JOC The Journal of Organic Chemistry

Note

Photo-Driven Photocatalyst-/Metal-Free Direct C-C/C-N Bond Formation: Synthesis of Indoles via EDA Complexes

Wei Guo, Kailiang Tao, Zhen Xie, Liuhuan Cai, Mingming Zhao, Wen Tan, Gongping Liu, Weijie Mei, Ling Deng, XiaoLin Fan, and Lvyin Zheng

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b01689 • Publication Date (Web): 18 Sep 2019

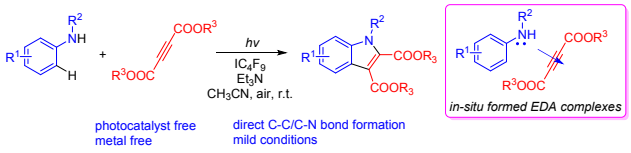
is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Photo-Driven Photocatalyst-/Metal-Free Direct C-C/C-N Bond Formation: Synthesis of Indoles via EDA Complexes

Wei Guo,*† Kailiang Tao,† Zhen Xie, Liuhuan Cai, Mingming Zhao, Wen Tan, Gongping Liu, Weijie Mei, Ling Deng, Xiaolin Fan,* Lvyin Zheng*

Key Laboratory of Organo-pharmaceutical Chemistry of Jiangxi Province, Gannan Normal University, Ganzhou 341000, China

Fax: (+86) 0797-8393536; *E-mail: guoweigw@126.com; fanxl2008@gnnu.edu.cn; zhenglvyin@126.com



ABSTRACT:

The photo-driven direct C-C/C-N bond formation initiated by electron donor-acceptor (EDA) complexes for the synthesis of indoles has been accomplished via [3 + 2] annulations of secondary arylamines with alkynes using IC_4F_9 as oxidants in the absent of any photocatalysts and metals. This green transformation exhibits the advantages of operational simplicity, good functional tolerances and mild reaction conditions. The in-situ generated EDA complexes derived from arylamines with alkynes were characterized by UV−vis absorption spectrometry and NMR titration experiments.

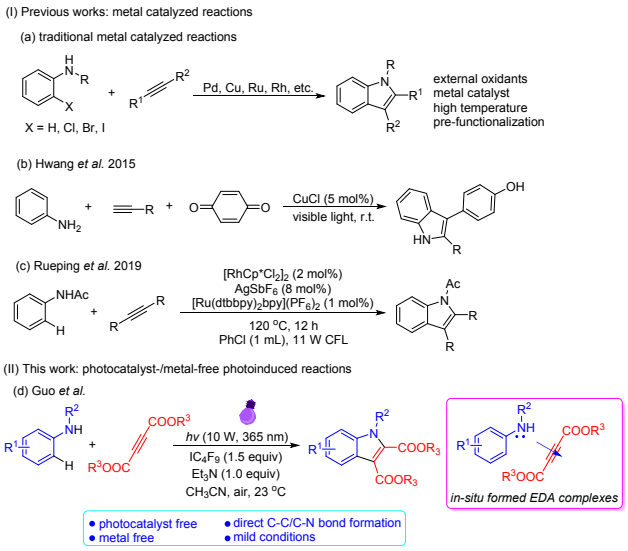
Electron donor-acceptor (EDA) complexes have known wide applications for the

construction of useful organic products by photochemical transformations in recent years.[1] Generally, typical EDA complexes derived from electron-rich and electron-deficient substrates undergo photochemical reaction *via* the photo-induced electron transfer process without the addition of external photocatalysts.[2] Moreover, the appearance of color change from EDA complex is visible, which can also be detected by optical absorption spectrum, exhibiting an obvious red shift.[3] Driven by light irradiation, the electron transfer within EDA complex plays an important role in accelerating the generation of active radical species, which further facilitates the subsequent transformation.[4] Despite the prevalence of photocatalyzed transformations, photochemical methodologies based on the formation of EDA complexes for the new applications are still highly desirable.

