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Graphical Abstract

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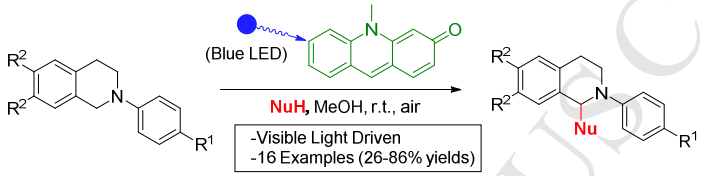

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ABSTRACT

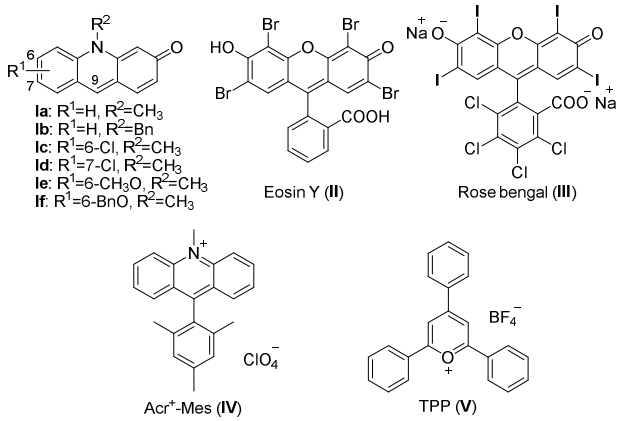
N-Substituted-3(10H)-acridones have been established as visible-light organic photocatalyst. These photosensitizers are efficient for oxidative coupling reaction of N-aryl tetrahydroisoquinolines with various nucleophiles. Notably, N-methyl-3(10H)-acridone (**Ia**) is stable and can be effectively prepared. It is a water-soluble and atom-economic catalyst, and thus holds promise for green chemical applications. Mechanistic studies confirm a single electron transfer (SET)-induced radical process and a rate-limiting step. Analysis of the photocatalytic reactivity−structure relationship reveals that the acridones are robust and tunable photosensitizers for photoredox catalysis.

Introduction

Visible light constitutes the major part of sunlight, which provides clean and renewable energy for the nature. Application of solar photocatalysts on an industrial scale has been an aspiration since a century ago.[1] Photocatalysts mainly include transition metal chromophores and organic chromophores. $[Ru(bpy)_3]Cl_2$ and iridium polypyridyl complexes are among the best organometallic photoredox catalysts with well demonstrated versatility in organic synthesis.[2] On the other hand, "metal-free" organic chromophores have long been recognized for their ability to initiate photoredox catalysis.[3] Despite the significant advances in the field of photoredox catalysis, development of robust, versatile and eco-friendly organic photocatalysts is still highly desirable. In this study, N-substituted-3(10H)-acridones **Ia~f** (Figure 1) are prepared as visible-light photosensitizers for organic photoredox catalysis.

As part of our program to develop inhibitors of epigenetic enzymes, we became interested in 3-hydroxy-N-methylacridinium ion (Ac^+OH) and its derivatives.[4] This compound could be synthesized according to the literature procedures. Interestingly, N-methyl-3(10H)-acridone (**Ia**) [5] was obtained as an orange red solid whose structure was confirmed by X-ray crystallography (see Supporting Information (SI): Figure S6). Given its unique chromophore structure and photophysical properties (see SI: Figures S2~5, Tables S1~2), we reasoned that **Ia** might find its utility as a visible-light organic photocatalyst. To the best of our knowledge, there are no any reports concerning its applications in organic photoredox catalysis.[6]

Figure 1. Visible-light photosensitizers for organic photoredox catalysis.

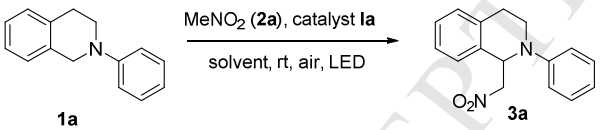


Result and Discussion

To test this hypothesis, photocatalytic oxidative coupling reaction of N-phenyl tetrahydroisoquinoline (**1a**) with nitromethane was chosen as the model reaction (Table 1). Firstly, different types of light sources were examined (entries 1~5, Table 1). To our delight, the desired product **3a** was obtained in 77% yield after 7 h of irradiation with blue LED at room temperature (entry 2, Table 1). It was found that the reaction was significantly affected by the volume of nitromethane (entries 8, 11, Table 1). A screening of solvents revealed that MeOH was the best solvent allowing for production of **3a** in 82% yield (see

in the supporting information). The catalyst loading also had a significant impact on the reaction. While 1~5 mol % catalyst loading afforded good product yields and appropriate reaction speed (entries 8, 12, 13, Table 1), 0.01~0.001 mol % catalyst loading resulted in decreased reaction speed and conversion rate (entries 15, 16, Table 1). Surprisingly, TON (turnover number) and TOF (turn over frequency) of **Ia** could reach approximately 79000 and 3950 h^{-1}, respectively (entry 16, Table 1). The reaction proceeded very poorly in the absence of air (entry 18, Table 1), indicating the critical role of oxygen. When the reaction was run under an oxygen atmosphere, the reaction proceeded very fast at the early stage, however, the overall conversion rate was not as good as with using air (entries 8, 19, Table 1). Notably, the reaction did not take place at all in the dark (entry 20, Table 1). The photocatalyst was also required for efficient conversion (entry 17, Table 1). To investigate the photocatalytic reactivity−structure relationship of acridones, a series of acridones **Ia~f** (Figure 1) were synthesized following the literature procedures [4,11] (see SI: Scheme S1 and experimental section). To compare the photocatalytic efficiency of **Ia~f**, the CDC reaction of **1a** with nitromethane was carried out (Table 1). Notably, all the acridones tested were efficient photocatalyts for this CDC reaction, leading to a complete conversion within 7.5 h. Acridone **Ia** exhibited almost the same reactivity with **Ib** (entries 8 and 22, Table 1), indicating the negligible effect caused by different N-substituted groups. Acridones **Ic** and **Id** with 6-Cl or 7-Cl substitution showed obviously decreased reaction rate (entries 23 and 24, Table 1), implying that electron-withdrawing groups might have negative effect on the photocatalytic activity. On the other hand, the introduction of a methoxy or benzyloxy group at the 6 position of **Ie** or **If** resulted in an increase in photocatalytic efficiency (entries 25 and 26, Table 1), indicating that electron-donating substituents on the benzene ring may be favorable for the photocatalytic activity. Together, various acridones represent a new class of robust and tunable organic photoredox catalysts. Finally, acridone **Ia** was found to be a novel and highly efficient organic photoredox catalyst.

