38 (m, 9H), 4.46 (m, 1H), 2.87 (m, 2H), 2.29–2.22 (m, 1H), 1.72–1.62 (m, 2H), 1.36 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.38, 172.68, 139.43, 134.28, 130.36, 129.70, 128.81, 128.63, 128.55, 128.14, 127.93, 127.58, 59.84, 48.70, 46.92, 30.61, 27.90, 24.33, 22.24.

4.2.3. N-Benzoyl-L-proline (**1c**)[9,11]

0.75 g, 34%, white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.44 (m, 5H), 4.80 (dd, *J* = 8.2, 5.0 Hz, 1H), 3.64–3.54 (m, 2H), 2.51 (m, 1H), 2.22–2.18 (m, 1H), 2.06–1.89 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.41, 171.65, 141.65, 140.15, 135.82, 129.46, 129.02, 127.92, 127.25, 126.06, 60.14, 50.71, 28.38, 25.29.

4.2.4. N-(3-Phenyl)benzoyl-L-proline (**1d**)[9]

2.18 g, 74%, white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.67 (m, 2H), 7.61–7.35 (m, 7H), 5.76 (br, 1H), 4.76 (m, 1H), 3.61 (m, 2H), 2.37–2.21 (m, 2H), 2.06–1.87 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.50, 171.68, 141.70, 141.66, 141.61, 140.21, 140.14, 139.99, 135.85, 135.81, 135.45, 129.58, 129.47, 129.33, 129.02, 127.98, 127.92, 127.58, 127.25, 126.06, 60.14, 50.83, 50.71, 50.64, 28.37, 25.29.

4.2.5. N-(4-Phenyl)benzoyl-L-proline (**1e**)[8b,9,12]

2.18 g, 74%, white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69–7.59 (m, 6H), 7.50–7.37 (m, 3H), 4.82 (dd, *J* = 8.1, 4.9 Hz, 1H), 3.72–3.62 (m, 2H), 2.53 (m, 1H), 2.24–2.11 (m, 1H), 2.11–1.91 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.66, 171.68, 141.66, 140.14, 135.81, 129.47, 129.02, 127.92, 127.25, 126.06, 60.14, 50.71, 28.37, 25.29.

4.2.6. N-(2-Methyl)benzoyl-L-proline (**1f**)[8b]

0.77 g, 33%, white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.21 (m, 4H), 4.78 (m, 0.9H), 4.11 (m, 0.1H), 3.79 (m, 0.1H), 3.27 (m, 2.9H), 2.45 (m, 1H), 2.30 (m, 3H), 2.18 (m, 1H), 2.02–1.97 (m, 1H), 1.90–1.87 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.31, 174.68, 171.52, 170.89, 136.23, 136.07, 134.47, 130.65, 129.44, 129.27, 125.93, 125.67, 60.89, 58.90, 49.26, 46.02, 31.28, 29.14, 24.76, 22.74, 19.03, 18.91.

*4.2.7. N-(2-Bromo)benzoyl-L-proline (**1g**)[13]*

2.20 g, 75%, white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (m, 1H), 7.45–7.29 (m, 3H), 4.82 (dd, J = 8.3, 3.6 Hz, 0.9H), 4.20 (m, 0.1H), 3.83 (m, 0.2H), 3.35–3.31 (m, 1.8H), 2.57 (m, 1H), 2.22–1.94 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.08, 171.45, 135.38, 130.73, 128.49, 127.34, 59.97, 50.55, 28.57, 25.29.

*4.2.8. N-(2-iso-Propyl)benzoyl-L-proline (**1h**)*

1.04 g, 40%, white solid; m.p. 132–131 °C; IR (KBr, cm^{-1}) 3432, 3051, 1732, 1625; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.37 (m, 2H), 7.24–7.16 (m, 2H), 4.80 (dd, J = 8.2, 4.0 Hz, 1H), 3.29–3.25 (m, 2H), 3.03–2.94 (m, 1H), 2.57–2.47 (m, 1H), 2.23–1.84 (m, 3H), 1.27–1.22 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.83, 171.38, 144.42, 134.05, 129.03, 125.27, 58.43, 48.98, 30.15, 29.79, 29.68, 27.70, 23.91, 23.34, 23.10; HRMS (FAB) calcd for $(M + H)^+$ $C_{15}H_{19}NO_3$: 262.1438, found 262.1451.