Indoles are often regarded as the most important structural scaffolds in natural and synthetic *N*-heterocycles, which are also considered as the privileged structures exiting in pharmaceuticals, agrochemicals and advanced functional materials.[5] Advances for the efficient construction of indole core skeletons have been receiving continuing attentions in the recent years.[6] Generally, great endeavors on the synthesis of indoles mainly are focus on the C-C/C-N bond formations from two or three starting materials by exploring various transition metals (e.g., Mn, Co, Ni, Cu, Ag, Au, Ru, Pd, Rh, Ir) as catalysts (Scheme 1a).[7] In recent years, photocatalyzed organic reactions have emerged as very powerful weapons in the ambitions of acquiring fine chemicals because of the advantage of sustainable and environmentally benign.[8] For examples, Hwang's group successfully developed an excellent copper catalyzed

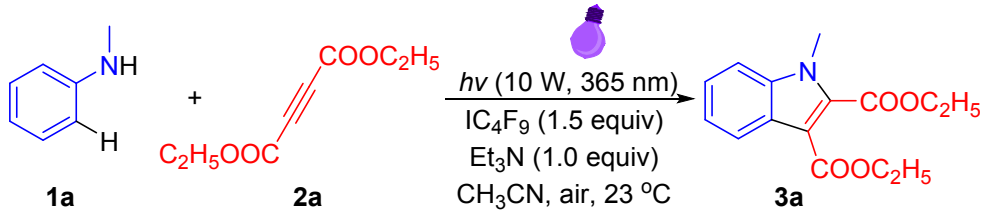
three-component coupling strategy for the synthesis of indoles from arylamines, terminal alkynes, and quinines under visible-light irradiation (Scheme 1b).[9] Subsequently, Rueping's group also succeeded in the photoredox catalyzed cyclization of acetanilides with alkynes for constructing of indoles using Rh(III)/Ag(I) as co-catalysts, Ru(III) as photocatalyst (Scheme 1c).[10] Although remarkable achievements in the field of transition metal catalyzed synthesis of indoles have been accomplished, eliminating the metallic residues is an extremely impending issue.

Recently, we have explored visible-light-promoted coupling annulations for the synthesis of 2-iminothiazolidin-4-ones via in situ formed EDA complexes without the need of any external metals and photocatalysts, in which the EDA complexes from electron donors and acceptors promote the reaction process.[11] We further envision that the preparation of indoles may be performed through investigating the appropriate electron-rich/electron-deficient substrates. In this context, we herein advance the photo-induced direct C-C/C-N bond formation concept for the construction of indoles from the [3 + 2] annulations of secondary arylamines with but-2-ynedioates in the absent of any photoredox catalysts and metals, in which the in situ generated EDA complexes derived from secondary arylamines and alkynes could be involved in the reaction (Scheme 1d).



Scheme 1. Synthesis of Indoles from Arylamines and Alkynes

Table 1. Screening of Reaction Conditions[a]



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

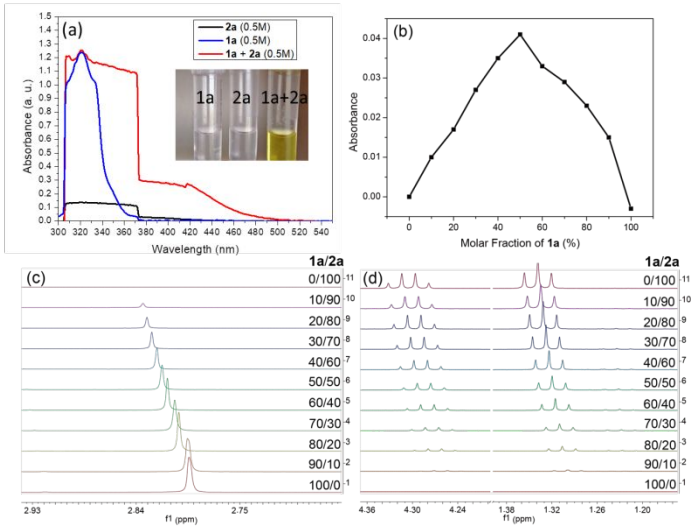
Entry	Variation of the initial conditions	**3a**, Yield (%)[b]
1	none	70
2	with Rose Bengal (1 mol %)	55
3	with Eosin B (1 mol %)	30
4	with Eosin Y (1 mol %)	59
5	with $Ir(ppy)_3$ (1 mol %)	49
6	with $RuCl_2(bpy)_3$ (1 mol %)	52
7	no Et_3N	trace
8	no IC_4F_9	0
9	no light	0
10	NaOH instead of Et_3N	50
11	K_2CO_3 instead of Et_3N	54
12	DABCO instead of Et_3N	8
13	DBU instead of Et_3N	44
14	TMEDA instead of Et_3N	57
15	IBr or ICl or KI or I_2 or KI/I_2 instead of IC_4F_9	<5
16	DMF instead of CH_3CN	56