Table 1. Photocatalytic Reaction of N-phenyl Tetrahydroisoquinoline with Nitromethane [a]



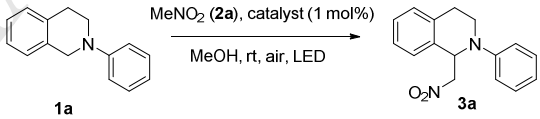
1a **3a**

entry	**Ia** (mol%)	LED Color	**2a** (mL)	time (h)	conv. (%)[b]	yield (%)[c]
1	1	white	0.5	7	96	70
2	1	blue	0.5	7	99	77
3	1	green	0.5	7	82	56
4	1	red	0.5	7	<10	8
5	1	yellow	0.5	7	<10	6
6	1	blue	0.1	6	91	61
7	1	blue	0.5	6	94	72
8	1	blue	1	6	100	82
9	1	blue	1.5	6	96	68
10	1	blue	2	6	97	66
11	1	blue	2.4	6	88	58
12	5	blue	1	4.5	100	79
13	2	blue	1	5	100	74
14	0.1	blue	1	11	100	-
15	0.01	blue	1	20	94	-
16	0.001	blue	1	20	79	-
17	0	blue	1	20	56	-
18[d]	1	blue	1	6	31	-
19[e]	1	blue	1	6	93	-
20[f]	1	-	1	6	0	-
21[g]	1	blue	1	6	24	-
22	**Ib (1)**	blue	1	6	100	80
23	**Ic (1)**	blue	1	7	100	82
24	**Id (1)**	blue	1	7.5	100	77
25	**Ie (1)**	blue	1	5	100	78
26	**If (1)**	blue	1	5	100	85

[a] Conditions: **1a** (0.25 mmol), **2a**, catalyst **Ia**, solvent (total solution volume 2.5 mL), air, r.t., blue LED irradiation (6W, λ= 450±10 nm). [b] Conversion rate was determined by ^{1}H-NMR, 1,1,2,2-tetrachloroethane as internal standard. [c] Isolated yields after column chromatography. [d] Reaction was run under nitrogen atmosphere.[e] Reaction was run under oxygen atmosphere. [f] Reaction was run in the dark. [g] One equivalent of TEMPO was added.

Next, we wanted to compare acridone **Ia** with the common photoredox catalysts, including Eosin Y (**II**),[6a] Rose Bengal (**III**),[6b] Acr^+-Mes (**IV**),[6c] TPP (**V**),[6d] and $[Ru(bpy)_3]Cl_2$.[2a,7] As shown in Table 2, photocatalytic reaction of N-phenyl tetrahydroisoquinoline with nitromethane was run in the presence of various photocatalysts. LED with different color was used to match the maximum absorption wavelength of each catalyst. To our delight, under the same reaction condition, **Ia** (1 mol%) showed the best photocatalytic capability, enabling an almost complete conversion after 6 h (entry 1, Table 2), while Acr^+-Mes (**IV**) induced only 81% conversion (entry 4, Table 2). Eosin Y (**II**) and Rose Bengal (**III**) showed moderate activity for photocatalysis (entries 2 and 3, Table 2). TPP (**V**) was a weak catalyst for this reaction with only 46% conversion (entry 5, Table 2). Notably, **Ia** had a slightly higher conversion rate than $[Ru(bpy)_3]Cl_2$ (entry 6, Table 2). Together, in this context, acridone **Ia** was more efficient than the common photocatalyst such as $[Ru(bpy)_3]Cl_2$ and Acr^+-Mes (**IV**). It is worth noting that **Ia** has a very good water-solubility, thus allowing for green chemical applications with using water as a solvent.

Table 2. Comparison of Acridone Ia with Common Photocatalysts [a]

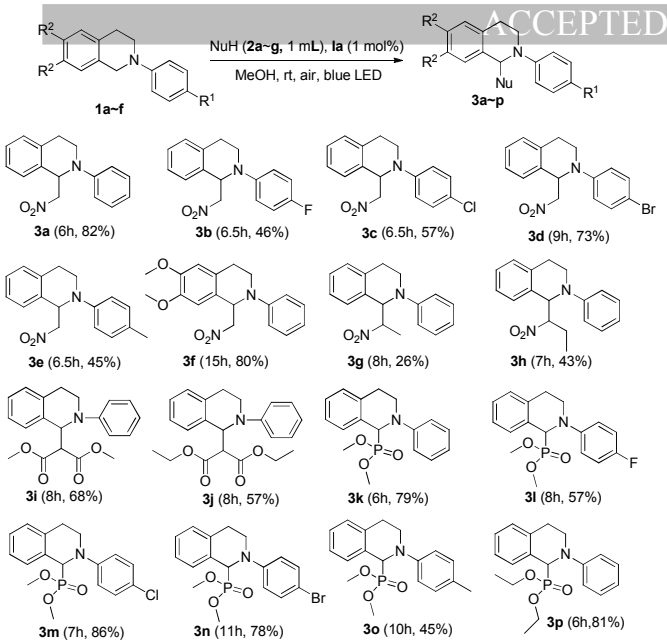


1a **3a**

entry	catalyst	LED color	time (h)	conversion (%)[b]	yield (%)[c]
1	**Ia**	blue	6	99	97
2	**II**	green	6	56	54
3	**III**	green	6	58	56
4	**IV**	blue	6	81	74
5	**V**	blue	6	46	41
6	$[Ru(bpy)_3]Cl_2$	blue	6	95	95

[a] Conditions: **1a** (0.25 mmol), **2a** (1 mL), catalyst (1 mol%), MeOH (1.5 mL), air, r.t., LED irradiation. [b,c] Conversion rate and yields were determined by ^{1}H-NMR, 1,1,2,2-tetrachloroethane as internal standard.

Scheme 1. The Substrate Scope of Coupling Reaction between N-Aryl Tetrahydroisoquinolines with Various Nucleophiles.

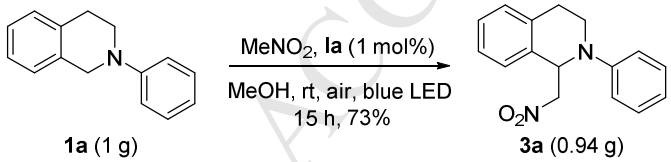


NuH (**2a~g**): CH_3NO_2 (**2a**); $CH_3CH_2NO_2$ (**2b**); $CH_3(CH_2)_2NO_2$ (**2c**); Dimethyl malonate (**2d**); Diethyl malonate (**2e**); Dimethyl phosphonate (**2f**); Diethyl phosphonate (**2g**).