*4.2.9. N-[2-(2′-Methyl)phenyl]benzoyl-L-proline (**1i**)*

1.05 g, 34%, white solid; m.p. 62–61 °C; IR (KBr, cm^{-1}) 3439, 3060, 1735, 1621; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.38 (br, 1H), 7.50–7.18 (m, 8H), 4.36 (m, 0.9H), 3.95 (m, 0.1H), 3.57 (m, 0.1H), 3.23–3.00 (m, 1.9H), 2.45–2.24 (m, 3H), 2.14–1.97 (m, 2H), 1.82–1.26 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.86, 173.95, 171.44, 169.85, 138.62, 136.48, 135.72, 130.58, 130.44, 129.88, 129.25, 128.00, 127.83, 127.61, 127.47, 126.76, 125.53, 59.25, 48.70, 45.52, 30.37, 28.14, 24.51, 22.41, 20.21, 20.04; HRMS (FAB) calcd for $(M + H)^+$ $C_{19}H_{19}NO_3$:310.01438, found 310.1444.

*4.2.10. N-(2-Phenyl)benzoyl-L-serine (**10**)[4a,9]*

White solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.35 (d, J = 8.0 Hz, 1H), 7.50–7.26 (m, 8H), 4.28–4.25 (m, 1H), 3.64–3.56 (m, 2H), 3.31 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.36, 169.60, 140.55, 139.91, 136.90, 130.47, 130.23, 129.00, 128.67, 128.59, 127.63, 127.50, 61.76, 55.61.

4.3. Procedure for the synthesis of N-benzoyl-2,2-dialkyl-4-oxazolidine carboxylic acids 5a–c and 7a,b from serine and threonine methyl esters

THF solution (20 mL) of the corresponding benzoyl chloride (20 mmol) was added dropwise to L-serine or threonine methyl esters (3.12 or 3.40 g, 20 mmol) in an aq. $NaHCO_3$ (3.36 g, 40 mmol) solution (40 mL) at 0 °C. The mixture was stirred overnight at room temperature, and then extracted with EtOAc, and washed with brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography using hexane/EtOAc = 4:1 as the eluent to yield the corresponding *N*-benzoyl-L-serine or threonine methyl esters (*N*-benzoyl-L-serine methyl ester: 1.90 g, 65%; *N*-(2-phenyl)benzoyl-L-serine methyl ester: 3.88 g, 34%; *N*-(2-phenyl)benzoyl-L-threonine methyl ester: 2.13 g, 34%).

The mixture of benzene (24 mL) and chloroform (14 mL) solution containing *N*-benzoyl-L-serine or threonine methyl esters (10 mmol, *N*-benzoyl-L-serine methyl ester: 2.24 g, *N*-(2-phenyl) benzoyl-L-serine methyl ester: 3.00 g, *N*-(2-phenyl)benzoyl-L-threonine methyl ester: 3.13 g), *p*-TsOH (20 mg, 0.1 mmol), and 2,2-dimethoxypropane or 1,1-dimethoxycyclohexane (2.45 or 3.04 mL, 20 mmol) was reflux for 4 h at 80 °C. The organic solvent was removed by distillation, and quenched by saturated aq. $NaHCO_3$ solution, and then extracted with EtOAc, and washed with brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography using hexane/EtOAc = 7:1 as the eluent to yield the corresponding *N*-benzoyl-2,2-dialkyl-4-oxazolidine methyl esters ((*4R*)-*N*-benzoyl-2,2-dimethyl-4-oxazolidine methyl ester: 1.84 g, 70%; (*4R*)-*N*-(2-phenyl)benzoyl-2,2-dimethyl-4-oxazolidine methyl ester: 2.54 g, 75%; (*4R*)-*N*-(2-phenyl)benzoyl-2-cyclohexyl-4-oxazolidine methyl ester: 2.80 g, 74%; (*4R*, *5R*)-*N*-(2-phenyl)benzoyl-2,2,5-trimethyl-4-oxazolidine methyl ester: 2.26 g, 64%).