17	DMSO instead of CH_3CN	48
18	CH_2Cl_2 instead of CH_3CN	31
19	H_2O or NMP instead of CH_3CN	trace
20	465 nm or 520 nm LEDs light sources instead of 365 nm	<45
21	under N_2	23
22	under O_2	65

[a]Reaction conditions: Unless otherwise stated, the reaction of *N*-methylaniline **1a** (0.10 mmol), diethyl but-2-ynedioate **2a** (0.10 mmol), IC_4F_9 (0.15 mmol) and Et_3N (0.10 mmol) was carried out at 23 °C in CH_3CN (1 mL) under 10 W UV (365 nm) LED irradiation for 12 h in the open air. [b]Isolated yields based on **1a**.

To verify our hypothesis, *N*-methylaniline (**1a**) was selected as the model electron donor to react with diethyl but-2-ynedioate (**2a**) as electron acceptor, and IC_4F_9 as initiator for investigating the feasibility of the designed transformation (Table 1). Initially, the reaction was performed in CH_3CN under the light irradiation of 365 nm UV LEDs at room temperature by using Et_3N as the base. To our delight, the target product **3a** was obtained in 70% isolated yield (Table 1, entry 1). Then, several organic and inorganic photocatalysts such as Rose Bengal, Eosin B, Eosin Y, $Ir(ppy)_3$ and $RuCl_2(bpy)_3$ were explored, however, none of them could give higher yields (Table 1, entries 2-6). Furthermore, control experiments showed that Et_3N, IC_4F_9, and light sources are all critical for the construction of indoles (Table 1, entries 7-9). Among various bases tested, Et_3N was the most effective one (Table 1, entries 10-14). In order to study the role of iodine, other iodine compounds were investigated and found to be inferior to IC_4F_9, showing that $\bullet C_4F_9$ radicals are playing a key role in the

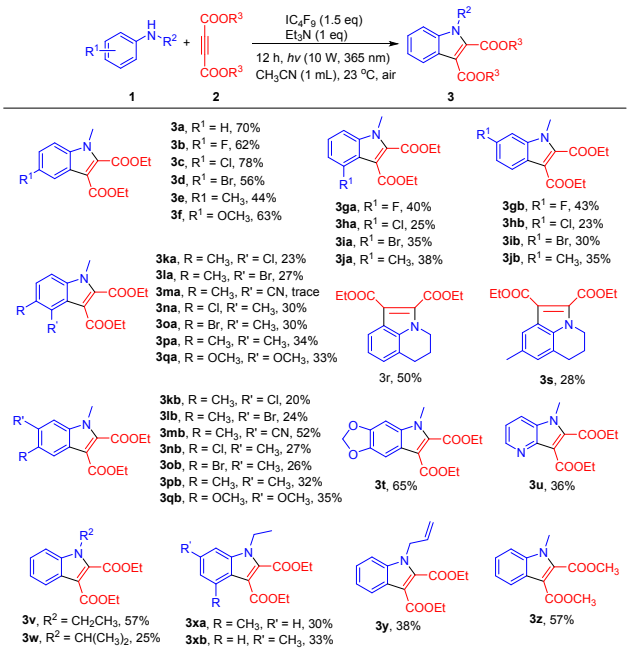
process. (Table 1, entry 15). The solvent investigations revealed that CH_3CN gave the highest yield (Table 1, entries 16-19). Other light sources were also performed in these reactions, however, the yields of **3a** were not further improved (Table 1, entry 20). The results revealed that UVA light is playing a key role to generate the $\bullet C_4F_9$ and iodine radicals with the assistance of Et_3N.[1c, 2a] When the reaction was carried out under N_2, only 23% yield of **3a** was obtained (Table 1, entry 21). However, when the reaction was performed under O_2, **3a** was obtained in 65% yield, indicating that O_2 is important for the reaction (Table 1, entry 21). As a result, the optimal reaction conditions were established as described in entry 1 of Table 1. Finally, a gram-scale reaction was successfully achieved under the optimal conditions, and the isolated yield of **3a** was 56% (see Experimental Section).