[a]Conditions: **1** (0.25 mmol), **2** (1 mL), catalyst **Ia** (1 mol%), MeOH (1.5 mL), air, r.t., blue LED irradiation. [b] Isolated yields after column chromatography.

With the optimal reaction conditions established, we further examined the substrate scope of the oxidative coupling reaction of N-aryl tetrahydroisoquinolines **1a~f** with various nucleophiles **2a~g** in the presence of photocatalyst **Ia**. Various N-aryl tetrahydroisoquinolines underwent smooth reactions with nitromethane to afford the corresponding products **3a~f** in 45~82% yields (Scheme 1). It seems that electron-donating groups are favorable for this reaction (**3f**), while electron-withdrawing groups are not (**3b**, **3c**). Reaction of **1a** with nitroethane or 1-nitro-propane gave **3g** (26%) or **3h** (43 %) in low yields, respectively. To further explore the substrate scope, other nucleophiles such as dimethyl malonate (**2d**), diethyl malonate (**2e**), dimethyl phosphonate (**2f**) and diethyl phosphonate (**2g**) were examined. Reaction of **1a** with **2d** or **2e** afforded **3i** or **3j** in moderate yields, respectively. Reaction of N-aryl-tetrahydroisoquinolines **1a~e** with dialkylphosphonates **2f~g** yielded α-amino phosphonates **3k~3p** in moderate to good yields.

Scheme 2. Gram-Scale Reaction

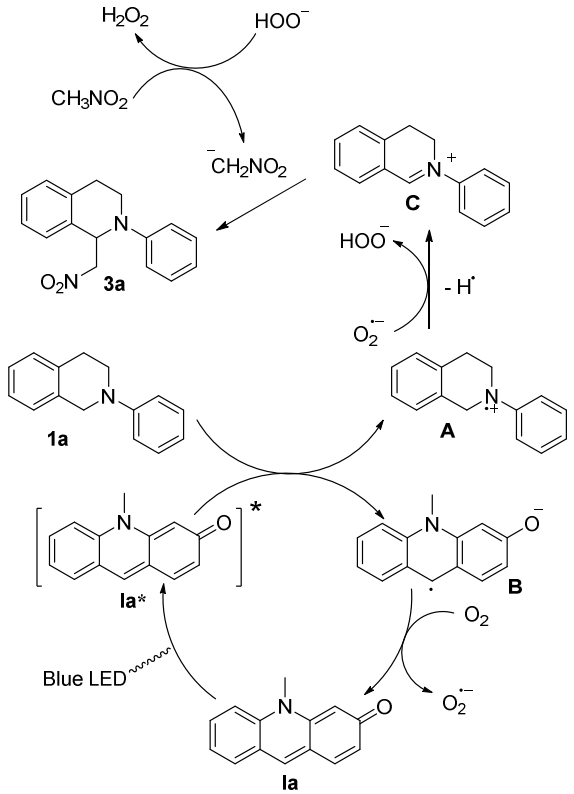


To demonstrate the practical utility of photocatalyst **Ia**, a gram-scale reaction (1.0 g) was carried out (Scheme 2). Thus, under the irradiation with blue LED, reaction of **1a** with nitromethane in the presence of **Ia** (1 mol%) in methanol for 15 h gave **3a** in 73% yield and 100% conversion.

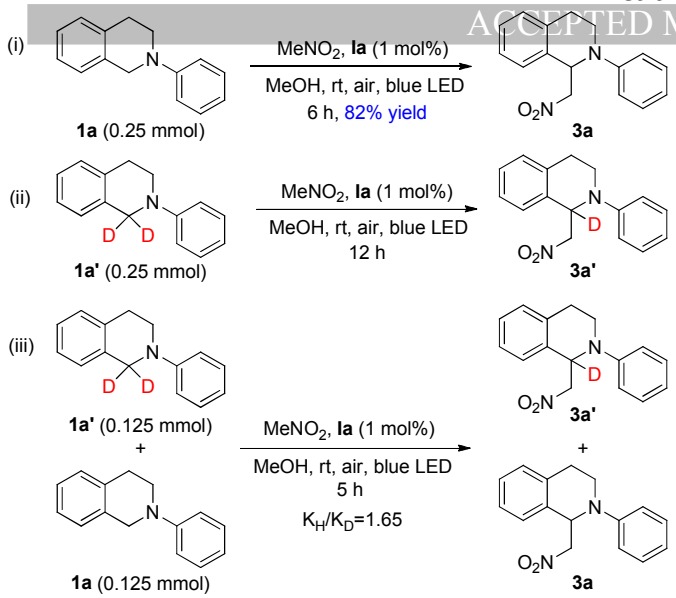
On the basis of our experimental results and the literature reports,[6a,7,8,9] a plausible mechanism for acridone-mediated photocatalytic cross-dehydrogenative-coupling (CDC) reaction is proposed (Scheme 3). Blue LED irradiation of acridone **Ia** provides the excited intermediate **Ia*** with enhanced oxidative ability. Oxidation of **1a** by **Ia*** via a single electron transfer (SET) process yields radical cation **A** together with radical anion **B**. Radical anion **B** is then oxidized by O_2 to allow for regeneration of **Ia** for the next catalytic cycle. Meanwhile, superoxide radical anion $O_2^{\bullet-}$ is formed, which abstracts hydrogen radical from **A** to afford iminium cation **C** together with hydroperoxide anion HOO^-. Deprotonation of nitromethane by hydroperoxide anion yields nitromethane anion, which undergoes nucleophilic attack at **C** to give **3a**.

