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Highlights

Aerobic oxidation under visible light conditions

No need for an external photocatalyst

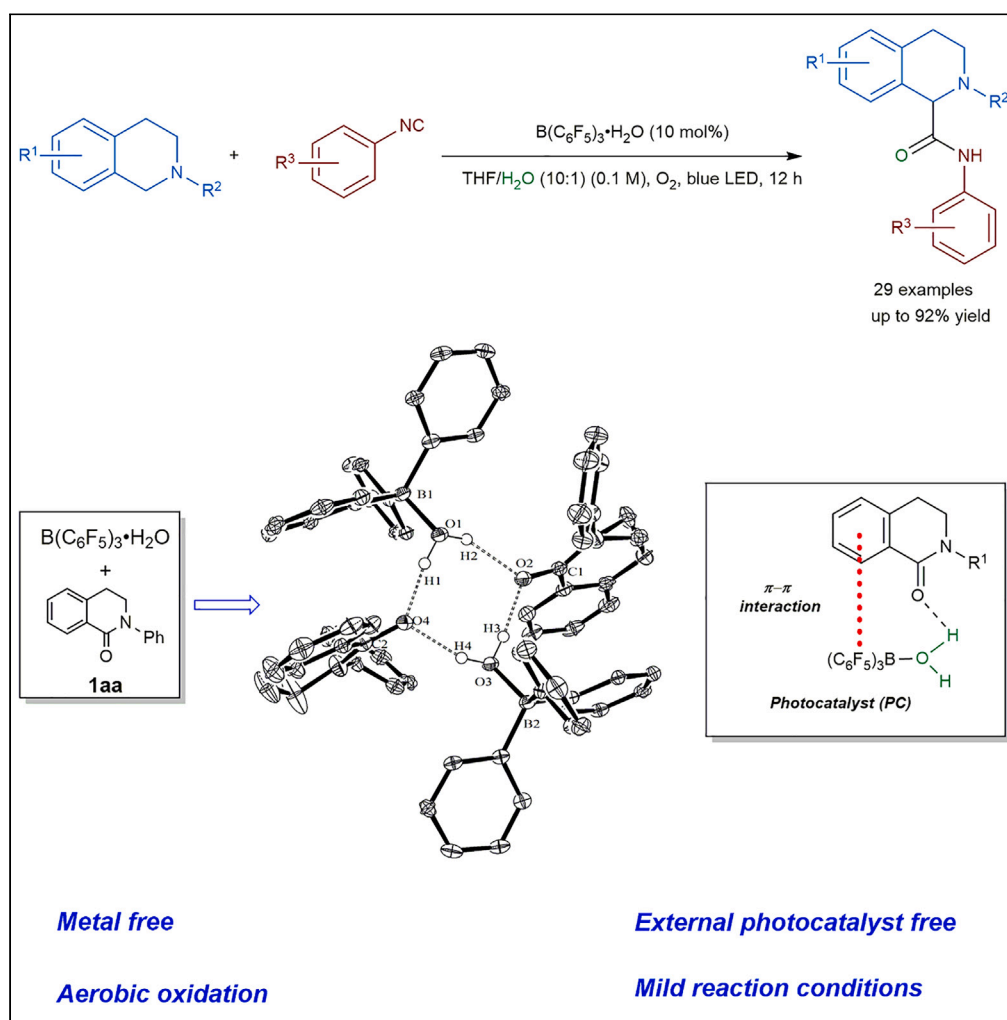Hydrogen bonds and π-π interactions between B(C₆F₅)₃·H₂O and amides were identified

Article

Synergistic effect of hydrogen bonds and π-π interactions of B(C$_6$F$_5$)$_3$·H$_2$O/amides complex: Application in photoredox catalysis

Shi-Jun Wang,[1] Long Wang,[1] and Xiang-Ying Tang[1,2,*]

SUMMARY

B(C$_6$F$_5$)$_3$·H$_2$O has been long recognized as a common Brønsted acid. The lack of X-ray crystal structure of B(C$_6$F$_5$)$_3$·H$_2$O with other substrates has greatly limited the development of a new catalytic mode. In this work, a complex of B(C$_6$F$_5$)$_3$·H$_2$O and amide 2-phenyl-3,4-dihydroisoquinolin-1(2H)-one with hydrogen bonds and π-π interactions is characterized by X-ray diffraction. Such noncovalent interactions in solution also exist, as verified by NMR, UV-Vis absorption, and fluorescence emission measurements. Moreover, the mixture of amide 2-phenyl-3,4-dihydroisoquinolin-1(2H)-one and B(C$_6$F$_5$)$_3$·H$_2$O, instead of other tested Brønsted acids, shows a tailing absorption band in the visible light region (400–450 nm). Based on the photoactive properties of the complex, a photoredox catalysis is developed to construct α-aminoamides under mild conditions.

INTRODUCTION

Tris(pentafluorophenyl)borane, B(C$_6$F$_5$)$_3$, as a main group Lewis acid, has been deeply investigated during the last decade.[1–8] Besides, with the discovery of crystal structure of B(C$_6$F$_5$)$_3$ with various molecules,[9–18] the catalytic mode of B(C$_6$F$_5$)$_3$ was further revealed.[19–31] On the other hand, owing to the moisture sensitivity of B(C$_6$F$_5$)$_3$, it is likely that the Brønsted acid B(C$_6$F$_5$)$_3$·H$_2$O acts as the real catalyst.[32,33] Although, there are some reports indicating that this effect can be attenuated in frustrated Lewis pairs (FLP) chemistry,[34–37] the strict anhydrous conditions are still necessary in most B(C$_6$F$_5$)$_3$ catalyzed transformations.

B(C$_6$F$_5$)$_3$·H$_2$O is a strong Brønsted acid[38–40] and the strength is similar to that of HCl in acetonitrile.[38] It has been reported that B(C$_6$F$_5$)$_3$·H$_2$O shows superior activity than other Brønsted acids in some transformations.[41–45] However, it is difficult to identify the real catalytic species under moist conditions, because Lewis acid and water-mediated pathways are competitive.[34–37,41–47] In the water-tolerant FLP-catalyzed hydrogenation, for instance, ethers could competitively replace water to coordinate with B(C$_6$F$_5$)$_3$ (Figure 1A).[34–37] Meanwhile, B(C$_6$F$_5$)$_3$·H$_2$O are mainly considered as a hydrogen bond donor. For instance, in the B(C$_6$F$_5$)$_3$·H$_2$O catalyzed ring opening reactions of epoxides,[46,47] hydrogen bond interactions between B(C$_6$F$_5$)$_3$·H$_2$O and epoxides/alcohols are revealed by microkinetic modeling and density functional theory calculations (Figure 1B).[44] Even though existing studies could account for the hydrogen bond interactions, other noncovalent interactions are barely considered. Thus, the direct and intuitive evidences such as X-ray single crystal diffraction are highly desirable.

A myriad of X-ray structures of four-coordinated complex via anhydrous B(C$_6$F$_5$)$_3$ were reported.[9–18] In contrast, there have been very limited reports involving X-ray structures of B(C$_6$F$_5$)$_3$·H$_2$O with other molecules,[38–40] resulting in difficulties understanding the difference between B(C$_6$F$_5$)$_3$·H$_2$O and other Brønsted acids. Herein, we wish to report an interesting X-ray crystal structure (**C1**) of B(C$_6$F$_5$)$_3$·H$_2$O and 2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (**1aa**), forming through intermolecular hydrogen bonds and π-π interactions. Meanwhile, the mixture of B(C$_6$F$_5$)$_3$·H$_2$O and **1aa** in tetrahydrofuran (THF) solution showed reinforcement both in UV-Vis absorption and fluorescence emission. On the basic of these observations, a photoredox oxidation reaction was developed using the combination of B(C$_6$F$_5$)$_3$·H$_2$O and **1aa** as the photocatalyst.

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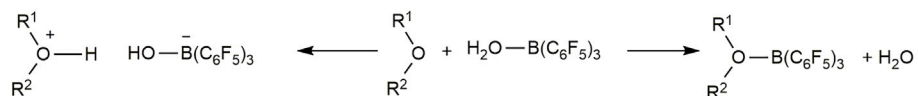
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A water-tolerant FLP-catalysis

B water- and alcohol-mediated catalysis
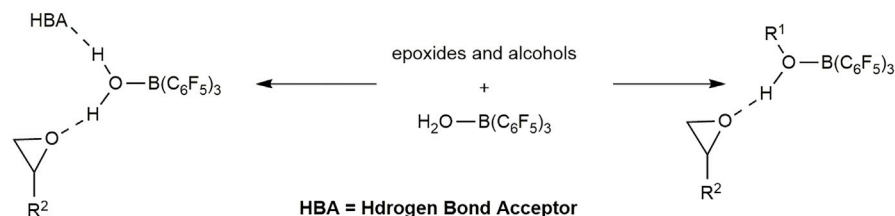

HBA = Hdrogen Bond Acceptor

Figure 1. Competitive boron Lewis acid, water-and alcohol-mediated pathways

RESULTS AND DISCUSSION

Identify noncovalent interactions between B(C₆F₅)₃·H₂O and amide 1aa

The crystals of **C1** suitable for X-ray crystal structure analysis were obtained by slowly solvent evaporation of the solution of **1aa** and $B(C_6F_5)_3 \cdot H_2O$ (1:1) in dichloromethane (Figure 2). The B-O bond lengths in **C1** are 1.5692(19) and 1.5557(19) Å, slightly shorter than that in aqua complexes of $B(C_6F_5)_3$.[38–40] Correspondingly, the C=O bond lengths are elongated to be 1.2579(19) and 1.2622(19), respectively.[48,49]

As can be seen from Figure 3, there are two π-π interactions between $-C_6F_5$ of $B(C_6F_5)_3$ and phenyl moiety of **1aa**. The twist angles of aromatic rings are 21.21(14) and 1.32(16) degree respectively. Besides, the distances between centroids are in the range of 3.30–3.80 Å.[50]
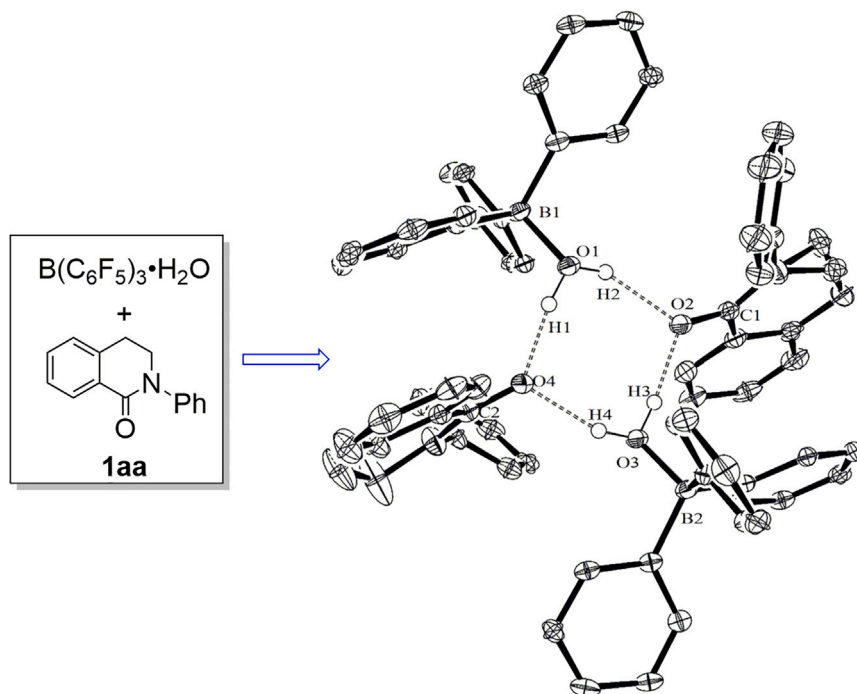