The obtained methyl esters (3 mmol, (*4R*)-*N*-benzoyl-2,2-dimethyl-4-oxazolidine methyl ester: 0.78 g, (*4R*)-*N*-(2-phenyl) benzoyl-2,2-dimethyl-4-oxazolidine methyl ester: 1.02 g, (*4R*)-*N*-(2-phenyl)benzoyl-2-cyclohexyl-4-oxazolidine methyl ester: 1.09 g, (*4R*, *5R*)-*N*-(2-phenyl)benzoyl-2,2,5-trimethyl-4-oxazolidine methyl ester: 1.06 g) were hydrolyzed by using NaOH (6 mmol, 0.24 g) in the mixture of THF (12 mL) and H_2O (4 mL) solution at room temperature until starting materials were consumed completely (by TLC monitoring, about 3 h). After each reaction is complete, the solution was washed by Et_2O, and then 1 M H_2SO_4 was added until pH = 3 and the solution was extracted with EtOAc. The organic layer was washed with H_2O and brine, and dried over with Na_2SO_4, and concentrated *in vacuo* giving a residue that was subjected to silica gel column chromatography using hexane/EtOAc = 1:1 as the eluent to yield the desired 4-oxazolidine carboxylic acids **5** and **7**. Compounds **5a**, **5c**, and **7a**, **7b** have been previously reported.

*4.3.1. (4R)-N-(2-Phenyl)benzoyl-2,2-dimethyl-4-oxazolidine carboxylic acid (**5a**)[5c,9]*

0.76 g, 78%, white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.67 (s, 1H), 7.46–7.23 (m, 9H), 3.85 (m, 1H), 3.72 (m, 1H), 3.24 (m, 1H), 1.72 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.35, 168.33, 139.42, 137.69, 136.08, 129.79, 129.43, 128.96, 128.84, 128.18, 127.74, 96.80, 66.64, 60.02, 25.48, 22.39.

*4.3.2. (4R)-N-(2-Phenyl)benzoyl-2-cyclohexyl-4-oxazolidine carboxylic acid (**5b**)*

0.73 g, 67%, white solid; m.p. 228–227 °C; IR (KBr, cm^{-1}) 3431, 3060, 1746, 1625; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.25 (m, 9H), 7.14–6.70 (m, 1H), 3.84 (dd, J = 8.3, 4.5 Hz, 1H), 3.73 (d, J = 5.9 Hz, 1H), 3.24–3.19 (m, 1H), 2.75–2.65 (m, 1H), 2.29–2.25 (m, 1H), 1.75–1.24 (m, 7H), 0.99–0.89 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.74, 168.80, 139.36, 137.56, 136.22, 129.69, 129.39, 128.97, 128.81, 128.17, 128.08, 127.66, 98.43, 66.51, 60.16, 33.53, 29.29, 24.52, 23.17, 23.11; HRMS (FAB) calcd for $(M + H)^+$ $C_{22}H_{23}NO_4$: 366.1700, found 366.1700.

*4.3.3. (4R)-N-Benzoyl-2,2-dimethyl-4-oxazolidine carboxylic acid (**5c**)[5b]*

0.43 g, 58%, white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 5H), 5.63 (br, 1H), 4.43 (m, 1H), 4.26–4.18 (m, 2H), 1.72 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.85, 168.99, 137.19, 129.91, 128.64, 126.13, 97.14, 67.11, 61.06, 24.91, 24.06.

*4.3.4. (4R, 5R)-N-(2-Phenyl)benzoyl-2,2,5-trimethyl-4-oxazolidine carboxylic acid (**7a**)[5c]*

0.86 g, 84%, white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.10 (br, 1H), 7.53–7.19 (m, 9H), 4.03 (m, 1H), 3.24 (d, J = 5.3 Hz, 1H), 1.63 (s, 3H), 1.53 (s, 3H), 0.84 (d, J = 13.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.07, 174.02, 168.90, 139.46, 138.08, 135.30, 130.04, 129.55, 129.37, 129.06, 128.82, 128.41, 127.41, 97.39, 74.93, 65.97, 25.44, 24.42, 19.61; HRMS (FAB) calcd for $(M + H)^+$ $C_{20}H_{20}N_2O_2$: 305.1649, found 305.1674.

*4.3.5. (4R, 5R)-N-Benzoyl-2,2,5-trimethyl-4-oxazolidine carboxylic acid (**7b**)[8a]*

0.81 g, 80%, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.46–7.38 (m, 5H), 4.24 (d, J = 6.0 Hz, 1H), 4.15–4.12 (m, 1H), 1.67

(s, 3H), 1.61 (s, 3H), 1.36 (d, $J = 5.0$ Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.08, 167.98, 137.40, 129.94, 128.24, 127.20, 95.78, 74.70, 67.45, 26.07, 23.20, 18.95.