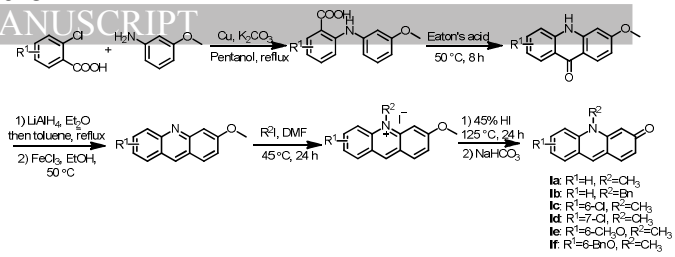
To validate the reaction mechanism, one equivalent of (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) was added to the reaction, leading to only 24% conversion rate (entry 30, Table 1). This suggests that the reaction should proceed through a radical process. Furthermore, to identify if hydrogen abstraction was a rate-limiting step, we carried out deuterium experiments with using deuterated N-phenyl tetrahydroisoquinoline (**1a'**) [10] as a substrate (Scheme 4). Thus, three reactions (equations i~iii) were performed with using **1a** (0.25 mmol), **1a'** (0.25 mmol), and **1a** (0.125 mmol) plus **1a'** (0.125 mmol) as the substrates, respectively. As expected, reaction of **1a** with nitromethane (equation i) proceeded quickly and smoothly to achieve completion in 6 h. Reaction of **1a'** with nitromethane (equation ii), however, underwent much slowly to take 12 h for a complete conversion. Reaction of **1a** plus **1a'** with nitromethane (equation iii) was stopped after 5 h, and after removal of the solvents, fast column chromatography provided a mixture of products **3a** and **3a'**. ^{1}H-NMR analysis of this product mixture revealed that production of **3a** from **1a** was much more than production of **3a'** from **1a'**, and the calculated K_H/K_D value was 1.65 (see SI: Figure S7). This demonstrates that the reaction rate of **1a'** was much slower than that of **1a** under the same condition, implying that hydrogen abstraction of the radical cation **A** to form iminium cation **C** should be a rate-limiting step (Scheme 3).

Scheme 3. Proposed Mechanism



Scheme 4. Deuterium Experiment for Determination of a Rate-Limiting Step





Conclusion

In conclusion, we demonstrate that N-substituted-3(10H)-acridones represent as visible-light photosensitizers for organic photoredox catalysis. These acridones are highly efficient for photocatalytic CDC reaction of N-aryl tetrahydroisoquinolines with various nucleophiles. This catalyst is stable and can be cost-effectively prepared. It has a high atom-economy and a good water-solubility, and thus holds promise for green chemical applications. Mechanistic study results support a single electron transfer (SET)-induced radical process, during which hydrogen abstraction of the radical cation by superoxide radical anion might be a rate-limiting step. Preliminary analysis of the photocatalytic reactivity−structure relationship shows that the acridones are robust and tunable photocatalysts. Further development of the acridone class of photosensitizers and exploration their applications in organic synthesis and photodynamic therapy (PDT) are undergoing in our laboratory.

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded on an ACF* 300Q Bruker or ACF* 500Q Bruker spectrometer. Low- and high-resolution mass spectra (LRMS and HRMS) were recorded in electron impact mode. The mass analyzer type used for the HRMS measurements was TOF. Reactions were monitored by TLC on silica gel 60 F254 plates (Qingdao Ocean Chemical Company, China). Column chromatography was carried out on silica gel (200-300 mesh, Qingdao Ocean Chemical Company, China). Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant (s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Commercially available reagents and solvents were used without further purification. Irradiation with blue light was performed using high-power LEDs (6W, λ = 450±10 nm, 1 m).

Synthesis of N-methyl-3(10H)-acridone (Ia)

2-((3-methoxyphenyl)amino)benzoic acid (6a)

An oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with **4a** (20 g, 128 mmol), Cu powder (0.658 g, 10.3 mmol), K_2CO_3 (20 g, 145 mmol), and **5** (16.8 mL, 135 mmol). The tube was evacuated and backfilled with argon three times, and then anhydrous degassed pentanol (170 mL) was added under a stream of nitrogen by syringe at room temperature. The tube was sealed, stirred, and heated to 140 ºC for 24 h. After being cooled to room temperature, the mixture was diluted with 100 mL water and acidfied with 2N HCl to pH = 3. The aqueous phase was extracted 200 mL CH_2Cl_2 (DCM) three times. The combined organic phase was washed with water (20 mL × 3) and dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using petroleum ether/EtOAc/AcOH (200:10:0.2) as the eluent to afford the product as a brown solid (27 g, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.04 (d, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.27 (m, 1H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.82 (s, 1H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 1H), 3.82 (s, 3H); ESI MS *m/z* 242.1 $[M-H]^-$.

3-methoxyacridin-9(10H)-one (7a) and 1-methoxy-9-oxo-9,10-dihydroacridin-2-ylium (isomer)

An oven dried flask was charged with PPA (111 g, 329 mmol) and **6a** (20 g, 82.2 mmol). The flask was evacuated and backfilled with argon three times. The mixture was heated to 110 ºC for 3 h. After being cooled to room temperature, the mixture was diluted with 100 mL water and stirred for 30 min. The solution was neutralized with NaOH to pH = 8 and then filtered. The combined solid was washed with water and ethyl ether to afford a pale yellow solid (**7a** and its isomer, 18 g, 97% yield). **isomer**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.59 (s, 1H), 8.16 (dd, *J* = 18.0, 8.5 Hz, 2H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.95-6.58 (m, 2H), 3.89 (s, 3H); **7a**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.41 (s, 1H), 8.12 (d, *J* = 7.7 Hz, 1H), 7.64 (t, *J* = 7.1 Hz, 1H), 7.56 (t, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.68 (d, *J* = 8.1 Hz, 1H), 3.85 (s, 3H); ESI MS *m/z* 224.1 $[M-H]^-$.

3-methoxyacridine (8a)

7a and its isomer (18 g, 80 mmol) was dissolved in 180 mL ethyl ether and cooled to 0 ºC. $LiAlH_4$ (12.5 g, 400 mmol) was added slowly to the solution. After stirring for 3 h, the mixture was diluted with 180 mL toluene and heated to 113 ºC for 12 h. After cooling to 0 ºC, the mixture was diluted with water and then filtered. The filtrate was collected and extracted with 5 portions of 100 mL DCM. The combined organic phase was washed with brine, dried with Na_2SO_4 and concentrated in vacuo. The residue was dissolved in 300 mL ethanol and 60 mL water and anhydrous $FeCl_3$ (39 g, 240 mmol) was added. The mixture was heated to 50 ºC for 30 min and then the solvent was evaporated. The residue was neutralized with 10% $NaHCO_3$ solution and then filtered. The solid was washed with DCM and the organic phase was collected. The aqueous phase was extracted with three portions of 100 mL DCM. The combined organic phase was washed with brine, dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by flash

chromatography on silica gel usingpetroleum ether/EtOAc (50:1) as the eluent to afford the product as a yellow solid (4.0 g, 24% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.18 (d, *J* = 8.7 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 9.2 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.20 (dd, *J* = 9.2, 1.9 Hz, 1H), 4.00 (s, 3H); ESI MS *m/z* 232.1 $[M+Na]^+$.