Figure 2. X-ray crystal structure of C1 (B(C₆F₅)₃·H₂O + 1aa)
F atoms and part of the hydrogen atoms are omitted for clarity. Selected bond distances (Å): B1–O1 1.5692(19), B2–O3 1.5557(19), C1–O2 1.2579(19), C2–O4 1.2622(19). CCDC (2207426).
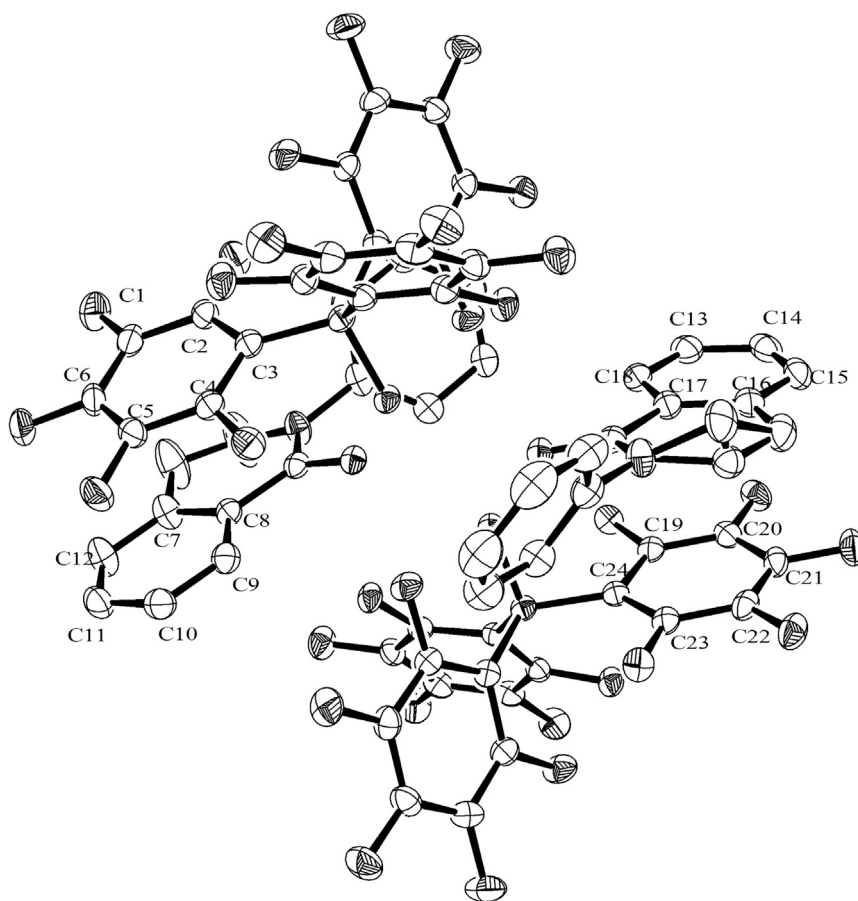
Figure 3. π-π interactions

Hydrogen atoms are omitted for clarity. Selected distances (Å) and angles (deg): plane centroid of C1–C6 to plane centroid of C7–C12 3.8065(10), plane centroid of C1–C6 to plane C7–C12 3.4126(16), plane to plane twist angle 21.21(14); plane centroid of C13–C18 to plane centroid of C19–C24 3.5511(10), plane centroid of C13–C18 to plane C19-C24 3.3748(12), plane to plane twist angle 1.32(16).

There are four oxygen atoms and four hydrogen atoms, forming an eight-membered ring in the conformation of boat-chair via hydrogen bond possessing the lowest transannular strain and energy (Figure 4).[51,52] The O … O distances in O–H … O hydrogen bond system range is 2.5627(15)−2.7583(15) Å, relatively shorter than the reported intermolecular O … O distances (2.70–3.00 Å),[53,54] suggesting the existence of stronger hydrogen bonds in crystal **C1**.
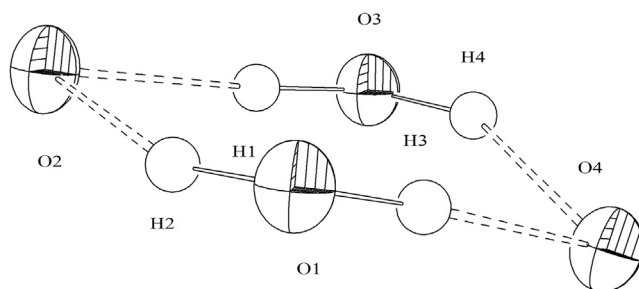

Figure 4. Structure analysis of eight-membered rings of hydrogen bond

Selected bond distances (Å): O1-H1 0.89(3), O1–H2 0.86(3), O3–H3 0.86(3), O3–H4 0.90 (3), O4 … H1 1.69(3), O2 … H2 1.97(3), O2 … H3 1.71(3), O4 … H4 1.83(3), O1 … O2 2.7583(15), O2 … O3 2.5627(15), O3 … O4 2.6578(15), O1 … O4 2.5659(15).
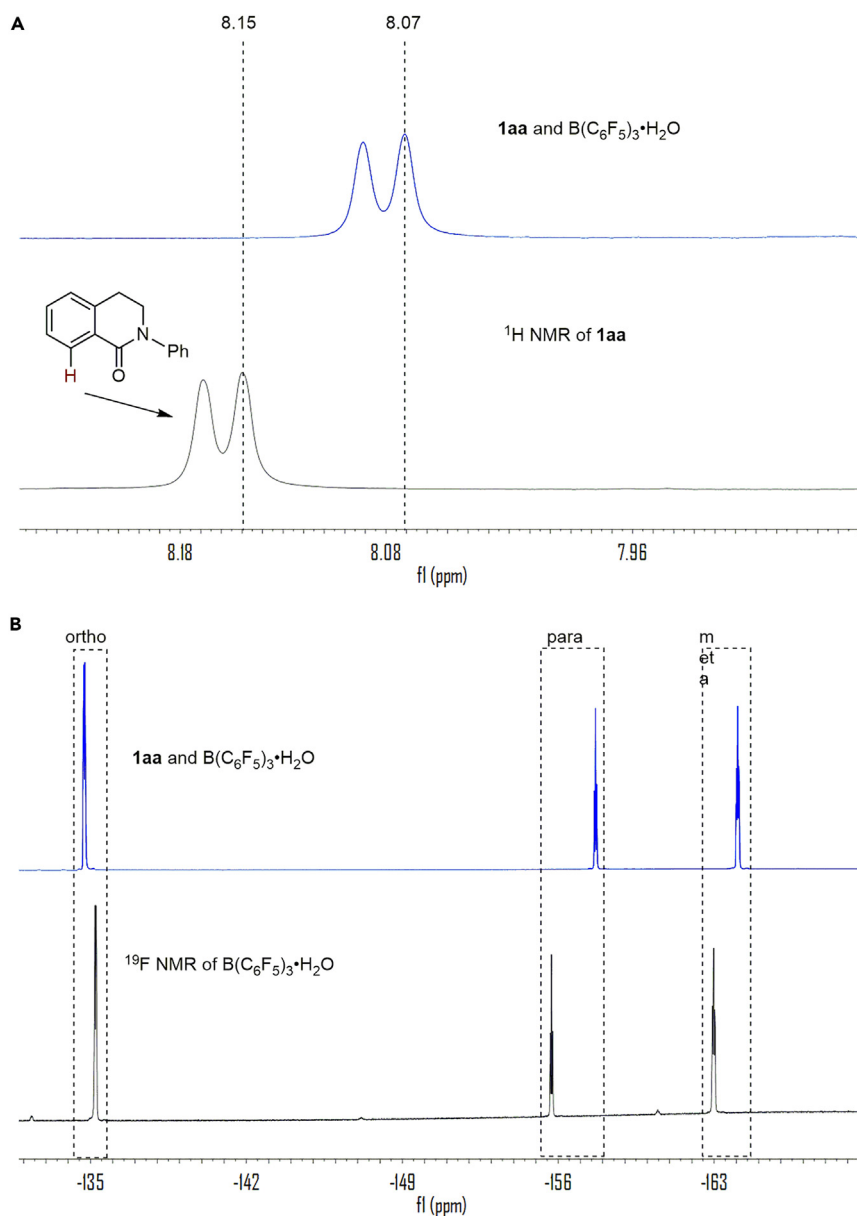
Figure 5. NMR experiments
0.05 mmol **1aa** was dissolved in 0.6 mL deuterated chloroform (CDCl$_3$).
(A) **1aa** (black); **1aa**/B(C$_6$F$_5$)$_3$·H$_2$O (1:1) (blue).
(B) B(C$_6$F$_5$)$_3$·H$_2$O (black); **1aa**/B(C$_6$F$_5$)$_3$·H$_2$O (1:1) (blue).

Encouraged by the above discoveries in **C1**, we considered that similar interactions might exist in so-lution. Compound **1aa** showed a ^{1}H NMR resonance at 8.15 ppm in CDCl$_3$ (Figure 5A, black curve). With the addition of B(C$_6$F$_5$)$_3$·H$_2$O (1.0 equiv), the resonance shifted to 8.07 ppm (Figure 5A, blue curve), indicating the formation of π-π interactions in solution.[55,56] The ^{19}F NMR of B(C$_6$F$_5$)$_3$·H$_2$O also changed on the addition of **1aa**. The original peaks of B(C$_6$F$_5$)$_3$·H$_2$O were observed at −135.2, −155.7 and −163.0 ppm (Figure 5B, black curve).[41] Upon addition of **1aa** (1.0 equiv), the characteristic peaks changed to −134.7, −157.7 and −164.0 ppm, respectively (Figure 5B, blue curve). According to previous reports,[36–38,41,42] intermolecular hydrogen bonds should exist between **1aa** and B(C$_6$F$_5$)$_3$·H$_2$O in solution.
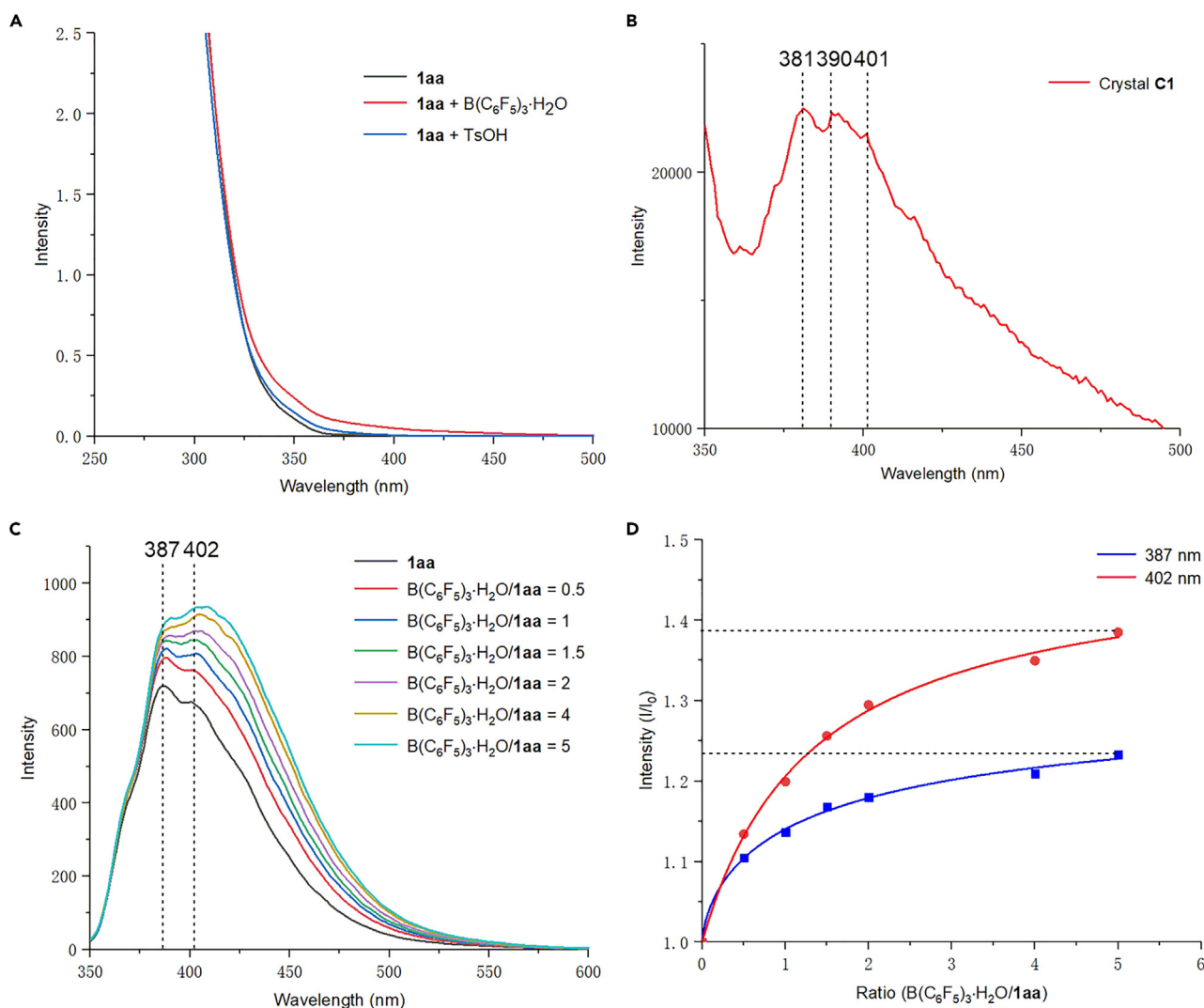
Figure 6. UV-Vis absorption and fluorescence emission measurements

(A) **1aa** in THF (10^{-3} M, black); **1aa** and $B(C_6F_5)_3 \cdot H_2O$ (1:1) in THF (10^{-3} M, red); **1aa** and *p*-toluenesulfonic acid (TsOH) (1:1) in THF (10^{-3} M, blue).

(B) Fluorescence emission spectra of **C1**, excitation wavelength, 330 nm.

(C) Fluorescence emission spectra of **1aa** in THF (10^{-4} M), $B(C_6F_5)_3 \cdot H_2O$ were added to the solution of **1aa**, excitation wavelength, 330 nm.

(D) Emission intensity, 387 nm and 402 nm.