4.4. General procedure for the photoreaction of 1 with 2

An aqueous CH_3CN solution (CH_3CN 36 mL, H_2O 4 mL) of **1** (10 mM), **2** (10 mM), NaOH (10 mM, 0.016g), Phen (3 mM, 0.0213g), and DCB (3 mM, 0.0153g) in Pyrex vessels (18 mm × 180 mm) was purged with Ar for 10 min. The mixture was irradiated with a 100 W high-pressure mercury lamp for 3 h, and then the solvent was removed under reduced pressure. The crude product was purified by silica-gel column chromatography using hexane/EtOAc = 4:1 as the eluent to yield adduct **3** and cyclized product **4**. Similar photoreactions of **5**, **7**, and **10** with **2** were carried out under the same conditions to yield **6**, **8**, **9**, **11**, and **12**. Compounds **4**, **11**, and **12** have been previously reported.

4.4.1. N-(2-Phenyl)benzoyl-2-pyrrolidinepropanenitrile (**3aA**) +48ee%

0.103 g, 85%, colorless oil; IR (neat, cm^{-1}) 2940, 2245, 1625; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52–7.40 (m, 9H), 4.16 (m, 1H), 3.46–3.25 (m, 0.5H), 2.96–2.88 (m, 1H), 2.71 (m, 0.5H), 2.32–1.25 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.49, 140.03, 139.82, 138.39, 136.83, 130.01, 129.73, 129.50, 128.82, 128.71, 128.55, 127.99, 127.85, 126.93, 119.86, 55.95, 48.04, 45.49, 30.06, 29.48, 29.39, 24.07, 21.99, 14.37, 14.25; HRMS (FAB) calcd for $(M + H)^+$ $C_{20}H_{20}N_2O$: 305.1649 found 305.1661.

4.4.2. N-(2-Phenyl)benzoyl-2-pyrrolidinepropanenitrile (**3bA**) −42ee%

0.098 g, 80%, colorless oil; IR (neat, cm^{-1}) 3060, 2246, 1621; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47–7.38 (m, 9H), 4.17 (m, 1H), 3.46–3.25 (m, 0.5H), 2.96–2.88 (m, 1H), 2.70 (m, 0.5H), 2.28–1.25 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.38, 170.07, 139.94, 139.72, 136.73, 129.91, 129.63, 129.50, 129.41, 128.72, 128.61, 128.45, 127.90, 127.76, 126.84, 119.77, 118.29, 55.86, 47.94, 45.39, 29.96, 29.68, 29.29, 28.31, 23.96, 21.89, 15.25, 15.08, 14.27, 14.15; HRMS (FAB) calcd for $(M + H)^+$ $C_{20}H_{20}N_2O$: 305.1649 found 305.1674.

4.4.3. N-Benzoyl-2-pyrrolidinepropanenitrile (**3cA**)

0.073 g, 80%, colorless oil; IR (neat, cm^{-1}) 2992, 2247, 1621; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.36 (m, 5H), 4.37–4.34 (m, 0.9H), 4.02 (m, 0.1H), 3.77 (m, 0.1H), 3.52–3.40 (m, 1.9H), 2.50–2.47 (m, 2H), 2.23–2.13 (m, 2H), 1.97–1.69 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.00, 136.78, 130.32, 128.39, 127.44, 119.95, 56.44, 50.37, 30.58, 30.15, 25.14, 14.44; HRMS (FAB) calcd for $(M + H)^+$ $C_{14}H_{16}N_2O$: 229.1336 found 229.1351.

4.4.4. N-(3-Phenyl)benzoyl-2-pyrrolidinepropanenitrile (**3dA**)

0.059 g, 48%, colorless oil; IR (neat, cm^{-1}) 2949, 2246, 1623; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76–7.35 (m, 9H), 4.44–4.39 (m, 1H), 3.57–3.51 (m, 2H), 2.56–2.51 (m, 2H), 2.30–2.17 (m, 2H), 2.01–1.74 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.88, 141.68, 140.18, 137.13, 128.98, 128.88, 127.79, 127.24, 126.18, 119.78, 56.52, 50.42, 30.62, 30.21, 25.14, 14.51; HRMS (FAB) calcd for $(M + H)^+$ $C_{20}H_{20}N_2O$: 305.1649 found 305.1661.