3-methoxy-10-methylacridin-10-ium iodide (9a)

8a (1.5 g, 7.2 mmol) and CH_3I (2.68 mL, 43 mmol) was dissolved in 50 mL DMF. The mixture was heated to 50 ºC for 28 h. After cooling to room temperature, the mixture was filtered. The solid was collected and washed with DCM and ethyl ether. The residue was dried to afford the product as a yellow solid (1.6 g, 64% yield). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.89 (s, 1H), 8.66 (d, *J* = 9.3 Hz, 1H), 8.51 (t, *J* = 8.9 Hz, 2H), 8.40-8.28 (m, 1H), 7.94 (t, *J* = 7.5 Hz, 1H), 7.78 (s, 1H), 7.66 (d, *J* = 9.2 Hz, 1H), 4.71 (s, 3H), 4.21 (s, 3H); ESI MS *m/z* 224.1 $[M-I]^+$;

10-methylacridin-3(10H)-one (Ia)

9a (1.4 g, 4.0 mmol) and HI (45% aqueous solution, 41 mL) were heated to 125 ºC for 24 h. After cooling to room temperature, $NaHCO_3$ solid was added to neutralize the solution to pH = 8. The aqueous solution was extracted with 6 portions of 50 mL DCM. The combined organic phase was washed with brine, dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography on silica gel using DCM/MeOH (50:1) as the eluent to afford the product as an orange solid (0.61 g, 63% yield).^{1}H NMR (300 MHz, CD_3OD) δ 8.44 (s, 1H), 8.05-7.78 (m, 3H), 7.64 (d, *J* = 9.3 Hz, 1H), 7.52-7.38 (m, 1H), 6.83 (d, *J* = 9.3 Hz, 1H), 6.42 (s, 1H), 3.91 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 182.43, 146.07, 141.02, 139.48, 134.11, 133.26, 130.48, 128.34, 123.33, 122.77, 121.71, 115.19, 99.03, 34.19; ESI MS *m/z* 210.1 $[M+H]^+$; HRMS for $C_{14}H_{11}NO$ $[M+H]^+$ cacld 210.0919, found 210.0912;

Synthesis of N-benzyl-3(10H)-acridone (Ib)

Following the procedure described for preparation of **Ia**, **Ib** was obtained as an orange red solid (60 mg, 22% yield). ^{1}H NMR (300 MHz, CD_3OD) δ 8.64 (s, 1H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.74 (dd, *J* = 11.6, 8.3 Hz, 3H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.33-7.15 (m, 3H), 7.06 (d, *J* = 7.1 Hz, 2H), 6.84 (d, *J* = 9.2 Hz, 1H), 6.38 (s, 1H), 5.72 (s, 2H); ^{13}C NMR (75 MHz, CD_3OD) δ 182.71, 146.05, 141.79, 139.57, 134.44, 134.13, 133.69, 130.74, 128.80, 128.54, 127.50, 125.67, 123.69, 123.21, 121.90, 115.48, 99.84, 51.01; ESI MS *m/z* 286.1 $[M+H]^+$; HRMS (ESI) for $C_{20}H_{16}NO$ $[M+H]^+$ calcd 286.1232, found 286.1238.

6-Chloro-N-methyl-3(10H)-acridone (Ic)

Following the procedure described for preparation of **Ia**, **Ic** was obtained as an orange red solid (114 mg, 82% yield). ^{1}H NMR (300 MHz, CD_3OD) δ 8.31 (s, 1H), 7.92-7.67 (m, 2H), 7.57 (d, *J* = 9.3 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 1H), 6.76 (d, *J* = 9.1 Hz, 1H), 6.32 (s, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 182.85, 152.45, 145.32, 139.50, 133.00, 131.29, 128.27, 123.29, 122.57, 119.65, 114.53, 99.08, 33.85; ESI MS *m/z* 244.1 $[M+H]^+$; HRMS (ESI) for $C_{14}H_{11}ClNO$ $[M+H]^+$ calcd 244.0529, found 244.0524.

7-Chloro-N-methyl-3(10H)-acridone (Id)

Following the procedure described for preparation of **Ia**, **Id** was obtained as an orange red solid (84 mg, 73% yield).^{1}H NMR (300 MHz, DMSO-d_6) δ 8.26 (s, 1H), 7.93 (d, *J* = 2.2 Hz, 1H), 7.83 (d, *J* = 9.3 Hz, 1H), 7.70 (dd, *J* = 9.2, 2.3 Hz, 1H), 7.57 (d, *J* = 9.5 Hz, 1H), 6.60 (d, *J* = 9.4 Hz, 1H), 6.10 (s, 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 182.85, 145.56, 138.43, 136.64, 133.29, 132.85, 131.35, 128.90, 126.54, 124.84, 122.33, 117.71, 100.63, 35.05; ESI MS *m/z* 244.1 $[M+H]^+$; HRMS (ESI) for $C_{14}H_{11}ClNO$ $[M+H]^+$ calcd 244.0529, found 244.0533.

Synthesis of 6-Methoxy-N-methyl-3(10H)-acridone (Ie)

A mixture of **9c** (3.5 g, 9.08 mmol), pyridine (17 mL) and acetic acid (50 mL) was stirred at 100 ^{o}C for 24 h. After cooling to room temperature, the excessive solvents were evaporated under reduced pressure. The residue was basified slowly with an aqueous saturated sodium bicarbonate solution (40 mL) to pH = 7-8, then MeOH (100 mL) was added and filtered. The filter was concentrated in vacuo. The crude product was subjected to column chromatography (CH_2Cl_2: MeOH = 25: 1) to give **Ie** as an orange yellow solid (2.0 g, 92% yield). ^{1}H NMR (300 MHz, CD_3OD) δ 8.21 (s, 1H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.48 (d, *J* = 9.2 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 2H), 6.74 (d, *J* = 9.0 Hz, 1H), 6.39 (s, 1H), 3.97 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 180.55, 164.78, 144.97, 141.18, 140.51, 132.66, 131.71, 126.05, 119.40, 116.22, 114.10, 98.85, 96.25, 54.85, 33.85; ESI MS *m/z* 240.1 $[M+H]^+$; HRMS (ESI) for $C_{15}H_{14}NO_2$ $[M+H]^+$ calcd 240.1025, found 240.1026.