Scheme 2. Interactions between **1a** and **2a**. (a) UV−vis absorption spectra of **1a**, **2a**, and the mixture of **1a** + **2a** in CH_3CN from 320 to 550 nm, respectively ([**1a**] = 0.5 M, [**2a**] = 0.5 M). (b) Job's plot of the EDA complexes for ratio between **1a** and **2a** with UV/vis absorption spectrometry. (c), (d) NMR titration experiments between **1a** and **2a**.

In order to further explore the formation of electron donor-acceptor (EDA) complexes from **1a** and **2a**, we investigated the UV−vis absorption spectroscopic properties of **1a**, **2a**, and the mixture of these two components in CH_3CN, respectively. Obviously, a yellow color appeared when colorless **1a** was mixed with colorless **2a**, which could ascribe to the generation of charge-transfer (CT) band (Scheme 2a).[12] Moreover, the UV−vis absorption spectrometry displays the new absorption bands in the 420 nm-550 nm region, which can be attributed to the presence of a new electronic transition from the amine to the alkyne within the [amine-alkyne] complex.[13] Furthermore, the Job's plot of the complex was explored by the UV−vis absorption spectrometry (details in the Supporting Information). The maximal absorption was observed when the ratio of **1a**/**2a** in CH_3CN is 1:1, which can be inferred that the charge-transfer complex is generated from **1a** and **2a** *via* a single-electron transfer (SET) process (Scheme 2b).[14] We further performed the NMR titration experiments to investigate the interactions of **1a** and **2a** (details in the Supporting Information).[15] The results revealed that the increasing amount of acceptors (**2a**) could withdraw higher electron from **1a,** leading to the down-field shift for the ^1H NMR signal of methyl group of **1a** (Scheme 2, c). As for **2a**, the chemical shifts of ethyl group moved to the higher field with the increase of amount of donators (**1a**) (Scheme 2, d). Considering the above results, the EDA complex is derived from *N*-methylanilines (using as the electron donators) and diethyl but-2-ynedioates (using as the electron acceptors).

Table 2. Scope of Secondary Arylamines and But-2-ynedioates[a]

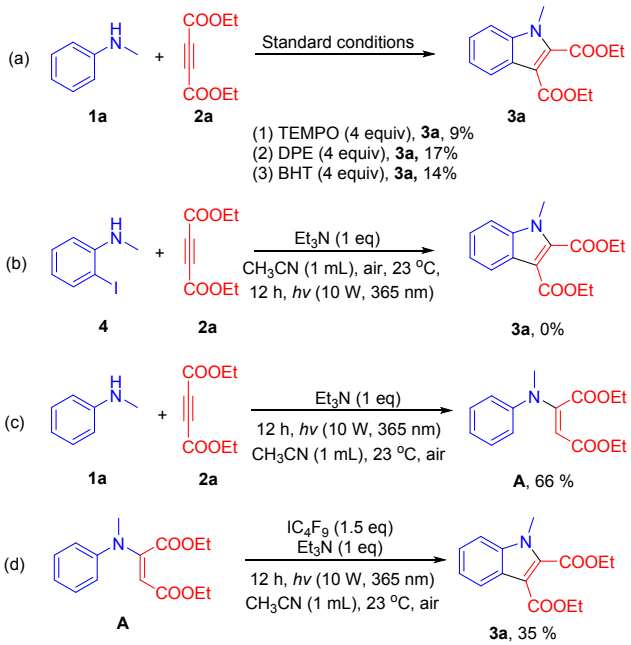


[a]Reaction conditions: **1** (0.10 mmol), **2** (0.10 mmol), IC_4F_9 (0.15 mmol) and Et_3N (0.10 mmol) in CH_3CN (1 mL) at 23 °C under 10 W UV (365 nm) LED irradiation for 12 h in the open air. [b]Isolated yields based on **1**.