4.4.5. N-(4-Phenyl)benzoyl-2-pyrrolidinepropanenitrile (**3eA**)

0.098 g, 80%, white solid; m.p. 119–118 °C; IR (KBr, cm^{-1}) 2952, 2336, 1621; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63–7.37 (m, 9H), 4.42 (m, 1H), 3.60–3.54 (m, 2H), 2.53 (m, 2H), 2.29–2.16 (m, 2H), 2.04–1.72 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.73, 143.12, 140.18, 135.35, 128.90, 128.00, 127.85, 127.37, 127.16, 126.98, 119.88, 56.45, 50.38, 30.51, 30.08, 25.13, 14.36; HRMS (FAB) calcd for $(M + H)^+$ $C_{20}H_{20}N_2O$: 305.1649 found 305.1656.

4.4.6. N-(2-Methyl)benzoyl-2-pyrrolidinepropanenitrile (**3fA**)

0.084 g, 77%, colorless oil; IR (neat, cm^{-1}) 2952, 2245, 1629; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.19 (m, 4H), 4.35–4.33 (m, 0.9H), 3.81 (m, 0.1H), 3.62 (m, 0.2H), 3.20–3.13 (m, 1.8H), 2.55–2.50 (m, 2H), 2.30 (s, 3H), 2.16–2.12 (m, 1H), 2.01–1.75 (m, 4H), 1.61 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.89, 137.45, 133.78, 130.59, 129.09, 126.06, 125.76, 119.86, 56.05, 48.82, 30.50, 30.21, 24.49, 19.12, 14.78; HRMS (FAB) calcd for $(M + H)^+$ $C_{15}H_{18}N_2O$: 243.1492 found 243.1485.

4.4.7. N-(2-Bromo)benzoyl-2-pyrrolidinepropanenitrile (**3gA**)

0.104 g, 85%, colorless oil; IR (neat, cm^{-1}) 2973, 2245, 1633; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58–7.54 (m, 1H), 7.36–7.21 (m, 3H), 4.36–4.34 (m, 0.9H), 3.93–3.69 (m, 0.1H), 3.63–3.39 (m, 0.1H), 3.25–3.15 (m, 1.9H), 2.62–2.51 (m, 2H), 2.25–2.03 (m, 2H), 1.97–1.73 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.08, 139.20, 132.90, 130.48, 127.98, 127.57, 119.96, 118.54, 57.79, 56.33, 48.34, 45.44, 30.40, 30.03, 24.22, 22.41, 14.82, 14.01; HRMS (FAB) calcd for $(M + H)^+$ $C_{14}H_{15}BrN_2O$: 307.0441 found 307.0468.

4.4.8. N-(2-iso-Propyl)benzoyl-2-pyrrolidinepropanenitrile (**3hA**)

0.079 g, 73%, colorless oil; IR (neat, cm^{-1}) 3007, 2248, 1628; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.30 (m, 2H), 7.21–7.13 (m, 2H), 4.33 (m, 0.9H), 3.80 (m, 0.1H), 3.57 (m, 0.1H), 3.15 (m, 1.9H), 3.00–2.94 (m, 1H), 2.56–2.46 (m, 2H), 2.28 (m, 1H), 2.14–2.09 (m, 1H), 2.02–1.76 (m, 4H), 1.27–1.19 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.94, 144.79, 136.49, 129.69, 129.40, 126.05, 126.00, 125.77, 119.89, 57.76, 56.04, 49.25, 30.64, 30.52, 30.17, 30.04, 24.42, 24.00, 14.72; HRMS (FAB) calcd for $(M + H)^+$ $C_{17}H_{22}N_2O$: 271.1805 found 271.1809.

4.4.9. N-[2'-(2''-Methyl)phenyl]benzoyl-2-pyrrolidinepropanenitrile (**3iA**)

0.120 g, 91%, colorless oil; IR (neat, cm^{-1}) 3060, 2245, 1630; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.21 (m, 8H), 4.14 (m, 1H), 3.13 (m, 1H), 3.00–2.79 (m, 1H), 2.32–2.17 (m, 3H), 2.05–1.98 (m, 2H), 1.73–1.49 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.21, 137.60, 130.58, 130.28, 129.04, 128.31, 128.18, 127.70, 120.00, 55.48, 48.41, 30.12, 29.86, 24.49, 24.24, 20.32, 13.88; HRMS (FAB) calcd for $(M + H)^+$ $C_{21}H_{22}N_2O$: 319.1805, found 319.1826.