Synthesis of 6-Benzyloxy-N-methyl-3(10H)-acridone (If)

Compound **Ie** (1.1 g, 4.43 mmol) was dissolved in 45% aqueous HI (45 mL, 274.67 mmol) and the resulting mixture was stirred at reflux for 24 h. After cooling to room temperature, the reaction mixture was basified slowly with an aqueous saturated sodium bicarbonate solution to pH = 7-8 and extracted with butyl alcohol (5 x 100 mL). The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was subjected to column chromatography (CH_2Cl_2:MeOH = 25:1) to give the crude intermediate **10** (about 900 mg). To a stirred mixture of **10** (90 mg, 0.40 mmol) and K_2CO_3 (165 mg, 1.20 mmol) in DMF (4 mL) was added slowly benzyl bromide (82 mg, 0.48 mmol). The reaction mixture was stirred at room temperature for 5 h. Then water (5 mL) was added and the mixture was extracted with CH_2Cl_2 (5 x 10 mL). The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was subjected to column chromatography (CH_2Cl_2:MeOH = 30: 1) to give **If** (64 mg, 46% yield). ^{1}H NMR (300 MHz, CD_3OD) δ 8.26 (s, 1H), 7.73 (d, *J* = 8.9 Hz, 1H), 7.57-7.46 (m, 3H), 7.45-7.28 (m, 3H), 7.16 (s, 1H), 7.09 (dd, *J* = 8.9, 2.0 Hz, 1H), 6.77 (dd, *J* = 9.2, 1.6 Hz, 1H), 6.41 (s, 1H), 5.26 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 181.98, 164.08, 145.76, 141.61, 140.76, 136.05, 133.18, 132.25, 128.28, 127.95, 127.47, 127.07, 120.15, 116.74, 114.65, 99.41, 98.11, 70.36, 34.27; ESI MS *m/z* 316.1 $[M+H]^+$; HRMS (ESI) for $C_{21}H_{18}NO_2$ $[M+H]^+$ calcd 316.1338, found 316.1345.

The typical procedure for synthesis and characterization of β-nitro amine derivatives 3a~h

In a 5 mL open snap vial equipped with magnetic stirring bar the tetrahydroisoquinoline derivative **1** (0.25 mmol, 1.0 eq.) and N-methyl-3(10H)-acridone (**Ia**, 0.01 eq.) were dissolved in nitroalkane **2** (1 mL) and methanol (1.5 mL). The resulting mixture was irradiated with blue LEDs until the reaction was completed (monitored by TLC). The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (petroleum ether/ethyl acetate 200: 1~100:1) to give β-nitro amine derivative **3** (43-82% yields).

1-Nitromethyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3a) [13] 55 mg, 82% yield; Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.08 (m, 6H), 7.00 (d, *J* = 7.8 Hz, 2H), 6.87 (t, *J* = 7.1 Hz, 1H), 5.57 (t, *J* = 7.0 Hz, 1H), 4.89 (dd, *J* = 11.3, 8.1 Hz, 1H),

4.58 (dd, *J* = 11.6, 6.6 Hz, 1H), 3.88-3.39 (m, 2H), 3.27-2.96 (m, 1H), 2.91-2.66 (m, *J* = 16.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.48, 135.31, 133.00, 129.54, 129.22, 128.15, 127.04, 126.74, 119.50, 115.19, 78.84, 58.23, 42.16, 26.53.

2-(4-Fluorophenyl)-1-nitromethyl-1,2,3,4-tetrahydroisoquinoline (3b)[14] 33 mg, 46% yield; Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.11 (m, 4H), 7.03-6.83 (m, *J* = 14.2, 6.8 Hz, 4H), 5.44 (dd, *J* = 8.1, 6.2 Hz, 1H), 4.84 (dd, *J* = 11.9, 8.6 Hz, 1H), 4.57 (dd, *J* = 12.0, 5.9 Hz, 1H), 3.72-3.48 (m, 2H), 3.11-2.96 (m, *J* = 15.8, 7.8 Hz, 1H), 2.73 (dt, *J* = 16.5, 4.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.21 (d, *J* = 239.2 Hz), 145.32, 135.24, 132.62, 129.43, 128.09, 126.94, 126.76, 117.99 (d, *J* = 7.6 Hz), 115.86 (d, *J* = 22.3 Hz), 78.88, 58.73, 42.90, 25.85; ^{19}F NMR (282 MHz, $CDCl_3$) δ -98.16.

2-(4-Chlorophenyl)-1-nitromethyl-1,2,3,4-tetrahydroisoquinoline (3c)[14] 43 mg, 57% yield; Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.04 (m, 6H), 6.90 (d, *J* = 9.0 Hz, 2H), 5.49 (t, *J* = 7.2 Hz, 1H), 4.85 (dd, *J* = 11.9, 8.1 Hz, 1H), 4.57 (dd, *J* = 11.9, 6.3 Hz, 1H), 3.73-3.55 (m, 2H), 3.19-2.96 (m, 1H), 2.95-2.57 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.15, 135.06, 132.54, 129.33, 129.30, 128.25, 126.97, 126.83, 124.41, 116.56, 78.69, 58.21, 42.26, 26.21.

2-(4-Bromophenyl)-1-nitromethyl-1,2,3,4-tetrahydroisoquinoline (3d)[13] 63 mg, 73% yield; Brown yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, *J* = 9.0 Hz, 2H), 7.30-7.08 (m, 4H), 6.85 (d, *J* = 9.0 Hz, 2H), 5.49 (t, *J* = 7.2 Hz, 1H), 4.84 (dd, *J* = 11.9, 8.0 Hz, 1H), 4.57 (dd, *J* = 11.9, 6.4 Hz, 1H), 3.75-3.50 (m, 2H), 3.21-2.94 (m, *J* = 14.8, 7.2 Hz, 1H), 2.88-2.62 (m, *J* = 16.4, 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.52, 135.04, 132.49, 132.25, 129.29, 128.29, 126.98, 126.85, 116.82, 111.61, 78.64, 58.12, 42.14, 26.23.

2-(4-Methylphenyl)-1-nitromethyl-1,2,3,4-tetrahydroisoquinoline (3e)[14] 32 mg, 45% yield; Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.12 (m, 4H), 7.09 (d, *J* = 8.3 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.51 (t, *J* = 7.1 Hz, 1H), 4.86 (dd, *J* = 11.8, 8.0 Hz, 1H), 4.56 (dd, *J* = 11.8, 6.4 Hz, 1H), 3.84-3.46 (m, 2H), 3.20-2.97 (m, 1H), 2.76 (dt, *J* = 16.4, 4.4 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.42, 135.35, 133.03, 129.98, 129.27, 129.16, 128.00, 126.97, 126.63, 115.98, 78.87, 58.40, 42.39, 26.30, 20.33.