With the optimized reaction conditions in hand, we then turned our attention to the exploration of the generality and limitation for the [3 + 2] annulations (Table 2). We were pleased to find that the *para*-substituted *N*-methylanilines bearing electron-donating and electron-withdrawing groups were reacted smoothly with **2a**, giving the corresponding products (**3a-3f**) in moderate to good yields. It is notable that *meta*-substituted *N*-methylanilines are useful substrates in this protocol, providing two different substituted target materials (**3ga-3jb**). These transformations afford diversity-oriented practical applications in organic and medicinal chemistry. To our delight, *N*-methylaniline substrates that include disubstituted groups at *meta*-/*para*-positions remain viable in this transformation, delivering the desired products with

two different configurations (**3ka-3qb**). Moreover, cyclic substrates are also tolerated and afford the respective 5,6-dihydro-4*H*-pyrrolo[3,2,1-ij]quinolines (**3r**, **3s**). Gratifyingly, hetercyclic-amines can be utilized in this new annulations protocol to afford the corresponding products (**3t**, **3u**) in moderate yields. Additionally, *N*-ethylaniline, *N*-isopropylaniline and *N*-allylaniline proceed smoothly to give the desired products **3v-3y**. Satisfactorily, the methyl but-2-ynedioate (**2b**) also worked well to accomplish the photo-driven C-C/C-N bond formation transformation, giving the desired product **3z** in 57% yield.

Scheme 3. Control Experiments

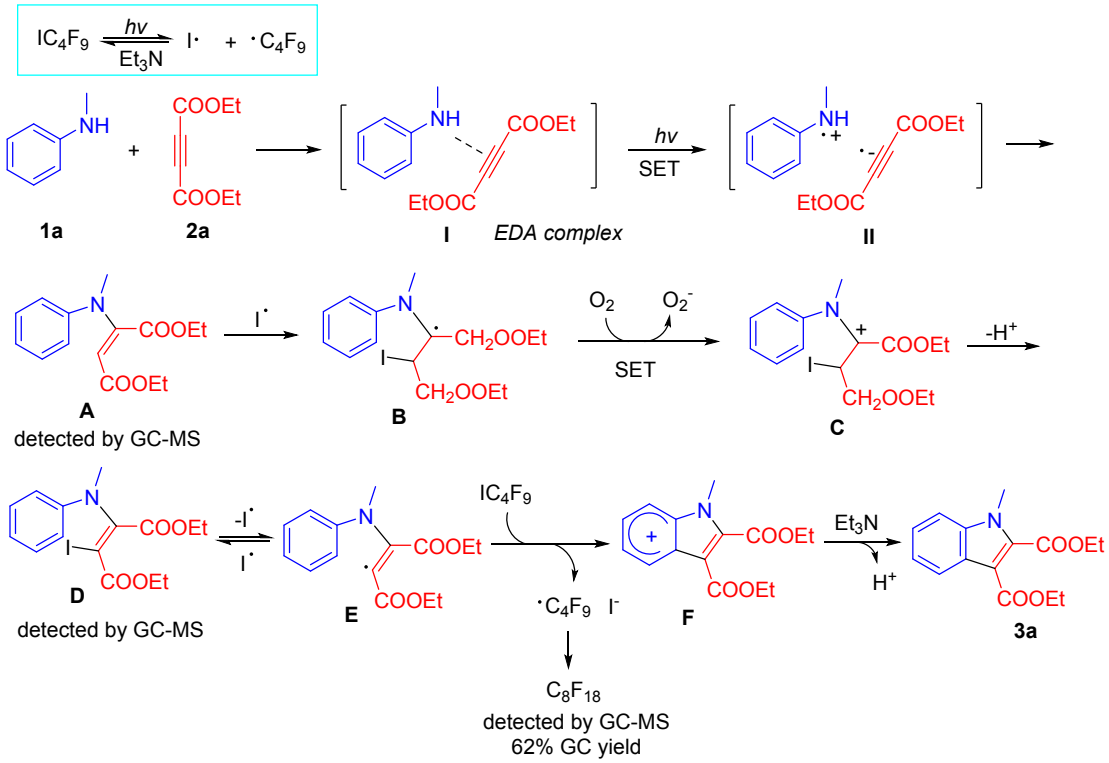


To gain more details about the reaction mechanism, we conducted some control experiments (Scheme 3). When four equivalents of radical inhibitors such as TEMPO, DPE and BHT were added in the reaction systems, the yields of **3a** were reduced from 70% to 9%, 17% and 14%, respectively, indicating radical reaction pathways involved