In tetrahydrofuran solution, **1aa** as well as the mixture of **1aa** and *p*-toluenesulfonic acid (TsOH), show no absorption in visible light region, respectively (Figure 6A, black and blue curves). Similarly, using other Brønsted acids instead of TsOH as hydrogen bond donors, such as phenylboronic acid, cyclohexanecarboxylic acid, and methanesulfonic acid, the corresponding mixtures also show no absorption in the visible light region (see supplmental information for detail, Figure S4). However, the mixture of **1aa** and $B(C_6F_5)_3 \cdot H_2O$ exhibits a tailing band from 400 to 450 nm (Figure 6A, red curve).

The fluorescence emission measurements of **C1** and **1aa**/$B(C_6F_5)_3 \cdot H_2O$ were attempted. The solid fluorescence emission spectrum of **C1** showed three peaks at 381 nm, 390 nm, and 401 nm (Figure 6B). Similar emission peaks were observed in solution. There were two fluorescent peaks at 387 nm and 402 nm, which are enhanced in terms of the emission intensity by increasing the $B(C_6F_5)_3 \cdot H_2O$ fraction (Figure 6C). When the ratio of $B(C_6F_5)_3 \cdot H_2O$/**1aa** is 1.5:1, the emission intensity was comparable at 387 nm and 402 nm. With the addition of $B(C_6F_5)_3 \cdot H_2O$, the emission intensity at 402 nm gradually became stronger than the emission intensity at 387 nm, indicating that the rotation of aromatic rings was more restricted because of
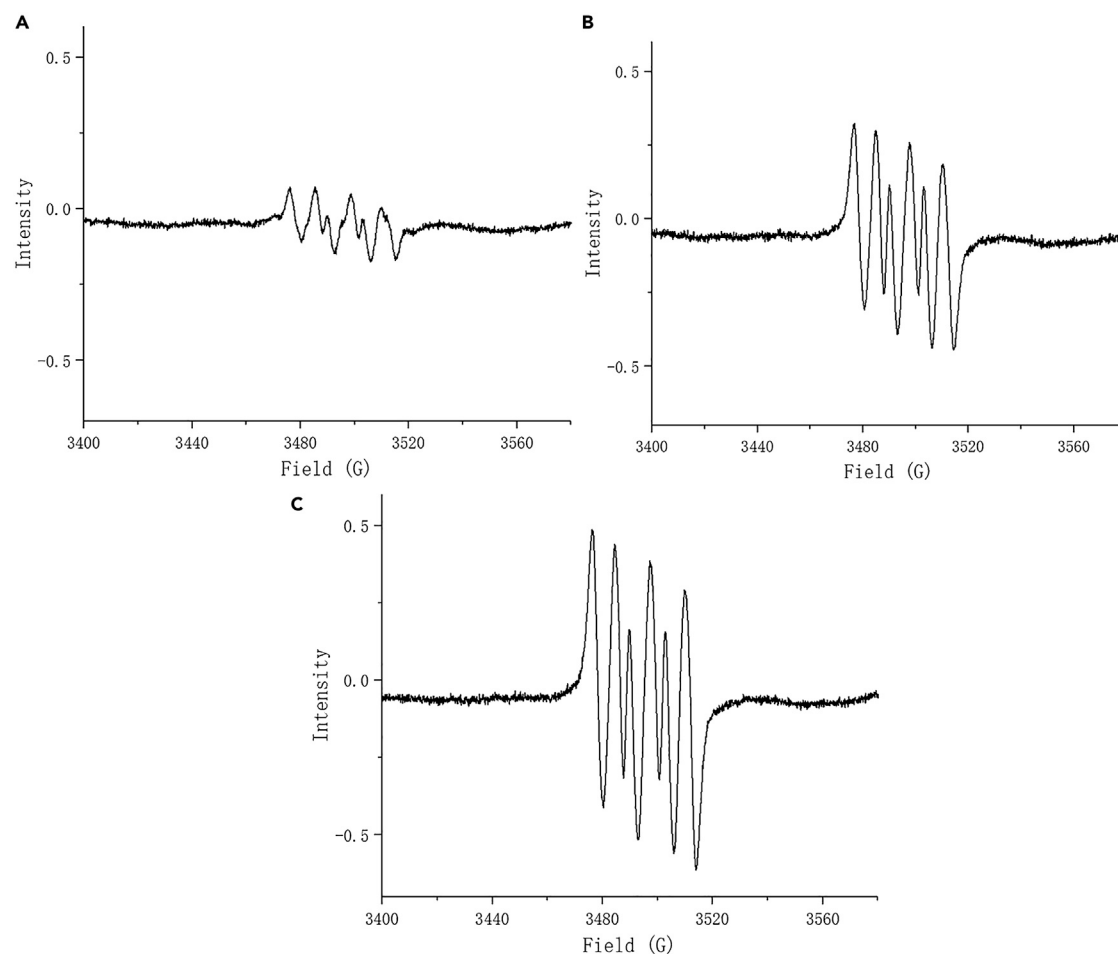
Figure 7. EPR measurements
0.05 mmol scale, **1aa**/DMPO/B(C$_6$F$_5$)$_3$·H$_2$O (1:1:1) in THF (1 mL) under air.
(A) in the dark.
(B) irradiated by blue LEDs for 2 min.
(C) irradiated by blue LEDs for 5 min.

increased π-π interactions.[55,56] In comparison to B(C$_6$F$_5$)$_3$·H$_2$O/**1aa** (5:1) and **1aa**, the fluorescence emission intensities at 387 nm and 402 nm were enhanced by 23% and 38%, respectively (Figure 6D).

To further explore the properties of mixture of B(C$_6$F$_5$)$_3$·H$_2$O and **1aa**, electron paramagnetic resonance (EPR) measurements were conducted. As can be seen in Figure 7, directly subjecting the THF solution of **1aa**, B(C$_6$F$_5$)$_3$·H$_2$O and 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO) to EPR, a weak radical signal was detected (Figure 7A). A strong signal appeared when the above solution was irradiated by blue light for 2 min (Figure 7B). As the irradiation time was extended to 5 min, further enhancement was observed (Figure 7C). According to previous reports, DMPO-O$_2^-$ species is formed (α_N = 13.1 G, α_H = 9.1 G), indicating that the mixture of B(C$_6$F$_5$)$_3$·H$_2$O and **1aa** can activate molecular oxygen probably through energy transfer on visible light irradiation.[57–60]

These observations of the complex of B(C$_6$F$_5$)$_3$·H$_2$O and **1aa** inspired us to further exploit its catalytic potential in photoredox catalysis. Therefore, the reaction of *N*-phenyl-tetrahydroisoquinoline (**1a**) and 4-isocyano-1,1'-biphenyl (**2a**) was investigated. As expected, the reaction gave corresponding product **3aa** in 58% yield in THF using 10 mol % of B(C$_6$F$_5$)$_3$·H$_2$O/**1aa** as photocatalyst (Figure 8A). Besides, in the absence of isocyanide, **1a** could be converted to **1aa** in 30% yield catalyzed by B(C$_6$F$_5$)$_3$·H$_2$O, with 61% **1a** recovered (Figure 8B). Thus, when **1a** and **2a** were treated by B(C$_6$F$_5$)$_3$·H$_2$O, the desired product
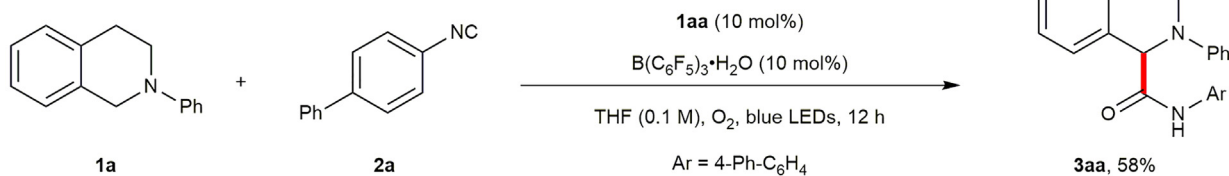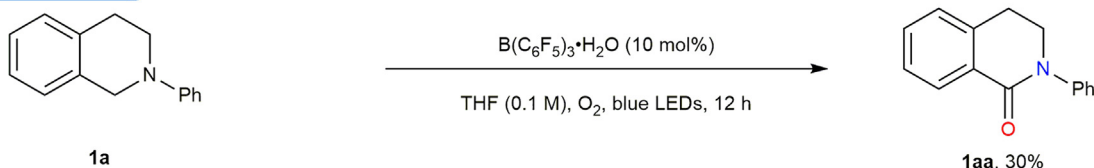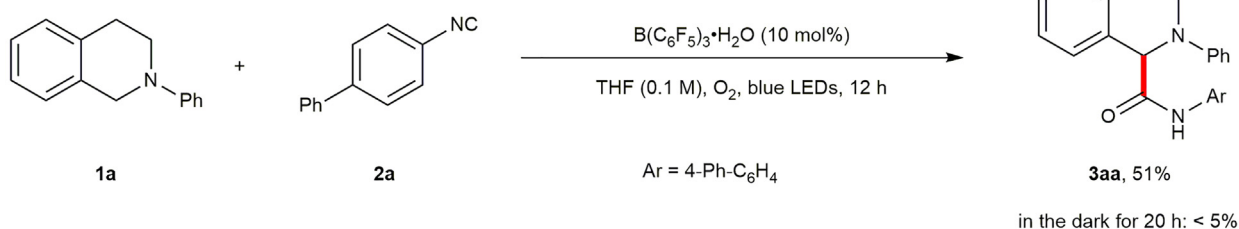
Figure 8. Catalytic properties of B(C₆F₅)₃·H₂O and 1aa

(A) **C1** Catalysis Experiment: **1a** (0.15 mmol), **2a** (0.1 mmol).

(B) generate **1aa** via **1a** direct oxidation, **1a** (0.1 mmol).

(C) **1a** was found to generate to **1aa**, subsequently combined with B(C₆F₅)₃·H₂O to catalyze the reaction. **1a** (0.15 mmol), **2a** (0.1 mmol).

3aa could still be obtained in 51% yield (Figure 8C). Meanwhile, only trace amount of **3aa** was formed in the dark (Figure 8C).

In addition, the UV-Vis absorption measurements of reaction mixture showed a tailing band from 400 to 450 nm (Figure 9A), similar to the absorption curve of B(C₆F₅)₃·H₂O/**1aa** (Figure 6A). The mixture of **1a** and B(C₆F₅)₃·H₂O in THF showed no absorption in visible light region (Figure 9B), different from the result that an Electron Donor-Acceptor (EDA) complex was formed between **1a** and anhydrous B(C₆F₅)₃.[61] EPR measurement of the reaction mixture with DMPO showed similar signals (Figure 9D) as those of the mixture of **1a**/DMPO/B(C₆F₅)₃·H₂O (Figure 9C), further confirming that the combination of B(C₆F₅)₃·H₂O and **1aa** (*in situ* formed from **1a**) acts the photocatalyst of the reaction.

Substrate Scope

Under the optimized reaction conditions (See supplmental information), the generality of the reaction was tested by variation of different tetrahydroisoquinolines (Figure 10). All reactions proceeded smoothly to give corresponding products **3** in moderate to good yields. **3aa** was obtained in 62% isolated yield in gram scale. Substrate with a β-naphthyl group was compatible with the reaction conditions, and the desired product **3ba** could be obtained in 83% yields. For tetrahydroisoquinoline with a hydrogen bond acceptor CN group, the reaction furnished product **3ca** in 57% yield. For substrate bearing a Cl atom on the *N*-aryl ring, the reaction delivered **3da** in 34% yield. Substrates having electron-donating methoxy substituent were also suitable for this transformation, giving **3ea** and **3fa** in 66% and 37% yields, respectively. For substrates with a *para*- and *meta*-Me on the *N*-aryl ring, corresponding products **3ga** and **3ha** were isolated in moderate yields. When substrates had two methoxy groups on the benzene ring (R¹), the reaction could still perform smoothly to give **3ia** in 52% yields. To our delight, bupivacaine analogue **3ja** could be
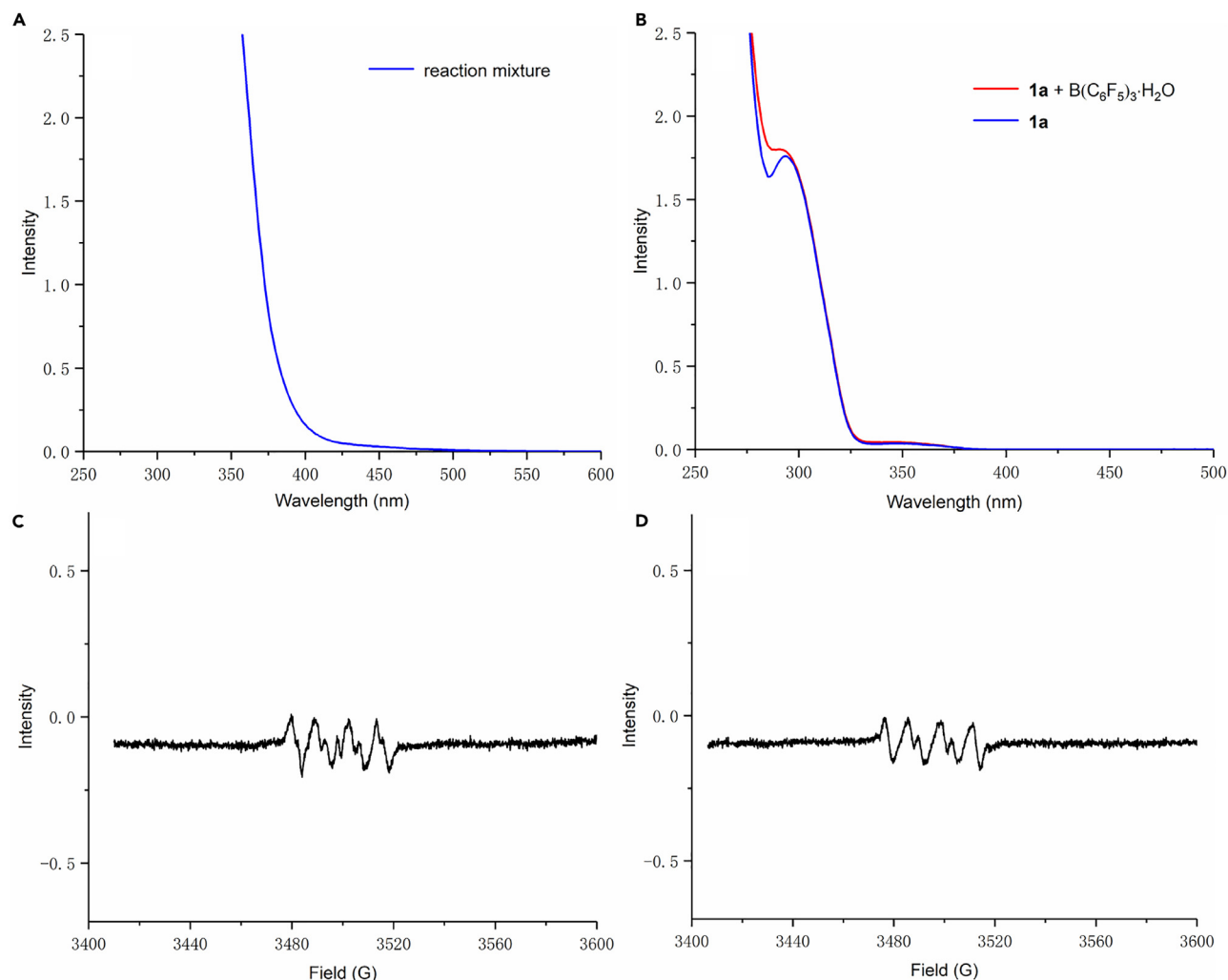
Figure 9. UV-Vis absorption spectra and EPR measurements