6,7-Dimethoxy-1-nitromethyl-2-phenyl-1,2,3,4–tetrahydroisoquinoline (3f)[13] 66 mg, 80% yield; Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (t, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.85 (t, *J* = 7.3 Hz, 1H), 6.63 (d, *J* = 12.4 Hz, 2H), 5.47 (t, *J* = 7.1 Hz, 1H), 4.85 (dd, *J* = 11.8, 8.0 Hz, 1H), 4.57 (dd, *J* = 11.8, 6.4 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.75-3.63 (m, 1H), 3.62-3.47 (m, 1H), 3.16-2.81 (m, 1H), 2.68 (dt, *J* = 16.1, 4.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.81, 148.61, 147.77, 129.44, 127.43, 124.60, 119.58, 115.55, 111.78, 109.69, 78.79, 57.97, 56.08, 55.91, 42.08, 25.83.

1-(1-Nitro-ethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3g)[13] A mixture of the two diastereoisomers. 18 mg, 26% yield, 1.5:1 dr; Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.10 (m, 5.2H), 7.09-6.97 (m, 2.4H), 6.90-6.82 (m, 0.8H), 5.33-5.24 (m, 1H), 5.14-5.01 (m, 0.6H, major isomer), 4.98-4.86 (m, 0.4H, minor isomer), 3.93-3.80 (m, 0.7H), 3.68-3.51 (m, 1.5H), 3.15-3.01 (m, 1.1H), 3.00-2.84 (m, 1.1H), 1.73 (d, *J* = 6.8 Hz, 1.2H, minor isomer), 1.57 (d, *J* = 6.6 Hz, 2.1H, major isomer); ^{13}C NMR (75 MHz, $CDCl_3$, minor isomer marked*): δ 149.21*, 148.93, 135.65, 134.83*, 133.86*, 132.07, 129.45*, 129.33 (major and minor isomers), 129.13*, 128.75*, 128.37, 128.22, 127.28*, 126.60*, 126.15, 119.35, 118.82*, 115.46, 114.55*, 88.96*, 85.47, 62.77, 61.19*, 43.56*, 42.70, 26.75*, 26.41, 17.42*, 16.40.

1-(1-Nitro-propyl)-2-phenyl-1,2,3,4–tetrahydroisoquinoline (3h)[13] A mixture of two diastereoisomers: 32 mg, 43% yield, 2.0:1 dr; Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.10 (m, 5H), 7.06-6.92 (m, 2H), 6.90-6.78 (m, 1H), 5.27 (d, *J* = 9.2 Hz, 0.3H, minor isomer), 5.17 (d, *J* = 9.5 Hz, 0.6H, major isomer), 5.01-4.80 (m, 0.6H, major isomer), 4.80-4.57 (m, 0.3H, minor isomer), 4.08-3.43 (m, 2H), 3.26-2.75 (m, 2H), 2.48-1.70 (m, 2H), 1.09-0.87 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, minor isomer marked*): δ 149.09, 149.01*, 135.55, 134.69*, 133.91*, 132.57, 129.41, 129.31, 129.17 (major and minor isomers), 128.66, 128.59*, 128.21*, 128.16, 127.22*, 126.61*, 125.89 (major and minor isomers), 119.39, 118.59*, 115.84, 114.16*, 96.14*, 93.05, 62.18, 60.70*, 43.53*, 42.34, 26.81*, 25.74, 24.98*, 24.60, 10.66 (major and minor isomers).

The typical procedure forsynthesis and Characterization of β-diester Amine Derivatives 3i and 3j

In a 5 mL open snap vial equipped with magnetic stirring bar 2-phenyl tetrahydroisoquinoline **1a** (0.25 mmol, 1.0 eq), dialkyl malonates **2d~e** (5 equiv.), and N-methyl-3(10H)-acridone (**Ia**, 0.01 equiv.) were dissolved in methanol (2.5 mL). The resulting mixture was irradiated with blue LED until the reaction was completed (monitored by TLC). The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (petroleum ether/ethyl acetate 200: 1~100:1) to give β-diester amine derivatives **3i~j** (57-68% yields).

2-(2-Phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-malonic acid dimethyl ester (3i)[13]

58 mg, 68% yield; Pale yellow oil;^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.07 (m, 6H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 5.71 (d, *J* = 9.3 Hz, 1H), 3.95 (d, *J* = 9.3 Hz, 1H), 3.81-3.60 (m, 5H), 3.55 (s, 3H), 3.08 (ddd, *J* = 15.5, 8.7, 6.5 Hz, 1H), 2.88 (dt, *J* = 16.5, 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.24, 167.37, 148.76, 135.65, 134.75, 129.07, 128.93, 127.59, 127.02, 126.00, 118.60, 115.19, 59.08, 58.14, 52.48, 42.17, 26.04.

2-(2-Phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-malonic acid diethyl ester (3j)[13]

51 mg, 57% yield; Light brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.10 (m, 6H), 7.01 (d, *J* = 8.3 Hz, 2H), 6.86-6.68 (m, 1H), 5.76 (d, *J* = 9.1 Hz, 1H), 4.30-3.98 (m, 4H), 3.93 (d, *J* = 9.1 Hz, 1H), 3.79-3.59 (m, 2H), 3.19-3.00 (m, 1H), 2.99-2.80 (m, 1H), 1.20 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.88, 167.07, 148.82, 135.92, 134.77, 129.00, 128.81, 127.44, 127.12, 125.93, 118.39, 115.04, 61.48, 59.50, 57.82, 42.24, 26.10, 13.85, 13.80.

The typical procedure for synthesis and characterization of α-amino Phosphonates 3k~p.

In a 5 mL open snap vial equipped with magnetic stirring bar tetrahydroisoquinoline derivative **1** (0.25 mmol, 1.0 equiv.) and N-methyl-3(10H)-acridone (**Ia**, 0.01 equiv.) were dissolved in dialkylphosphonate **2** (1 mL) and methanol (1.5 mL). The resulting mixture was irradiated with blue LEDs until the reaction was completed (monitored by TLC). The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (petroleum ether/ethyl acetate 50: 1~5:1) to give α-amino phosphonates **3k~p** (45-86% yields).