4.4.10. N-(2-Phenyl)benzoyl-2-pyrrolidine methyl propionate (**3aB**)

0.092 g, 68% (using hexane/EtOAc = 2:1 as the eluent), colorless oil; IR (neat, cm^{-1}) 2980, 1737, 1634; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.32 (m, 9H), 4.14 (m, 1H), 3.70 (s, 3H), 3.55 (m, 1H), 3.44–3.39 (m, 0.5H), 3.20 (m, 0.5H), 2.91–2.84 (m, 1H), 2.40–2.05 (m, 1H), 1.93 (m, 1H), 1.72–1.26 (m, 5H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 173.82, 172.88, 169.91, 139.92, 137.11, 136.26, 132.24, 129.54, 129.44, 129.23, 128.75, 128.61, 128.49, 128.42, 127.77, 127.64, 127.07, 57.33, 56.20, 51.60, 47.71, 45.06, 42.06, 30.99, 30.56, 29.76, 29.33, 29.25, 23.89, 21.81; HRMS (FAB) calcd for $(M + H)^+$ $C_{21}H_{23}NO_3$: 338.1751, found 338.1760.

4.4.11. N-(2-Phenyl)benzoyl-2-pyrrolidine t-butyl propionate (**3aC**)

0.091 g, 60% (using hexane/EtOAc = 5:1 as the eluent), colorless oil; IR (neat, cm^{-1}) 2926, 1725, 1622; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51–7.34 (m, 9H), 4.11 (m, 1H), 3.27 (m, 0.5H), 2.87 (m, 1H), 2.63 (m, 0.5H), 2.22–1.63 (m, 4H), 1.52–1.30 (m, 13H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.68, 171.91, 169.77, 139.90, 137.17, 136.33, 129.51, 129.20, 128.75, 128.59, 128.44, 128.40, 127.76, 127.61, 127.09, 80.36, 80.13, 57.62, 56.31, 47.68, 45.11, 32.52, 32.10, 29.64, 29.44, 29.24, 28.11, 28.00, 23.86, 21.84; HRMS (FAB) calcd for $(M + H)^+$ $C_{24}H_{29}NO_3$: 380.2220, found 380.2210.

*4.4.12. N-(2-Phenyl)benzoyl-2-pyrrolidine N′-t-butyl propionamide (**3aD**)*

0.077 g, 50% (using hexane/EtOAc = 1:1 as the eluent), colorless oil; IR (neat, cm^{-1}) 2967, 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49–7.37 (m, 9H), 6.67 (br, 1H), 4.11 (m, 1H), 2.85 (m, 2H), 2.05 (m, 1H), 1.91 (m, 1H), 1.52–1.29 (m, 13H), 1.24 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.12, 170.41, 139.93, 136.87, 129.66, 129.34, 128.75, 128.59, 128.50, 128.36, 127.74, 126.90, 56.10, 51.04, 47.72, 34.90, 31.59, 30.42, 30.16, 28.83, 28.74, 25.36, 23.69, 22.66, 14.15; HRMS (FAB) calcd for $(M + H)^+$ $C_{24}H_{30}N_2O_2$: 379.2380, found 379.2378.

*4.4.13. Spirodihydroisoquinolinone (**4**)[9]*

0.007 g, 7% in the case of **2B** or 0.019 g, 19% in the case of **2C** or 0.013 g, 13% in the case of **2D** (using hexane/EtOAc = 7:1 as the eluent), white solid; ^1H NMR (300 MHz, $CDCl_3$) δ 8.11–8.08 (m, 1H), 7.48–7.42 (m, 1H), 7.37–7.31 (m, 1H), 7.27–7.23 (m, 1H), 6.24–6.18 (m, 1H), 5.84–5.80 (m, 1H), 5.63–5.54 (m, 2H), 3.89–3.76 (m, 2H), 3.64–3.56 (m, 1H), 2.78–2.75 (m, 2H), 2.02–1.77 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.92, 144.90, 131.98, 128.79, 128.37, 127.95, 127.50, 127.04, 126.61, 126.51, 125.40, 63.95, 45.77, 44.03, 28.66, 26.74, 22.85.