(A) **1a**, **2a** and $B(C_6F_5)_3 \cdot H_2O$ (1:1:1) in THF (10^{-3} M) irradiated by blue LEDs for 2 h.

(B) **1a** in THF (10^{-3} M, blue); **1a** and $B(C_6F_5)_3 \cdot H_2O$ (1:1) in THF (10^{-3} M, red).

(C) 0.1 mmol **1a**/DMPO and $B(C_6F_5)_3 \cdot H_2O$ (0.01 mmol) THF (1 mL) irradiated by blue LEDs for 30 s.

(D) 0.1 mmol **1a**/**2a**/DMPO (1:1:1) and $B(C_6F_5)_3 \cdot H_2O$ (0.01 mmol) in THF (1 mL), irradiated by blue LEDs for 30 s.

obtained in 32% yield from *N*-Ph piperidine, and the reaction of *N*-Ph proline also provided corresponding product **3ka** in 39% yield.

Next, a variety of isocyanides were examined and the results are presented in Figure 11. For isocyanide bearing a methoxy group on the benzene ring, the reaction produced the desired product **3 ab** in 86% yield. The reactions of electron-deficient aromatic isocyanides provided the corresponding amides **3ac-3ag** in moderate yields. 2-biphenylyl isocyanide led to amide product **3ah** in 77% yield. Similarly, for other 2-biaryl substituted isocyanides, products **3ai-3ak** were obtained in moderate to good yields (73%–84%). Aliphatic isocyanides were also suitable for this transformation and gave the desired products **3 aL-3ar** in 56–90% yields. Notably, ester tethered isocyanide furnished the target product **3as** in 92% yield.

Mechanistic studies

Light on/off experiments were conducted to investigate the effect of light. The mixture of **1a**, **2b** and $B(C_6F_5)_3 \cdot H_2O$ in THF/H_2O was stirred for 2 h, alternating between 10-min periods of blue LED irradiation and 30 min in the dark. It was noted that the reaction proceeded smoothly on light irradiation, but the
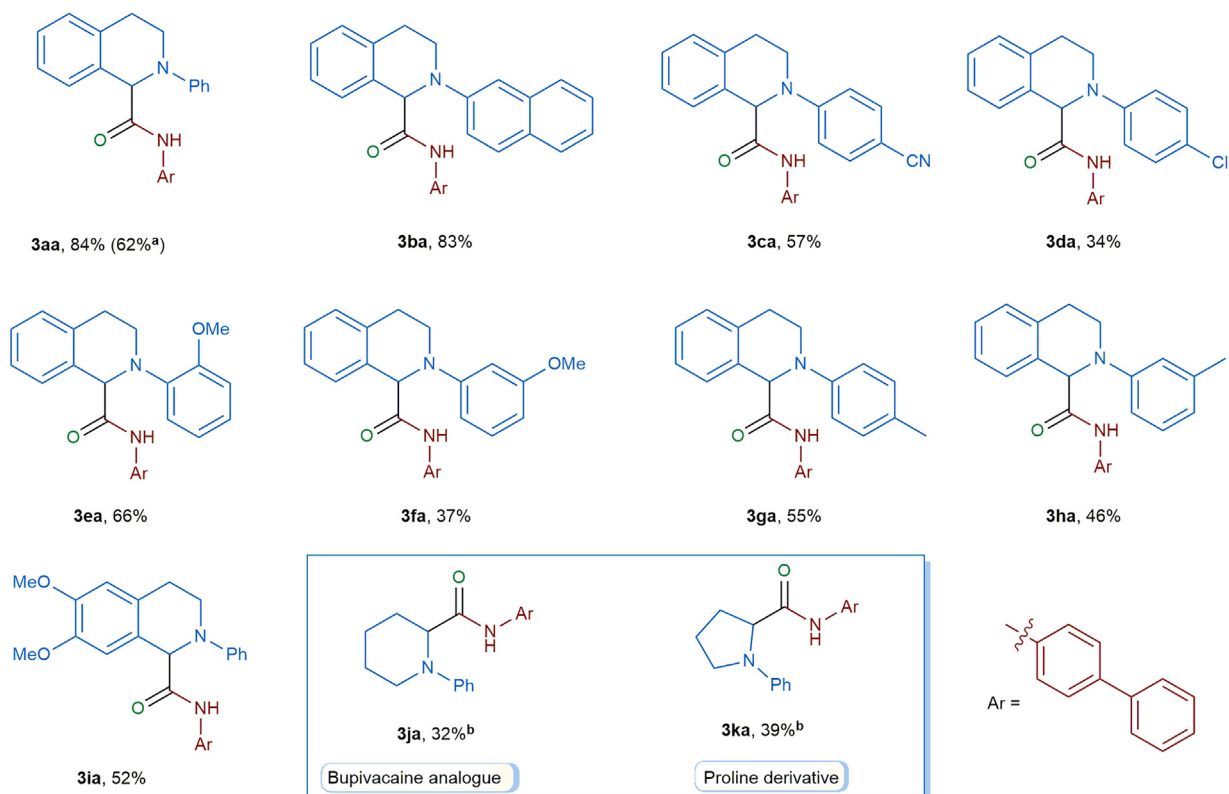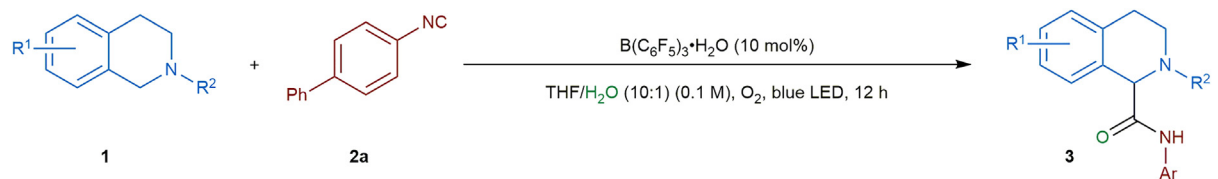
Figure 10. Substrate scope of tetrahydroisoquinolines

Reaction condition: **1** (0.15 mmol), **2a** (0.1 mmol), B(C₆F₅)₃ (10 mol %), THF: H₂O = 10: 1 (1 mL), blue LED, O₂ atmosphere at room temperature. a, Gram scale reaction. b, Reaction time: 36 h.

consumption of the isocyanide **2b** immediately stalled without light, indicating that continuous light irradiation is essential for the reaction. (Figure 12).

The reaction mixture was monitored by ^{19}F NMR after completion of the reaction. As shown in Figure 13, the resonance shifts appeared at −135.7, −160.7 and −165.2 ppm, suggesting that B(C₆F₅)₃·H₂O is remained after the reaction.[62] Moreover, potassium iodide-starch test showed discoloration, implying that oxidizing substances were formed in the reaction. Subsequently, H₂O₂ was observed by a reported method using Ti(SO₄)₂ as the chromogenic agent, the characteristic peak was monitored at 405 nm (see supplmental information for detail).[63]

Plausible reaction mechanism

Based on the aforementioned results and reported photoredox aerobic oxidations,[64–66] a plausible mechanism is proposed (Figure 14). Initially, amide is formed via autoxidation of **1**.[67] Then, the photocatalyst species **PC** is formed via hydrogen bond and π-π interactions between B(C₆F₅)₃·H₂O and amide. In addition, for **1j** and **1k**, N-phenyl group of the corresponding amides might take part in the π-π interactions. Next, singlet oxygen ($^1O_2$) is generated via energy transfer (EnT) by excited **PC***. Subsequent oxidation of compounds **1** by $^1O_2$ gives imine cation intermediate, together with the formation of H₂O₂ as a
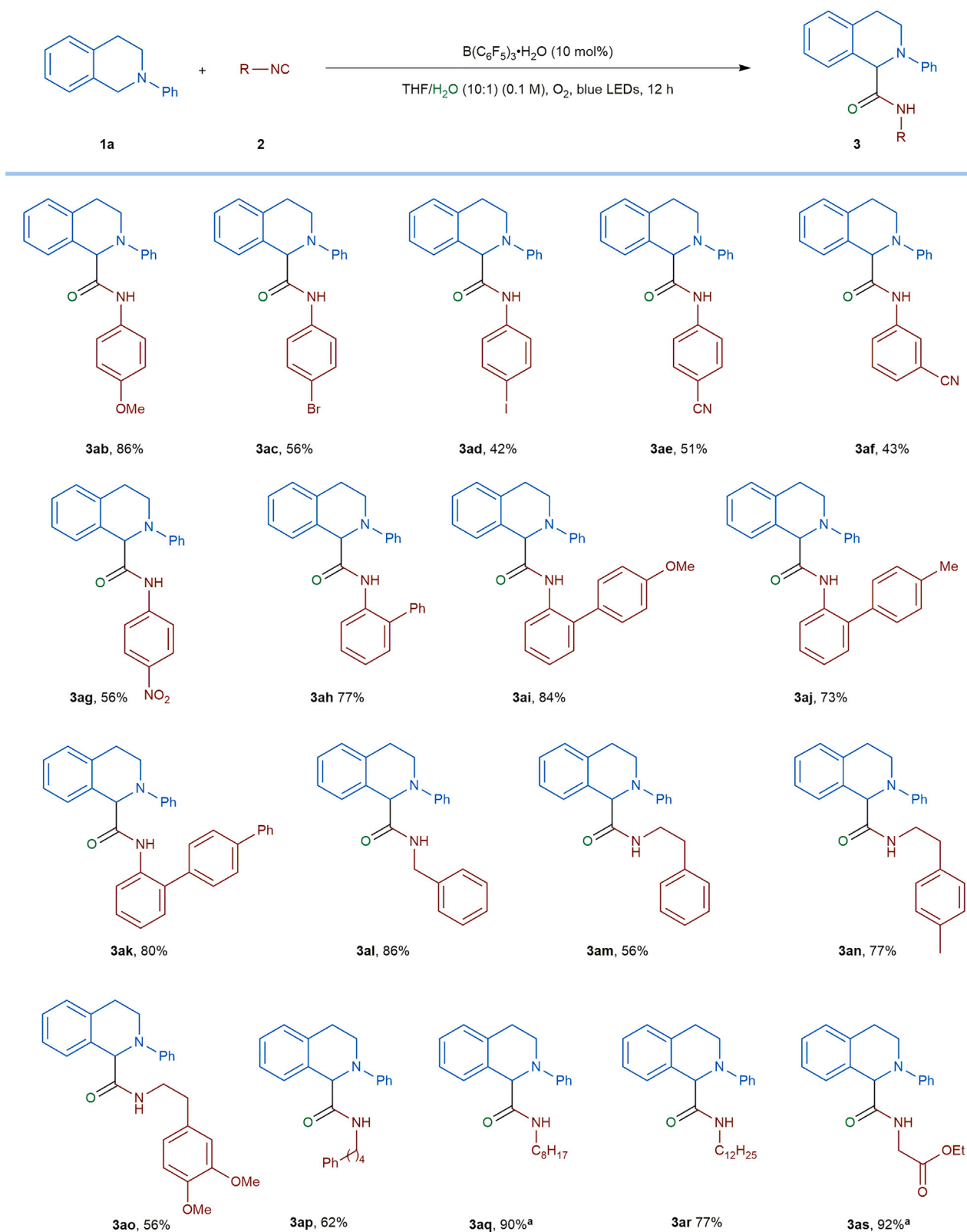
Figure 11. Substrate scope of Isocyanide