in this transformation (Scheme 3a).[16] When **1a** was replaced with 2-iodo-*N*-methylaniline (**4**) under the standard conditions, no desired product **3a** was obtained (Scheme 3b). However, when the reaction was performed in the absence of IC_4F_9, compound **A** was obtained in 66% yield (Scheme 3c). Furthermore, when compound **A** was performed under the standard conditions, **3a** was obtained in 35% isolated yield (Scheme 3d). This result implied that compound **A** might a possible intermediate.

Based on the above experiments, a proposed mechanism for the novel photo-driven annulations is outlined in Scheme 4. At first, the in situ generated EDA complex (**I**) from *N*-methylaniline **1a** and diethyl but-2-ynedioate **2a** delivers the radical ion pair (**II**) via the light-induced single-electron transfer (SET) process.[17] Coupling of the radical ion pair (**II**) generates intermediate **A**.[17,18] Then, addition of iodine radical to intermediate **A** affords the radical intermediate **B**, which is further converted into intermediate **C** through SET process under the condition of air/O_2 atmosphere. Elimination of a proton from intermediate **C** gives intermediate **D**,[19] which is then fragmented to give intermediate **E**. The intermediate **E** is further oxidized by C_4F_9I to produce intermediate **F**, C_4F_9 radical and iodine anion. Subsequently, C_8F_{18} was obtained through radical coupling process in 62% GC yield. Finally, the desired product **3a** is obtained from intermediate **F** through the elimination of a proton.[16,20]

Scheme 4. Possible Reaction Mechanism



In conclusion, we have exhibited the utility of in situ formed EDA complexes for the preparation of indoles via direct C-C/C-N bond formation under the irradiation of light. Compared with previously reported method, this photo-driven [3 + 2] annulation does not require any photocatalysts and metals. Furthermore, this protocol features operational simplicity, good functional tolerances and mild reaction conditions, and allows for the construction of a diverse collection of valuable indole products. Mechanistic experiments have provided obvious evidence supporting for the generation of a donor-acceptor complex while facilitating the photo-driven reaction process. We anticipate that this EDA complexes concept will prove powerful for pursuing new green photo-induced organic transformations in the near future.

EXPERIMENTAL SECTION

General Information. Melting points were tested using a melting point instrument and are uncorrected. IR spectra were obtained with an infrared spectrometer on either potassium bromide pellets or liquid films between two potassium bromide pellets.^{1}H and ^{13}CNMR spectra were performed on a 400 MHz NMR spectrometer. GC−MS data were obtained using electron ionization. HRMS data were collected from a high-resolution mass spectrometer (LCMS-IT-TOF). The reaction was carried out on the photoreaction instrument (WP-TEC-1020L, WATTCAS, China) using a condenser system. The distance from the light source to the irradiation vessel is 5 mm. TLC was used on commercially available 100−400 mesh silica gel plates (GF254). The starting materials including **1a**, **1b**, **1c**, **1d**, **1e**, **1f**, **1g**, **1h**, **1i**, **1j**, **1r**, **1s**, **1u**, **1v**, **1w**, **1x**, **1y**, **2a** and **2b** were purchased from a commercial way. Other materials (**1k**, **1l**, **1m**, **1n**, **1o**, **1p**, **1q** and **1t**) were synthesized by our lab. Unless otherwise noted, all purchased chemicals were used without further purification.

General Procedure for Synthesis of *N*-methylanilines.

A solution of dimethyl sulfates (0.252 g, 2 mmol) and anilines (0.186 g, 2 mmol) in 10 mL H_2O was stirred of 1 h under ice bath. After completion of the reaction monitored by TLC, 30% sodium hydroxide solution (10 mL) was added. The mixture was extracted by ethyl acetate (3 × 15 mL), and then washed with water (2 × 10 mL). The combined organic phase was dried over $MgSO_4$, filtered, and then concentrated in vacuum. The residue was purified by flash chromatography on silica gel to give the

desired products (using the mixture of petroleum ether and ethyl acetate (5:1) as eluent).