*4.4.14. N-(2-Phenyl)benzoyl-2,2-dimethyl-4-oxazolidinepropanenitrile (**6aA**)*

0.104 g, 75%, white solid; m.p. 115–114 °C; IR (KBr, cm^{-1}) 3060, 2246, 1635; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56–7.39 (m, 9H), 3.42 (d, J = 9.3 Hz, 1H), 3.32 (m, 1H), 2.98 (m, 1H), 2.17–1.93 (m, 2H), 1.68 (s, 3H), 1.58 (s, 3H), 1.30–1.25 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.91, 139.55, 137.81, 136.35, 130.06, 129.99, 129.15, 128.84, 128.10, 127.90, 127.79, 117.98, 95.56, 65.91, 56.67, 29.16, 27.11, 21.77, 14.18; HRMS (FAB) calcd for $(M + H)^+$ $C_{21}H_{22}N_2O_2$: 335.1754, found 335.1768.

*4.4.15. N-(2-Phenyl)benzoyl-2-cyclohexyl-4-oxazolidinepropanenitrile (**6bA**)*

0.106 g, 70%, white solid; m.p. 76–75 °C; IR (KBr, cm^{-1}) 2932, 2336, 1633; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54–7.39 (m, 9H), 3.40 (d, J = 9.2 Hz, 1H), 3.28 (m, 1H), 2.92 (m, 1H), 2.77 (m, 1H), 2.30 (m, 1H), 2.02–1.92 (m, 2H), 1.65–1.26 (m, 9H), 0.98 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.11, 139.50, 137.69, 136.68, 130.04, 129.88, 129.16, 128.80, 128.08, 127.86, 127.77, 118.00, 97.10, 65.62, 56.64, 35.46, 29.26, 28.42, 24.48, 23.27, 23.05, 14.21; HRMS (FAB) calcd for $(M + H)^+$ $C_{24}H_{26}N_2O_2$: 375.2067, found 375.2086.

*4.4.16. N-Benzoyl-2,2-dimethyl-4-oxazolidinepropanenitrile (**6cA**)*

0.082 g, 76% (using hexane/EtOAc = 6:1 as the eluent), colorless.s oil; IR (neat, cm^{-1}) 2983, 2245, 1635; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.40 (m, 5H), 4.13–4.09 (m, 2H), 3.82 (d, J = 5.3 Hz, 1H), 2.20–2.10 (m, 2H), 1.73–1.60 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.80, 137.29, 129.88, 128.78, 126.04, 95.62, 66.56, 57.35, 29.44, 26.82, 23.41, 14.04; HRMS (FAB) calcd for $(M + H)^+$ $C_{15}H_{18}N_2O_2$: 259.1441, found 259.1426.

*4.4.17. N-(2-Phenyl)benzoyl-2,2,5-triimethyl-4-oxazolidinepropanenitrile (**8**)*

0.060 g, 44% in the case of 10 mM of **2A** or 0.098 g, 70% in the case of 20 mM of **2A** or 0.110 g, 78% in the case of 30 mM of **2A** (using hexane/EtOAc = 10:1 as the eluent), white solid; m.p. 94–93 °C; IR (KBr, cm^{-1}) 3059, 2247, 1633; ^1H NMR (500 MHz, $CDCl_3$) δ 7.60–7.36 (m, 9H), 3.79–3.75 (m, 1H), 2.98–2.96 (m, 1H), 1.97–1.95 (m, 1H), 1.89–1.87 (m, 1H), 1.74–1.63 (m, 1H), 1.60–1.54 (m, 6H), 1.48–1.44 (m, 1H), 0.41 (d, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.26, 139.61, 137.60, 136.26, 130.33, 130.13, 129.29, 128.96, 128.35, 128.27, 127.85, 117.77, 96.03, 62.14, 29.82, 27.59, 26.50, 20.55, 14.17; HRMS (FAB) calcd for $(M + H)^+$ $C_{22}H_{24}N_2O_2$: 349.1911, found 349.1898.