Reaction conditions: **1a** (0.1 mmol), **2** (0.15 mmol), B(C$_6$F$_5$)$_3$·H$_2$O (10 mol %). a, Reaction time: 14 h.
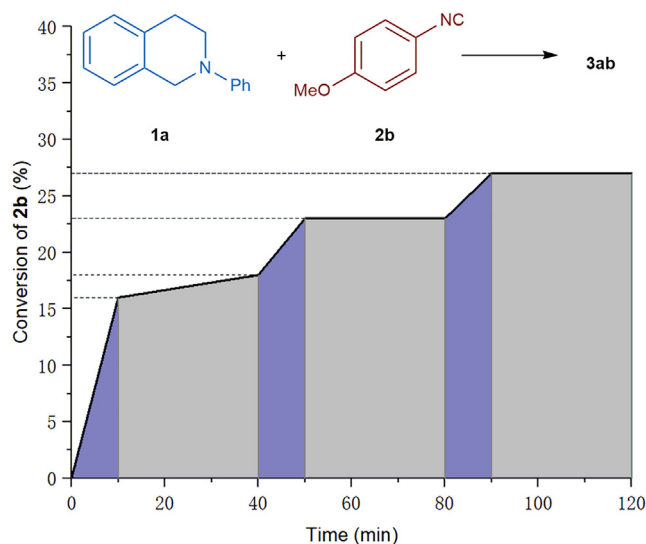
Figure 12. Light on/off experiment
1a (0.15 mmol), **2b** (0.1 mmol), $B(C_6F_5)_3 \cdot H_2O$ (0.01 mmol), THF/H_2O 10:1, the conversion of **2b** was monitored by GC.

byproduct. Finally, the multiple component reaction occurs between imine cation, isocyanide and H_2O delivers the final products **3**.

Conclusion

In summary, the crystal structure of $B(C_6F_5)_3 \cdot H_2O$ and amide **1aa** was obtained, from which hydrogen bond and π-π interactions are observed. This crystal was composed of six molecules with an eight-membered ring via hydrogen bonds. The boat-chair conformation of the eight-membered ring possesses the lowest energy and the hydrogen bond strength is stronger than normal ones reported in the literature.[50–52] Moreover, similar noncovalent interactions were also observed in solution as confirmed by NMR measurements, UV-Vis absorption and fluorescence emission spectra. The π-π interactions demonstrate the specific
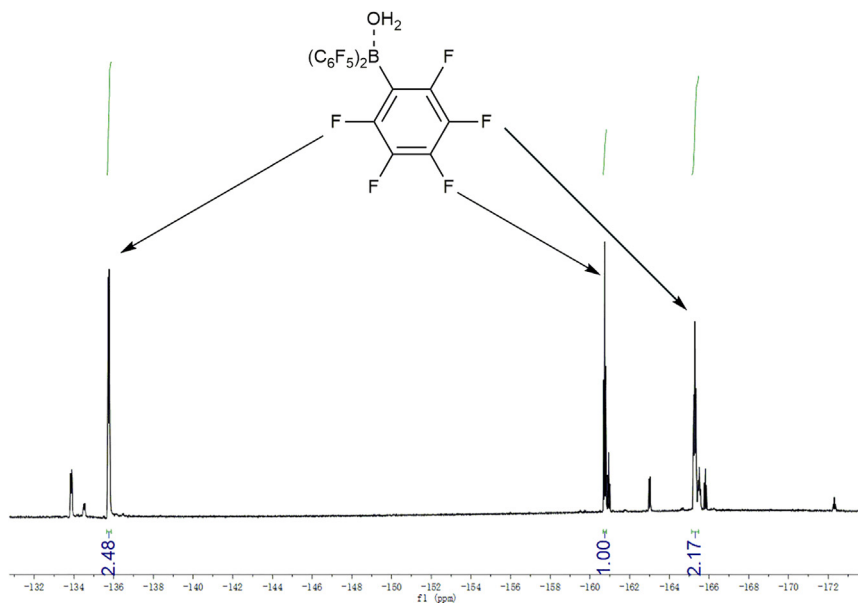
Figure 13. ^{19}F NMR measurement after completion of the reaction
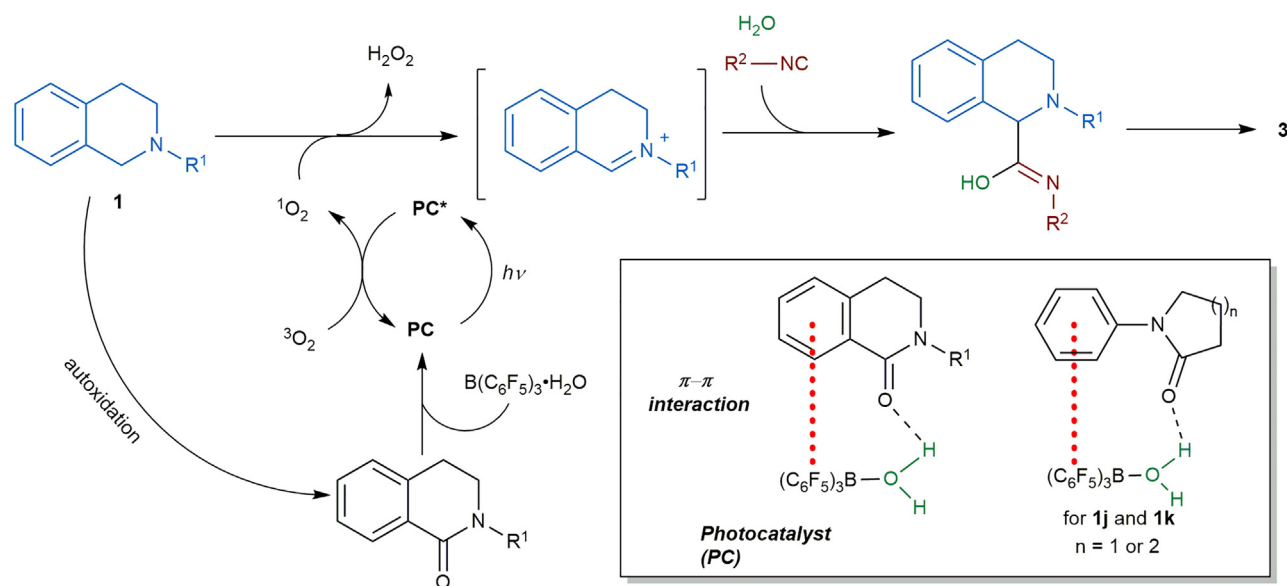
Figure 14. Plausible mechanism

characteristics of B(C₆F₅)₃·H₂O among other Brønsted acids. Based on the synergistic effect of hydrogen bonds and π-π interactions in B(C₆F₅)₃·H₂O/amides complex, a photoredox catalysis under visible light is developed using the complex as the photocatalyst.

Limitations of the study

The reaction works well with *N*-aryl tetrahydroisoquinolines; for *N*-alkyl substituted tetrahydroisoquinolines, very low yields were obtained.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- RESOURCE AVAILABILITY
  - Lead contact
  - Materials availability
  - Data and code availability
- METHOD DETAILS
  - General information
  - General procedure
  - Spectroscopic data

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2023.106528.

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AUTHOR CONTRIBUTIONS

X-Y.T. conceived and supervised the study. S-J.W. performed the syntheses, the spectroscopic characterizations and the X-ray crystal diffraction analysis. S-J.W., L.W., and X-Y.T. analyzed the data and wrote the manuscript.

DECLARATION OF INTERESTS

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Chemicals, peptides, and recombinant proteins		
1,2,3,4-Tetrahydro-2-isoquinoline	Meryer	CAS: 91-21-4
1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinolin	Meryer	CAS: 1745-07-9
4-Aminobiphenyl	Meryer	CAS: 92-67-1
4-Chlorobromobenzene	Energy Chemical	CAS: 106-39-8
4-Bromobenzonitrile	Energy Chemical	CAS: 623-00-7
2-Bromoanisole	Energy Chemical	CAS: 578-57-4
4-Bromoanisole	Adamas	CAS: 104-92-7
3-Bromoanisole	Adamas	CAS: 2398-37-0
4-Bromotoluene	Adamas	CAS: 106-38-7
3-Bromotoluene	Adamas	CAS: 591-17-3
4-Bromoaniline	Adamas	CAS: 106-40-1
4-Iodoaniline	Adamas	CAS: 540-37-4
p-Anisidine	Adamas	CAS: 104-94-9
4-Aminobenzonitrile	Adamas	CAS: 873-74-5
4-Nitroaniline	Adamas	CAS: 100-01-6
2-Aminobiphenyl	Adamas	CAS: 90-41-5
4′-Methyl-Bpphenyl-2-ylamine	Adamas	CAS: 1204-43-9
4′-Methoxy-Bpphenyl-2-ylamine	Adamas	CAS: 38089-03-1
Deposited data		
Complex of $B(C_6F_5)_3 \cdot H_2O$ and amide **1aa**.	CCDC	CCDC-2207426
Other		
Silica gel (200-300 mesh)	Huanghai	https://www.aladdin-e.com/
AVIII 400 MHz	Bruker	https://www.bruker.com

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Xiang-Ying Tang (xtang@hust.edu.cn).

Materials availability

All materials generated in this study are available within the article and the supplemental information or from the lead contact upon reasonable request.

Data and code availability

- The original crystal structure of $B(C_6F_5)_3 \cdot H_2O$ with **1aa** has been deposited at CCDC and is publicly available as of the date of publication. CCDC number is listed in the key resources table.

- This paper does not report original code.

- Any additional information required to reanalyze the data reported in this paper can be obtained from the lead contact upon request.

METHOD DETAILS

General information

The nuclear magnetic resonance spectra were recorded on the Bruker Avance III 400 MHz with tetramethyl-silane (TMS) as an internal standard. High resolution mass spectra were recorded using analyses by BrukerDaltonics SolariX 7.0T. Organic solvents used were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. Flash column chromatography was performed using 300-400 mesh silica gel. For thin-layer chromatography (TLC), silica gel plates (Huanghai GF254) were used. EPR (electron paramagnetic resonance) spectra were recorded by Bruker EMXmicro-6/1 instrument. X-Ray diffraction were collected by XtaLAB PRO MM007HF Cu (Rigaku, Japan). UV-vis spectra were obtained on a UV-2600 (Shimadzu). Fluorescence spectroscopic studies were performed with a RF-5301PC (Shimadzu). All heat sources are oil bath. All light sources are 3 W blue LED bands and the wavelength of peak is 427 nm. The distance from the light source to the container is 3-5 cm.

General procedure

Synthesis of substrate isoquinolines
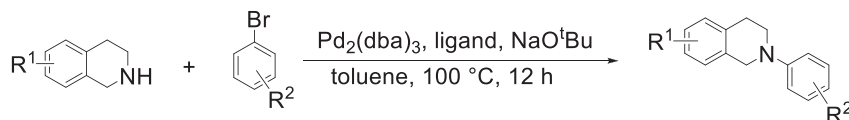
A mixture of $Pd_2(dba)_3$ (3 mol%) and ligand (2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl) (8 mol%) were placed into an oven dried reaction tube. Subsequently, the reaction tube was degassed with N_2 for three times. Then, dry toluene, bromoarene (1.0 equiv.), 1,2,3,4-tetrahydroisoquinoline (1.2 equiv.) and ^tBuONa (1.4 equiv.) were sequentially added under nitrogen protection. Then the reaction mixture was heated to 100 °C for 12 h. After completion, the resulting reaction mixture was slowly cooled to room temperature, quenched by brine and extracted with ethylacetate. The organic layer was dried over-Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel. In addition, **1a-1h** are known compound.

Synthesis of isocayanides
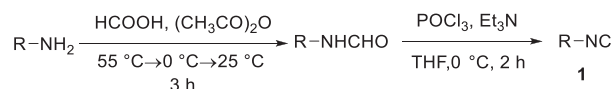
A mixture of HCOOH (2.0 equiv) and $(CH_3CO)_2O$ (2.0 equiv.) were stirred at 55 °C for 2 h. Before aniline (1.0 equiv.) was added the reaction mixture was cooled down at 0 °C, then continued stirring for 2hat room temperature. After consumption of aniline, all the volatiles were removed under reduced pressure and the crude product was directly used in the next step without further purification.