1-Phenyl-2-dimethylphosphonate-1,2,3,4-tetrahydroisoquinoline (3k)[15]

63 mg, 79% yield; White solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, *J* = 6.2 Hz, 1H), 7.27 (t, *J* = 7.9 Hz, 2H), 7.22-7.12 (m, 3H), 6.98 (d, *J* = 8.3 Hz, 2H), 6.82 (t, *J* = 7.2 Hz, 1H), 5.21 (d, *J* = 20.0 Hz, 1H), 4.03 (ddd, *J* = 13.1, 8.4, 5.0 Hz, 1H), 3.71-3.59 (m, 7H), 3.15-2.92 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.24 (d, *J* = 5.9 Hz), 136.40 (d, *J* = 5.6 Hz), 130.41, 129.23, 128.82 (d, *J* = 2.6 Hz), 127.93 (d, *J* = 4.7 Hz), 127.52 (d, *J* = 3.5 Hz), 126.03 (d, *J* = 2.9 Hz), 118.66, 114.77, 58.73 (d, *J* = 159.3 Hz), 53.88 (d, *J* = 7.1 Hz), 52.90 (d, *J* = 7.7 Hz), 43.54, 26.66; ^{31}P NMR (121 MHz, $CDCl_3$) δ 24.50.

1-(4-Fluorophenyl)-2-dimethylphosphonate-1,2,3,4–tetrahydroisoquinoline (3l)

48 mg, 57% yield; White solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.31 (m, 1H), 7.28-7.09 (m, 3H), 7.01-6.84 (m, 4H), 5.07 (d, *J* = 20.3 Hz, 1H), 4.08-3.92 (m, 1H), 3.65 (d, *J* = 10.5 Hz, 6H), 3.59-3.48 (m, 1H), 3.06-2.93 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.57 (d, *J* = 238.2 Hz), 146.02 (dd, *J* = 7.0, 2.0 Hz), 136.23 (d, *J* = 5.8 Hz), 130.49 (d, *J* = 52.0 Hz), 128.87 (d, *J* = 2.6 Hz), 127.95 (d, *J* = 4.6 Hz), 127.55 (d, *J* = 3.6 Hz), 126.07 (d, *J* = 2.8 Hz), 116.68 (d, *J* = 7.5 Hz), 115.72, 115.43, 59.28 (d, *J* = 159.0 Hz), 53.79 (d, *J* = 7.2 Hz), 52.89 (d, *J* = 7.6 Hz), 44.38, 26.41; ^{19}F NMR (282 MHz, $CDCl_3$) δ -99.72; ^{31}P NMR (121 MHz, $CDCl_3$) δ 24.34; HRMS (ESI) for $C_{17}H_{19}FNN_aO_3P$ $[M+Na]^+$ calcd 358.0979, found 358.0983.

1-(4-Chlorophenyl)-2-dimethylphosphonate-1,2,3,4–tetrahydroisoquinoline (3m)[16]

76 mg, 86% yield; white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.31 (m, 1H), 7.29-7.10 (m, 5H), 6.91 (d, *J* = 9.0 Hz, 2H), 5.14 (d, *J* = 19.3 Hz, 1H), 4.05-3.89 (m, 1H), 3.72-3.49 (m, 7H), 3.23-3.08 (m, 1H), 3.07-2.91 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.75 (d, *J* = 5.2 Hz), 136.23 (d, *J* = 5.6 Hz), 130.14, 129.00, 128.74 (d, *J* = 2.6 Hz), 127.93 (d, *J* = 4.8 Hz), 127.71 (d, *J* = 3.6 Hz), 126.16 (d, *J* = 2.8 Hz), 123.38, 115.71, 58.72 (d, *J* = 159.7 Hz), 53.78 (d, *J* = 7.2 Hz), 52.98 (d, *J* = 7.7 Hz), 43.77, 26.79; ^{31}P NMR (121 MHz, $CDCl_3$) δ 24.16.

1-(4-Bromophenyl)-2-dimethylphosphonate-1,2,3,4–tetrahydroisoquinoline (3n)[16]

77 mg, 78% yield; white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.28 (m, 3H), 7.29-7.13 (m, 3H), 6.86 (d, *J* = 9.0 Hz, 2H), 5.14 (d, *J* = 19.1 Hz, 1H), 4.06-3.88 (m, 1H), 3.72-3.47 (m, 7H), 3.24-3.07 (m, 1H), 3.07-2.90 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.13 (d, *J* = 5.1 Hz), 136.22 (d, *J* = 5.5 Hz), 131.89, 130.13, 128.72 (d, *J* = 2.7 Hz), 127.92 (d, *J* = 4.8 Hz), 127.74 (d, *J* = 3.5 Hz), 126.18 (d, *J* = 2.7 Hz), 116.08, 110.52, 58.61 (d, *J* = 159.7 Hz), 53.78 (d, *J* = 7.2 Hz), 53.00 (d, *J* = 7.7 Hz), 43.67, 26.83; ^{31}P NMR (121 MHz, $CDCl_3$) δ 24.10.

1-(4-Methylphenyl)-2-dimethylphosphonate-1,2,3,4–tetrahydroisoquinoline (3o)[16]

37 mg, 45% yield; white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.32 (m, 1H), 7.30-7.13 (m, 3H), 7.09 (d, *J* = 8.3 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.17 (d, *J* = 20.7 Hz, 1H), 4.11-3.95 (m, 1H), 3.76-3.55 (m, 7H), 3.08-2.92 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.25 (d, *J* = 7.1 Hz), 136.43 (d, *J* = 5.6 Hz), 130.38, 129.75, 128.89 (d, *J* = 2.5 Hz), 128.21, 127.95 (d, *J* = 4.5 Hz), 127.43 (d, *J* = 3.5 Hz), 125.99 (d, *J* = 2.8 Hz), 115.33, 58.95 (d, *J* = 159.4 Hz), 53.97 (d, *J* = 7.2 Hz), 52.88 (d, *J* = 7.7 Hz), 43.90, 26.38, 20.27; ^{31}P NMR (121 MHz, $CDCl_3$) δ 24.54.

1-Phenyl-2-diethylphosphonate-1,2,3,4–tetrahydroisoquinoline (3p)[13,15]

70 mg, 81% yield; Clear oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, *J* = 6.0 Hz, 1H), 7.32-7.08 (m, 5H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.79 (t, *J* = 7.2 Hz, 1H), 5.19 (d, *J* = 20.0 Hz, 1H), 4.17–3.82 (m, 5H), 3.74-3.53 (m, 1H), 3.16-2.90 (m, 2H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.34 (d, *J* = 12.7 Hz), 136.41 (d, *J* = 5.6 Hz), 130.66, 129.09, 128.70 (d, *J* = 2.5 Hz), 128.10 (d, *J* = 4.7 Hz), 127.38 (d, *J* = 3.5 Hz), 125.82 (d, *J* = 2.8 Hz), 118.42, 114.76, 63.24 (d, *J* = 7.2 Hz), 62.27 (d, *J* = 7.7 Hz), 59.83, 57.72, 43.45, 26.73, 16.36 (t, *J* = 5.9 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 22.28.

THE ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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