*4.4.18. 2,2,4-Trimethyl-3-oxo-spirodihydroisoquinolinone (**9**)*

0.032 g, 27% in the case of 10 mM of **2A** or 0.019 g, 16% in the case of 20 mM of **2A** or 0.015 g, 13% in the case of 30 mM of **2A** (using hexane/EtOAc = 7:1 as the eluent), white solid; m.p. 174–173 °C; IR (KBr, cm^{-1}) 3053, 1654; ^1H NMR (300 MHz, $CDCl_3$) δ 8.08–8.06 (m, 1H), 7.50–7.44 (m, 1H), 7.38–7.33 (m, 1H), 7.29–7.23 (m, 1H), 6.30–6.26 (m, 1H), 5.85–5.82 (m, 1H), 5.72–5.62 (m, 2H), 4.19–4.10 (m, 1H), 3.51 (d, J = 9.0 Hz, 1H), 2.78 (m, 2H), 1.80 (s, 3H), 1.69 (s, 3H), 1.37–1.34 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.78, 144.30, 132.89, 132.40, 129.19, 128.90, 127.99, 127.38, 127.18, 126.47, 126.35, 125.28, 117.11, 116.79, 93.42, 73.36, 67.85, 42.08, 26.71, 26.43, 24.12, 19.12; HRMS (FAB) calcd for $(M + H)^+$ $C_{19}H_{21}NO_2$:296.164500, found 296.1649.

*4.4.19. 4-Hydroxymethyl-4-[N-(2′-phenyl)benzoyl] aminobutyronitrile (**11**)[4a]*

0.067 g, 53%, colorless oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 7.7 Hz, 1H), 7.58–7.39 (m, 3H), 7.30–7.08 (m, 5H), 4.70 (d, J = 9.2 Hz, 1H), 3.96–3.83 (m, 2H), 3.64 (m, 1H), 1.91–1.63 (m, 2H), 1.25–1.14 (m, 1H), 0.95–0.83 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.77, 168.34, 142.23, 142.16, 140.09, 139.41, 135.57, 131.87, 131.04, 130.70, 130.46, 130.15, 129.82, 128.79, 128.61, 128.52, 128.33, 128.29, 128.20, 127.77, 127.57, 127.48, 119.05, 66.33, 47.05, 27.17, 13.88; HRMS (FAB) calcd for $(M + H)^+$ $C_{18}H_{18}N_2O_2$: 295.1441, found 295.1439.

*4.4.20. 2,2-Dimethyl-3-oxo-spirodihydroisoquinolinone (**12**)[9]*

0.039 g, 35% (using hexane/EtOAc = 7:1 as the eluent), white solid; ^1H NMR (300 MHz, $CDCl_3$) δ 8.10–8.07 (m, 1H), 7.51–7.45 (m, 1H), 7.40–7.35 (m, 1H), 7.27–7.21 (m, 1H), 6.26–6.22 (m, 1H), 5.89–5.86 (m, 1H), 5.69–5.61 (m, 2H), 4.09–4.02 (m, 2H), 3.95–3.91 (m, 1H), 2.78 (m, 2H), 1.78 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.75, 144.35, 132.33, 129.32, 129.12, 128.07, 127.34, 126.48, 126.42, 125.78, 95.24, 66.15, 62.10, 42.08, 26.66, 25.57, 23.89.

4.5. Chiral-HPLC analysis of the retention of α-chirality in the photoinduced decarboxylative radical addition

In order to measure the retention of α-chirality of adducts in the photoinduced decarboxylative radical addition, chiral HPLC analysis of adducts were carried out under these conditions. (1) For **3 aA**–**iA**, **3 aB**, **6 aA**–**iA, 8**, and **11**, Column: Daicel CHIRALPAK OD-H, eluent: hexane/2-propanol = 15/1, flow rate: 0.2 mLmin^{-1}, room temperature, UV detector: l = 254 nm. (2) For **3 aC**, Column: Daicel CHIRALPAK OD-H, eluent: hexane/2-propanol = 50/1, flow rate: 0.2 mLmin^{-1}, room temperature, UV detector: l = 254 nm. (3) For **3aD**, Column: Daicel CHIRALPAK OD-H, eluent: hexane/2-propanol = 30/1, flow rate: 0.2 mLmin^{-1}, room temperature, UV detector: l = 254 nm. Microanalyses should be included whenever possible. Under appropriate circumstances, high-resolution mass spectra may serve in lieu of microanalysis, if accompanied by suitable NMR criteria for sample homogeneity.

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Appendix A. Supplementary data

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