To a stirred solution of crude product in dry THF at 0 °C were added Et_3N (5.0 equiv.) and $POCl_3$ (1.2 equiv.) dropwise sequentially. After stirring for 2hat 0 °C, the reaction was quenched with water and extracted with ethylacetate (EA) for three times. The organic layer was washed with brine and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude prod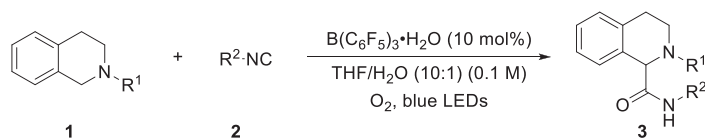uct was purified by column chromatography on silica gel to observed pure product **2**. In addition, **2a-2s** are known compound.

Synthesis of compounds 3

To a stirred solution of **1** (0.15 mmol, 1.5 equiv.) in mixed solvent (1 mL, THF: H_2O = 10:1) were added **2** (0.1 mmol, 1.0 equiv.) and boron catalyst (10 mol%). The resulting solution was stirred in the presence of O_2 under blue light irradiation. The reaction was monitored by TLC, the crude products were purified by flash column chromatography to provide a series of amide compounds **3**. In addition, **3aa** was known compound.

Gram scale reaction
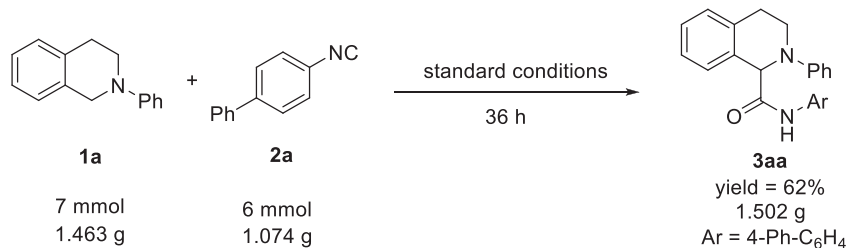
To a stirred solution of **2a** (6 mmol, 1.074 g) in mixed solvent (50 mL, THF: H_2O = 10:1) were added to **1a** (7 mmol, 1.463 g) and boron catalyst (10 mol%, 0.307 g). The resulting solution was stirred at blue LED and O_2 for 36 h. The crude product was purified by flash column chromatography to provide a series of amide compound **3aa** (1.502 g, 62%).

Oxidation reaction of 1a
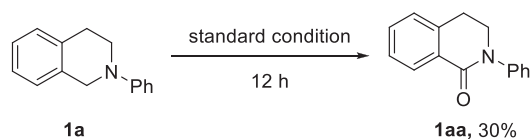
To a stirred solution of **1a** (0.1 mmol, 20.9 mg, 1.0 equiv.) in mixed solvent (1 mL, THF: H_2O = 10:1) was added to boron catalyst (10 mol%). The resulting solution was stirred at blue LEDs and 1 atm O_2 for 12 h. The crude product was purified by flash column chromatography to provide 1aa (6.6 mg, 30%) and **1a** (12.7 mg, 61%).

X-ray crystal structure analysis for 1aa
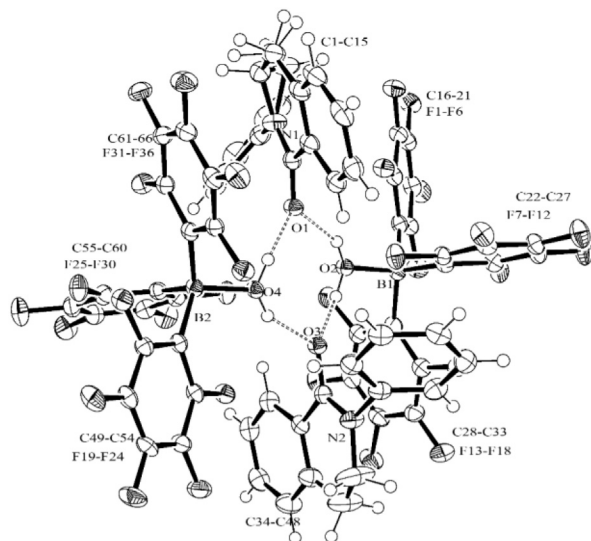
X-ray crystal structure analysis of **C1**. A clear colorless plate. Formula $C_{33}H_{15}BF_{15}NO_2$, $M = 753.27$, $0.25*0.2*0.05$ mm, $a = 12.0787(1)$, $b = 11.9169(1)$, $c = 41.6237(3)$ Å, $\beta = 97.510(1)°$, $V = 5939.95(8)$ Å^3, $\mu = 1.518$ mm^{-1}, $0.651 \leq T \leq 1.000$, Theta(max) = 74.296°, $R = 0.0381$, $wR^2 = 0.1036$, temperature = 293 K, hydrogen atoms calculated and refined as riding atoms.

Light on/off experiments
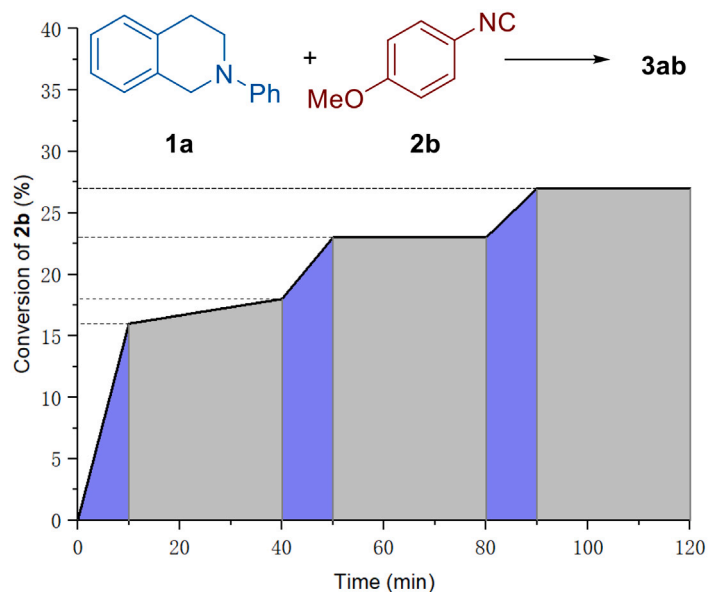
To a stirred solution of the 1-isocyano-4-methoxybenzene (**2b**, 0.1 mmol, 1.0 equiv.) and boron catalyst (10 mol%) in mixed solvent (1mL, THF: H$_2$O = 10:1) was added the N-phenyl-1,2,3,4-tetrahydroisoquinoline (**1a**, 0.15 mmol, 1.5 equiv.). Besides, 0.1 mmol dodecane was added as internal

standard. The light was kept on for ten minutes then kept off for thirty minutes. The reaction mixture 0.05 mL was taken and diluted with 1,2-dichloroethane (DCE) to 2 mL for gas chromatography (GC) monitoring.

Spectroscopic data

N-([1,1'-biphenyl]-4-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3aa)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (33.7 mg, 84% yield). m.p.: 192−194 °C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.88 (s, 1H), 7.65 (d, J = 6.8 Hz, 1H), 7.57−7.49 (m, 6H), 7.36−7.27 (m, 4H), 7.26−7.23 (m, 1H), 7.18 (d, J = 7.2 Hz, 1H), 7.02 (d, J = 8.0 Hz, 2H), 6.95 (dd, $J_1 = J_2$ = 7.6 Hz, 1H), 5.09 (s, 1H), 3.94 (dt, J = 9.6 Hz, J = 4.4 Hz, 1H), 3.40 (td, J = 10.8 Hz, J = 4.0 Hz, 1H), 3.16-3.00 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.6, 149.4, 140.5, 137.3, 136.7, 134.5, 132.1, 129.6, 129.1, 127.8, 127.7, 127.5, 127.1, 126.9, 120.4, 120.1, 115.3, 66.5, 45.4, 28.8. IR ν 3298, 3034, 2251, 2228, 1662, 1287, 858, 690 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{28}$H$_{25}$N$_2$O [M+H]$^+$ 405.1961; found 405.1960.

N-([1,1'-biphenyl]-4-yl)-2-(naphthalen-2-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ba)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (37.6 mg, 83% yield). m.p.: 141−143 °C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.89 (s, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.75−7.67 (m, 3H), 7.54−7.45 (m, 6H), 7.44−7.35 (m, 3H), 7.33−7.24 (m, 6H), 7.17 (d, J = 7.2 Hz, 1H), 5.24 (s, 1H), 4.03 (dt, J = 10.8 Hz, J = 4.0 Hz, 1H), 3.50 (td, J = 10.8 Hz, J = 4.0 Hz, 1H), 3.18−3.01 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 147.0, 140.5, 137.4, 136.7, 134.5, 134.4, 132.0, 129.5, 129.2, 128.8, 128.6, 127.9, 127.8, 127.6, 127.5, 127.1, 126.94, 126.9, 126.8, 126.7, 123.9, 120.1, 117.5, 66.2, 45.9, 28.8. IR ν 3303, 3052, 2924, 1667, 1596, 1386, 1112, 834 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{32}$H$_{27}$N$_2$O [M+H]$^+$ 455.2118; found 455.2117.

N-([1,1'-biphenyl]-4-yl)-2-(4-cyanophenyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ca)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (24.5 mg, 57% yield). m.p.: 137−139 °C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.37 (s, 1H), 7.61−7.58 (m, 1H), 7.55−7.48 (m, 8H), 7.40 (dd, $J_1 = J_2$ = 8.0 Hz, 2H), 7.33−7.28 (m, 3H), 7.23−7.20 (m, 1H), 6.95 (d, J = 8.8 Hz, 2H), 5.18 (s, 1H), 4.06−4.00 (m, 1H), 3.43 (td, J = 11.2 Hz, J = 3.6 Hz, 1H), 3.25−3.16 (m, 1H), 3.07 (dt, J = 15.6 Hz, J = 3.6 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 169.4, 152.0, 140.3, 137.8, 136.3, 134.4, 133.8, 131.7, 128.8, 128.4, 127.8, 127.6, 127.3, 127.27, 126.9, 120.4, 119.8, 113.7, 101.5, 65.6, 44.5, 28.7. IR ν 3319, 3026, 2831, 2246, 1662, 1318, 904, 722 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{29}$H$_{24}$N$_3$O [M+H]$^+$ 430.1914; found 430.1907.

N-([1,1'-biphenyl]-4-yl)-2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3da)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (14.9 mg, 34% yield). m.p.: 188−190 °C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.72 (s, 1H), 7.63 (d, J = 6.8 Hz, 1H), 7.55−7.48 (m, 6H), 7.42−7.37 (m, 2H), 7.33−7.24 (m, 5H), 7.17 (d, J = 6.8 Hz, 1H), 6.92 (d, J = 9.2 Hz, 2H), 5.03 (s, 1H), 3.94−3.88 (m, 1H), 3.35 (td, J = 10.8 Hz, J = 3.6 Hz, 1H), 3.16−3.08 (m, 1H), 3.01 (dt, J = 12.0 Hz, J = 3.2 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.2, 148.0, 140.4, 137.5, 136.6, 134.3, 131.8, 129.4, 129.0, 128.8, 127.9, 127.8, 127.6, 127.2, 127.0, 126.9, 125.5, 120.1, 116.4, 66.4, 45.6, 28.8. IR ν 3255, 3061, 2920, 2851, 1596, 1331, 1052, 840 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{28}$H$_{24}$N$_2$OCl [M+H]$^+$ 439.1572; found 439.1571.

N-([1,1'-biphenyl]-4-yl)-2-(2-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ea)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (28.6 mg, 66% yield). m.p.: 66-68°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 9.98 (s, 1H), 7.72 (d, J =7.2 Hz, 1H), 7.60-7.50 (m, 6H), 7.40 (dd, $J_1 = J_2$ = 7.6 Hz, 2H), 7.32-7.22 (m, 3H), 7.17-7.10 (m, 3H), 6.97-6.87 (m, 2H), 5.08 (s, 1H), 4.00 (s, 3H), 3.48-3.31 (m, 2H), 3.03-2.84 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.5, 153.8, 140.6, 139.0, 137.6, 136.6, 134.6, 132.1, 129.0, 128.7, 128.6, 127.5, 127.2, 127.0, 126.8, 126.2, 125.6, 123.3, 121.3, 119.5, 111.5, 65.2, 55.6, 47.7, 28.0. IR ν 3298, 3026, 2849, 2228, 1490, 1035, 904, 720 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{29}$H$_{27}$N$_2$O$_2$[M+H]$^+$ 435.2067; found 435.2066.

N-([1,1'-biphenyl]-4-yl)-2-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3fa)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (16.1 mg, 37% yield). m.p.: 64-66°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.81 (s, 1H), 7.63 (d, J = 7.2 Hz, 1H), 7.57-7.48 (m, 6H), 7.42-7.38 (m, 2H), 7.33-7.21 (m, 4H), 7.17 (d, J = 6.8 Hz, 1H), 6.62-6.56 (m, 2H), 5.10 (s, 1H), 3.95-3.89 (m, 1H), 3.80 (s, 3H), 3.39 (td, J = 10.8 Hz, J = 4.0 Hz, 1H), 3.15-2.99 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.4, 160.8, 150.8, 140.5, 137.3, 136.7, 134.5, 132.1, 130.3, 129.1, 128.8, 127.7, 127.5, 127.1, 126.8, 120.1, 108.0, 105.0, 101.9, 66.4, 55.3, 45.3, 28.8. IR ν 3319, 3025, 2920, 2847, 1662, 1445, 1166, 757 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{29}$H$_{27}$N$_2$O$_2$[M+H]$^+$ 435.2067; found 435.2066.

N-([1,1'-biphenyl]-4-yl)-2-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ga)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (22.9 mg, 55% yield). m.p.: 160-162°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.94 (s, 1H), 7.65 (d, J = 7.2 Hz, 1H), 7.56-7.47 (m, 6H), 7.41-7.37 (m, 2H), 7.32-7.22 (m, 3H), 7.17-7.11 (m, 3H), 6.93 (d, J = 8.8 Hz, 2H), 5.04 (s, 1H), 3.88 (dt, J = 10.4 Hz, J = 4.4 Hz, 1H), 3.35 (td, J = 11.2 Hz, J = 4.0 Hz, 1H), 3.13-2.96 (m, 2H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.7, 147.3, 140.5, 137.2, 136.8, 134.5, 132.1, 130.1, 129.0, 128.8, 127.8, 127.6, 127.5, 127.1, 126.8, 126.77, 120.1, 115.8, 66.5, 45.9, 28.8, 20.4. IR ν 3303, 3022, 2920, 2850, 1913, 1671, 1499, 1149 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{29}$H$_{27}$N$_2$O [M+H]$^+$ 419.2118; found 419.2119.

N-([1,1'-biphenyl]-4-yl)-2-(m-tolyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ha)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (19.3 mg, 46% yield). m.p.: 137-139°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.88 (s, 1H), 7.66-7.63 (m, 1H), 7.58-7.49 (m, 6H), 7.42-7.37 (m, 2H), 7.33-7.15 (m, 5H), 6.84-6.76 (m, 3H), 5.09 (s, 1H), 3.92 (dt, J = 11.2 Hz, J = 4.4 Hz, 1H), 3.40 (td, J = 10.4 Hz, J = 4.0 Hz, 1H), 3.14-2.99 (m, 2H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.6, 149.5, 140.5, 139.4, 137.3, 136.8, 134.6, 132.2, 129.4, 129.2, 128.8, 127.7, 127.66, 127.5, 127.1, 126.85, 126.8, 121.3, 120.1, 116.0, 112.4, 66.4, 45.4, 28.8, 21.9. IR ν 3326, 3031, 2917, 2827, 1671, 1487, 1113, 835 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{29}$H$_{26}$N$_2$ONa [M+Na]$^+$ 441.1937; found 441.1935.

N-([1,1'-biphenyl]-4-yl)-6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ia)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 2:1 as the eluent). Yellow solid (24.1 mg, 52% yield). m.p.: 197-198°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.85 (s, 1H), 7.56-7.48 (m, 6H), 7.42-7.37 (m, 2H), 7.35-7.28 (m, 3H), 7.18 (s, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.95 (dd, J_1 = J_2 = 7.2 Hz, 1H), 6.65 (s, 1H), 5.01 (s, 1H), 3.93-3.86 (m, 7H), 3.44-3.37 (m, 1H), 3.07-2.90 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.8, 149.5, 148.5, 147.8, 140.5, 137.3, 136.8, 129.6, 128.8, 127.6, 127.1, 126.8, 126.6, 123.8, 120.5, 120.2, 115.6, 111.8, 110.6, 65.9, 56.1, 56.0, 45.6, 28.2. IR ν 3263, 3021, 2911, 2828, 1657, 1217, 1114, 992 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{30}$H$_{29}$N$_2$O$_3$[M+H]$^+$ 465.2173; found 465.2172.

N-([1,1'-biphenyl]-4-yl)-1-phenylpiperidine-2-carboxamide (3ja)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (11.4 mg 32% yield). m.p.: 139-141°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.45 (s, 1H), 7.55-7.48 (m, 6H), 7.41 (dd, J_1 = J_2 = 7.6 Hz, 2H), 7.33-7.29 (m, 3H), 7.07 (d, J =8.0 Hz, 2H), 6.94 (dd, J_1 = J_2 = 7.2 Hz, 1H), 4.19 (t, J = 5.2 Hz, 1H), 3.36-3.34 (m, 2H), 2.21-2.17 (m, 1H), 2.01-1.94 (m, 1H), 1.80-1.61 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 171.3, 150.7, 140.6, 137.1, 137.0, 129.6, 128.8, 127.6, 127.1, 126.8, 121.2, 120.0, 117.8, 62.8, 49.5, 26.4, 24.0, 21.7. IR ν 3323, 3025, 1671, 1484, 1241, 830, 759, 695. HRMS (ESI) m/z: calcd for C$_{24}$H$_{25}$N$_2$O [M+H]$^+$ 357.1961; found 357.1958.

([1,1'-biphenyl]-4-yl)-1-phenylpyrrolidine-2-carboxamide (3ka)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (13.3 mg, 39% yield). m.p.: 207-208°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.44 (s, 1H), 7.59-7.51 (m, 6H), 7.41 (dd, J_1 = J_2 = 7.6 Hz, 2H), 7.33-7.27 (m, 3H), 6.89-6.84 (m, 1H), 6.73 (d, J = 8.0 Hz, 2H), 4.12-4.08 (m, 1H), 3.79-3.75 (m, 1H), 3.31-3.24 (m, 1H), 2.42-2.28 (m, 2H), 2.10-1.99 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 172.3, 147.6, 140.5, 137.4, 136.6, 129.5, 128.8, 127.6, 127.2, 126.9, 120.3, 118.9, 113.5, 65.4, 50.1, 31.6, 24.4. IR ν 3326, 2967, 2818, 1663, 1497, 1005, 755, 713. HRMS (ESI) m/z: calcd for C$_{23}$H$_{23}$N$_2$O [M+H]$^+$ 343.1875; found 343.1803.

N-(4-methoxyphenyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ab)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (30.7 mg, 86% yield). m.p.: 132-134°C . ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.70 (s, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.38-7.29 (m, 4H), 7.28-7.21 (m, 2H), 7.16 (d, J = 6.8 Hz, 1H), 6.99 (d, J = 8.0 Hz, 2H), 6.93 (dd, J_1 = J_2 = 6.8 Hz, 1H), 6.81-6.76 (m, 2H), 5.06 (s, 1H), 3.94-3.89 (m, 1H), 3.74 (s, 3H), 3.37 (td, J = 10.8 Hz, J = 4.0 Hz, 1H), 3.14-2.97 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.3, 156.5, 149.5, 134.6, 132.2, 130.6, 129.5, 129.1, 127.7, 127.6, 126.8, 121.6, 120.2, 115.1, 114.0, 66.3, 55.5, 45.3, 28.8. IR ν 3298, 3029, 2900, 2850, 1498, 888, 814 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{23}$H$_{23}$N$_2$O$_2$[M+H]$^+$ 359.1754; found 359.1753.

N-(4-bromophenyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ac)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (22.7 mg, 56% yield). m.p.: 154-155°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.83 (s, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.36-7.22 (m, 8H), 7.17 (d, J = 6.8 Hz, 1H), 7.00-6.92 (m, 3H), 5.06 (s, 1H), 3.91 (dt, J =11.2 Hz, J = 4.4 Hz, 1H), 3.38 (td, J =10.8 Hz, J = 4.0 Hz, 1H), 3.12-2.97 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 170.7, 149.3, 136.5, 134.5, 131.9, 131.8, 129.6, 129.1, 127.81, 127.8, 126.9, 121.4, 120.5, 117.0, 115.3, 66.3, 45.4, 28.7. IR ν 3298, 3028, 2915, 2228, 1597, 1320, 992, 690 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{22}$H$_{20}$N$_2$OBr [M+H]$^+$ 407.0754; found 407.0752.

N-(4-iodophenyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ad)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (19.0 mg, 42% yield). m.p.: 122-124°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.80 (s, 1H), 7.63-7.59 (m, 1H), 7.57-7.53 (m, 2H), 7.35-7.22 (m, 6H), 7.18-7.15 (m, 1H), 7.00-6.92 (m, 3H), 5.06 (s, 1H), 3.90 (dt, J = 11.2 Hz, J = 4.8 Hz, 1H), 3.42-3.35 (m, 1H), 3.11-2.97 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ. 170.6, 149.3, 137.8, 137.2, 134.5, 131.8, 129.6, 129.1, 127.8, 127.77, 126.9, 121.7, 120.6, 115.4, 87.6, 66.4, 45.4, 28.7. IR ν 3323, 3027, 2919, 2242, 2242, 1597, 1178, 818 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{22}$H$_{20}$N$_2$OI [M+H]$^+$ 455.0615; found 455.0614.

N-(4-cyanophenyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ae)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (18.1 mg, 51% yield). m.p.: 74-76°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 9.05 (s, 1H), 7.62-7.58 (m, 3H), 7.55-7.51 (m, 2H), 7.36-7.30 (m, 2H), 7.28-7.24 (m, 2H), 7.19-7.16 (m, 1H), 7.02-6.94 (m, 3H), 5.09 (s, 1H), 3.91 (dt, J = 11.2 Hz, J = 4.8 Hz, 1H), 3.43-3.36 (m, 1H), 3.11-2.98 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 171.2, 149.2, 141.4, 134.5, 133.2, 131.4, 129.7, 129.1, 129.0, 128.0, 127.9, 126.9, 120.9, 119.7, 118.8, 115.6, 107.3, 66.4, 45.6, 28.7. IR ν 3323, 3030, 2915, 2224, 1921, 1672, 1402, 933 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{23}$H$_{20}$N$_3$O [M+H]$^+$ 354.1601; found 354.1602.

N-(3-cyanophenyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3af)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (15.5 mg, 43% yield). m.p.: 138-140°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 8.97 (s, 1H), 7.88-7.87 (m, 1H), 7.67-7.60 (m, 2H), 7.37-7.31 (m, 4H), 7.30-7.23 (m, 2H), 7.19-7.16 (m, 1H), 7.02-6.94 (m, 3H), 5.09 (s, 1H), 3.92 (dt, J = 11.2 Hz, J = 4.4 Hz, 1H), 3.42-3.35 (m, 1H),3.13-2.99 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 171.2, 149.3, 138.3, 134.5, 131.5, 129.8, 129.7, 129.0, 127.94, 127.9, 127.8, 126.9, 123.9, 123.0, 120.8, 118.3, 115.5, 113.0, 66.3, 45.6, 28.7. IR ν 3298, 3043, 2899, 2251, 2227, 1499, 1036, 888 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{23}$H$_{20}$N$_3$O [M+H]$^+$ 354.1601; found 354.1599.

N-(4-nitrophenyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ag)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 5:1 as the eluent). Yellow oil (20.8 mg, 56% yield). ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 9.19 (s, 1H), 8.13 (d, J = 9.2 Hz, 2H), 7.67-7.60 (m, 3H), 7.34-7.25 (m, 5H), 7.18 (d, J = 6.8 Hz, 1H), 7.02-6.95 (m, 3H), 5.11 (s, 1H), 3.96-3.89 (m, 1H), 3.43-3.38 (m, 1H), 3.11-3.01 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 171.3, 149.2, 143.7, 143.2, 134.5, 131.3, 129.7, 129.0, 128.04, 128.0, 127.0, 121.0, 119.3, 115.7, 66.4, 45.7, 28.6.

N-([1,1'-biphenyl]-2-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ah)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (31.1 mg, 77% yield). m.p.: 53-54°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 9.18 (s, 1H), 8.50 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 7.2 Hz, 1H), 7.34-7.24 (m, 4H), 7.23-7.13 (m, 5H), 7.09 (d, J = 7.2 Hz, 1H), 7.05-7.02 (m,

3H), 6.91 (dd, $J_1 = J_2 = 7.2$ Hz, 1H), 6.77 (d, $J = 8.0$ Hz, 2H), 4.91 (s, 1H), 3.28 (dt, $J = 10.8$ Hz, $J = 3.6$ Hz, 1H), 2.98 (td, $J = 10.8$ Hz, $J = 3.2$ Hz, 1H), 2.67 (dt, $J = 10.2$ Hz, $J = 3.2$ Hz, 1H), 2.46-2.38 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$, TMS) δ 170.5, 148.9, 137.8, 135.0, 134.4, 132.1, 131.7, 129.6, 129.3, 129.2, 129.1, 128.9, 128.8, 128.5, 127.7, 127.6, 127.5, 126.9, 123.8, 119.7, 119.3, 114.4, 66.6, 44.3, 28.6. IR ν 3323, 3028, 2916, 2242, 1672, 1489, 1295, 1037 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{28}$H$_{25}$N$_2$O [M+H]$^+$ 405.1961; found 405.1960.

N-(4'-methoxy-[1,1'-biphenyl]-2-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ai)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (36.4 mg, 84% yield). m.p.: 128-130°C. ^1H NMR (400 MHz, CDCl$_3$, TMS) δ 9.17 (s, 1H), 8.46 (dd, $J_1 = 8.0$ Hz, $J_2 = 0.8$ Hz, 1H), 7.58 (d, $J = 7.2$ Hz, 1H), 7.32-7.26 (m, 3H), 7.25-7.17 (m, 2H), 7.15-7.12 (m, 1H), 7.10-7.05 (m, 2H), 6.98-6.89 (m, 3H), 6.77 (d, $J = 8.0$ Hz, 2H), 6.71-6.67 (m, 2H), 3.82 (s, 3H), 3.34 (dt, $J = 10.8$ Hz, $J = 4.0$ Hz, 1H), 3.03 (td, $J = 11.2$ Hz, $J = 3.6$ Hz, 1H), 2.73 (dt, $J = 16.0$ Hz, $J = 3.2$ Hz, 1H), 2.58-2.50 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$, TMS) δ 170.4, 159.0, 148.9, 135.1, 134.5, 132.2, 131.4, 130.3, 129.8, 129.7, 129.3, 128.8, 128.2, 127.6, 127.4, 126.9, 123.7, 119.6, 119.3, 114.3, 114.1, 66.6, 55.3, 44.3, 28.6. IR ν 3316, 3061, 2914, 2846, 2247, 1598, 1035, 834 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{29}$H$_{27}$N$_2$O$_2$[M+H]$^+$ 435.2067; found 435.2068.

N-(4'-methyl-[1,1'-biphenyl]-2-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3aj)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (30.5 mg, 73% yield). m.p.: 136-138°C. ^1H NMR (400 MHz, CDCl$_3$, TMS) δ 9.17 (s, 1H), 8.46 (d, $J = 9.6$ Hz, 1H), 7.56 (d, $J = 7.2$ Hz, 1H), 7.32-7.12 (m, 6H), 7.10 -7.04 (m, 2H), 6.98 (d, $J = 8.0$ Hz, 2H), 6.94-6.88 (m, 3H), 6.73 (d, $J = 8.0$ Hz, 2H), 4.90 (s, 1H), 3.29 (dt, $J = 10.4$ Hz, $J = 4.4$ Hz, 1H), 3.02 (td, $J = 11.2$ Hz, $J = 3.2$ Hz, 1H), 2.70 (dt, $J = 15.6$ Hz, $J = 3.6$ Hz, 1H), 2.54-2.45 (m, 1H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$, TMS) δ 170.3, 148.9, 137.4, 135.1, 134.7, 134.5, 132.2, 131.8, 129.6, 129.5, 129.2, 129.0, 128.9, 128.3, 127.6, 127.5, 126.9, 123.7, 119.7, 119.3, 114.3, 66.5, 44.3, 28.5, 21.3. IR ν 3327, 3057, 2950, 2917, 1683, 1493, 1271, 930 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{29}$H$_{27}$N$_2$O [M+H]$^+$ 419.2118; found 419.2116.

N-([1,1':4',1''-terphenyl]-2-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ak)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (38.4 mg, 80% yield). m.p.: 119-121°C. ^1H NMR (400 MHz, CDCl$_3$, TMS) δ 9.23 (s, 1H), 8.50 (dd, $J_1 = 8.8$ Hz, $J_2 = 1.2$ Hz, 1H), 7.65-7.61 (m, 2H), 7.58 (d, $J = 7.2$ Hz, 1H), 7.54-7.49 (m, 2H), 7.44-7.39 (m, 3H), 7.36-7.31 (m, 1H), 7.28-7.16 (m, 5H), 7.13-7.08 (m, 3H), 7.04 (d, $J = 7.2$ Hz, 1H), 6.90 (dd, $J_1 = J_2 = 7.2$ Hz, 1H), 6.75 (d, $J = 8.0$ Hz, 2H), 4.92 (s, 1H), 3.28 (dt, $J = 10.4$ Hz, $J = 4.4$ Hz, 1H), 2.98 (td, $J = 11.2$ Hz, $J = 3.2$ Hz, 1H), 2.68 (dt, $J = 15.6$ Hz, $J = 3.6$ Hz, 1H), 2.55-2.46 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$, TMS) δ 170.4, 148.9, 140.4, 140.3, 136.7, 135.0, 134.4, 132.2, 131.4, 129.6, 129.54, 129.5, 129.3, 129.0, 128.9, 128.6, 127.7, 127.6, 127.53, 127.5, 127.4, 127.1, 127.0, 126.9, 123.8, 119.8, 119.4, 114.4, 66.6, 44.4, 28.5. IR ν 3300, 3025, 2849, 2247, 1685, 1111, 906, 841 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{34}$H$_{29}$N$_2$O [M+H]$^+$ 481.2274; found 481.2273.

N-benzyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3al)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 10:1 as the eluent). White solid (29.3 mg, 86% yield). m.p.: 154-156°C. ^1H NMR (400 MHz, CDCl$_3$, TMS) δ 7.64-7.61 (m, 1H), 7.32-7.14 (m, 9H), 7.04-7.00 (m, 2H), 6.93-6.88 (m, 3H), 5.06 (s, 1H), 4.43-4.32 (m, 2H), 3.82 (dt, $J = 10.8$ Hz, $J = 4.4$ Hz, 1H), 3.28 (td, $J = 10.4$ Hz, $J = 3.6$ Hz, 1H), 3.07-2.91 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$, TMS) δ 172.4, 149.4, 138.1, 134.5, 132.6, 129.4, 128.9, 128.6, 127.7, 127.5, 127.4, 127.3, 126.8, 119.7, 114.9, 65.6, 45.2, 43.4, 29.0. IR ν 3319, 3025, 2831, 2247, 1489, 1055, 903, 756 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{23}$H$_{23}$N$_2$O [M+H]$^+$ 343.1805; found 343.1803.

N-phenethyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3am)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 5:1 as the eluent). White solid (19.9 mg, 56% yield). m.p.: 123-125°C. ^1H NMR (400 MHz, CDCl$_3$, TMS) δ 7.60-7.57 (m, 1H), 7.32-7.23 (m, 4H), 7.19-7.11 (m, 4H), 6.93-6.84 (m, 6H), 4.94 (s, 1H), 3.71 (dt, $J = 11.2$ Hz, $J = 4.0$ Hz, 1H), 3.52-3.36 (m, 2H), 3.19 (td, $J = 11.2$ Hz, $J = 3.6$ Hz, 1H), 2.89-2.60 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$, TMS) δ 172.3, 149.2, 138.7, 134.6, 132.6, 129.4, 128.8, 128.7, 128.5, 127.5, 127.46, 126.8, 126.4, 119.4, 114.3, 65.6, 44.6, 40.6, 35.4, 28.8. IR ν 3298, 3028, 2899, 2228, 1663, 1516, 943, 791 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{24}$H$_{25}$N$_2$O [M+H]$^+$ 357.1961; found 357.1960.

N-(4-methylphenethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3an)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 5:1 as the eluent). White solid (28.5 mg, 77% yield). m.p.: 97-99°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 7.59-7.56 (m, 1H), 7.31-7.21 (m, 4H), 7.14-7.11 (m, 1H), 6.97 (d, J = 7.6 Hz, 2H), 6.90-6.79 (m, 6H), 4.93 (s, 1H), 3.71 (dt, J = 11.2 Hz, J = 4.8 Hz, 1H), 3.49-3.34 (m, 2H), 3.20 (td, J = 10.4 Hz, J = 4.4 Hz, 1H), 2.90-2.75 (m, 2H), 2.71-2.55 (m, 2H), 2.29 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 172.3, 149.3, 135.8, 135.6, 134.6, 132.7, 129.4, 129.2, 128.9, 128.7, 128.6, 127.5, 127.4, 126.7, 119.4, 114.3, 65.6, 44.7, 40.7, 35.0, 28.8, 21.0. IR ν 3262, 3063, 2831, 2241, 1598, 1442, 1426, 987 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{25}$H$_{27}$N$_2$O [M+H]$^+$ 371.2118; found 371.2120.

N-(3,4-dimethoxyphenethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ao)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 2:1 as the eluent). White solid (23.3 mg, 56% yield). m.p.: 105-106°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 7.58-7.55 (m, 1H), 7.31-7.20 (m, 4H), 7.13-7.10 (m, 1H), 6.93-6.82 (m, 4H), 6.66 (d, J = 8.4 Hz, 1H), 6.54 (d, J = 2.0 Hz, 1H), 6.46 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 4.93 (s, 1H), 3.84 (s, 3H), 3.72-3.65 (m, 4H), 3.48-3.41 (m, 2H), 3.20 (td, J = 11.2 Hz, J = 3.6 Hz, 1H), 2.89-2.57 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 172.3, 149.3, 148.9, 147.5, 134.5, 132.7, 131.1, 129.4, 128.9, 127.5, 127.4, 126.7, 120.6, 119.4, 114.2, 111.6, 111.2, 65.7, 55.9, 55.7, 44.6, 40.5, 35.0, 28.8. IR ν 3028, 2915, 2850, 2251, 1662, 1061, 889, 752 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{26}$H$_{29}$N$_2$O$_3$[M+H]$^+$ 417.2173; found 417.2171.

2-phenyl-N-(4-phenylbutyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ap)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 5:1 as the eluent). White solid (23.8 mg, 62% yield). m.p.: 146-148°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 7.60-7.57 (m, 1H), 7.31-7.19 (m, 6H), 7.17-7.12 (m, 2H), 7.05-7.02 (m, 2H), 6.91-6.84 (m, 4H), 4.96 (s, 1H), 3.83 (dt, J = 11.2 Hz, J = 4.4 Hz, 1H), 3.31-3.11 (m, 3H), 3.06-2.91 (m, 2H), 2.50 (t, J = 6.8 Hz, 2H), 1.51-1.36 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 172.2, 149.4, 142.1, 134.4, 132.8, 129.4, 128.9, 128.3, 127.5, 127.4, 126.8, 125.7, 119.6, 114.5, 65.6, 45.0, 39.2, 35.4, 29.1, 29.0, 28.5. IR ν 3254, 3061, 2941, 2828, 1676, 1559, 1217, 827 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{26}$H$_{29}$N$_2$O [M+H]$^+$ 385.2274; found 385.2272.

N-octyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3aq)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 5:1 as the eluent). White solid (32.8 mg, 90% yield). m.p.: 129-130°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 7.60-7.57 (m, 1H), 7.32-7.27 (m, 2H), 7.25-7.19 (m, 2H), 7.15-7.12 (m, 1H), 6.92-6.87 (m, 4H), 4.97 (s, 1H), 3.85 (dt, J = 10.8 Hz, J = 4.0 Hz, 1H), 3.28 (td, J = 10.8 Hz, J = 4.0 Hz, 1H), 3.23-3.11 (m, 2H), 3.10-2.94 (m, 2H), 1.41-1.32 (m, 2H), 1.26-1.10 (m, 11H), 0.86 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 172.1, 149.4, 134.4, 132.8, 129.4, 128.9, 127.5, 127.4, 126.7, 119.5, 114.5, 65.6, 45.0, 39.5, 31.7, 29.5, 29.2, 29.1, 29.0, 26.8, 22.6, 14.1. IR ν 3264, 3060, 2950, 2847, 1673, 1425, 1220, 1053 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{24}$H$_{33}$N$_2$O [M+H]$^+$ 365.2587; found 365.2585.

N-dodecyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (3ar)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 5:1 as the eluent). White solid (32.3 mg, 77% yield). m.p.: 101-103°C. ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 7.61-7.57 (m, 1H), 7.33-7.20 (m, 4H), 7.16-7.13 (m, 1H), 6.92-6.87 (m, 4H), 4.97 (s, 1H), 3.86 (dt, J = 10.8 Hz, J = 4.4 Hz, 1H), 3.30 (td, J = 10.8 Hz, J = 4.0 Hz, 1H), 3.25-3.11 (m, 2H), 3.10-2.94 (m, 2H), 1.43-1.12 (m, 20H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 172.1, 149.4, 134.4, 132.8, 129.4, 128.9, 127.5, 127.4, 126.7, 119.5, 114.5, 65.6, 44.9, 39.5, 31.9, 29.65, 29.64, 29.54, 29.51, 29.49, 29.4, 29.2, 29.0, 26.8, 22.7, 14.2. IR ν 3317, 3027, 2918, 2246, 1663, 1488, 904, 723 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{28}$H$_{41}$N$_2$O [M+H]$^+$ 421.3213; found 421.3212.

Ethyl (2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonyl)glycinate (3as)

Purified by silica gel chromatography (petroleum ether/ethyl acetate 5:1 as the eluent). Colorless oil (31.1 mg, 92% yield). ^{1}H NMR (400 MHz, CDCl$_3$, TMS) δ 7.55-7.52 (m, 1H), 7.45-7.42 (m, 1H), 7.33-7.22 (m, 4H), 7.17-7.13 (m, 1H), 6.96-6.87 (m, 3H), 5.03 (s, 1H), 4.16-4.06 (m, 3H), 3.91-3.83 (m, 2H), 3.37-3.30 (m, 1H), 3.20-3.11 (m, 1H), 3.02-2.95 (m, 1H), 1.20 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$, TMS) δ 172.6, 169.6, 149.3, 135.0, 132.5, 129.4, 129.1, 127.6, 127.56, 126.7, 119.5, 114.4, 65.4, 61.5, 44.8, 41.3, 28.6, 14.1. IR ν 3298, 2918, 2250, 1598, 1318, 1036, 791, 692 cm^{-1}. HRMS (ESI) m/z: calcd for C$_{20}$H$_{23}$N$_2$O$_3$[M+H]$^+$ 339.1703; found 339.1701.