3-chloro-N,4-dimethylaniline (1k): yellow liquid, 55% yield (169 mg); IR (KBr, cm^{-1}) 2923, 2811, 1616, 1512, 1442, 1315, 1254, 1159, 1038, 997, 805, 694; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.00−6.98 (d, J = 8 Hz, 1H), 6.60 (s, 1H), 6.43−6.41 (dd, J = 8 Hz, 1H), 2.78 (s, 3H), 2.24 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 148.5, 134.8, 131.2, 124.0, 112.6, 111.4, 30.8, 18.9; Ms (EI, 70 eV): m/z = 154, 125, 120, 91, 77; HRMS (ESI) calcd for $C_8H_{11}ClN$ $[M + H]^+$ m/z 156.0575; found m/z 156.0578.

3-bromo-N,4-dimethylaniline (1l): yellow liquid, 58% yield (231 mg); IR (KBr, cm^{-1}) 2922, 2815, 1611,1509, 1445, 1313, 1252, 1162, 1026, 983, 838, 805,688; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.01−6.99 (d, J = 8 Hz, 1H), 6.80−6.79 (d, J = 4 Hz, 1H), 6.48−6.46 (dd, J = 8 Hz, 1H), 2.79 (s, 3H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 148.5, 131.0, 125.8, 125.4, 115.7, 112.0, 30.8, 21.6; Ms (EI, 70 eV): m/z = 199, 184, 120, 91, 71; HRMS (ESI) calcd for $C_8H_{11}BrN$ $[M + H]^+$ m/z 200.0069; found m/z 200.0067.

2-methyl-5-(methylamino)benzonitrile (1m): yellow solid, 52% yield (151 mg); mp 47-49 ^oC. IR (KBr, cm^{-1}) 2922, 2813, 2219, 1613, 1520, 1470, 1332, 1268, 1172, 1067, 824; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.08−7.06 (d, J = 8 Hz, 1H), 6.75 (s, 1H), 6.73−6.71 (dd, J = 8 Hz, 1H), 2.81 (s, 3H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 147.4, 130.9, 129.8, 118.8, 117.5, 114.5, 112.9, 30.6, 19.2; Ms (EI, 70 eV): m/z = 145, 116, 89, 77; HRMS (ESI) calcd for $C_9H_{10}N_2H$ $[M + H]^+$ m/z

147.0917; found *m/z* 147.0915.

4-chloro-N,3-dimethylaniline (1n): yellow liquid, 54% yield (166 mg); IR (KBr, cm^{-1}) 2924, 2858, 1604, 1501, 1323, 1254, 1185, 1044, 840, 801, 688; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.15−7.13 (d, J = 8 Hz, 1H), 6.49 (s, 1H), 6.42−6.40 (dd, J = 8 Hz, 1H), 2.83 (s, 3H), 2.33 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 148.0, 136.4, 129.4, 122.3, 114.6, 111.2, 30.8, 20.3; Ms (EI): *m*/*z* = 154, 125, 118, 91, 77; HRMS (EI, 70 eV) calcd for $C_8H_{11}ClN$ $[M + H]^+$ *m/z* 156.0575; found *m/z* 156.0581.

4-bromo-N,3-dimethylaniline (1o): yellow liquid, 47% yield (187 mg); IR (KBr, cm^{-1}) 2922, 2819, 1600, 1501, 1392, 1322, 1255, 1157, 1021, 845, 801, 688; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.28−7.26 (d, J = 8 Hz, 1H), 6.48−6.47 (d, J = 4 Hz, 1H), 6.32−6.30 (dd, J = 8 Hz, 1H), 2.79 (s, 3H), 2.31 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 148.6, 138.2, 132.6, 114.7, 111.6, 111.6, 30.8, 23.1; Ms (EI, 70 eV): *m*/*z* = 199, 184, 119, 91, 77; HRMS (ESI) calcd for $C_8H_{11}BrN$ $[M + H]^+$ *m/z* 200.0069; found *m/z* 200.0076.

N,3,4-trimethylaniline (1p):[21] yellow liquid, 56% yield (150 mg); IR (KBr, cm^{-1}) 2923, 2810, 1617, 1513, 1446, 1320, 1263, 1153, 1075, 1002, 847, 804; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 6.95−6.93 (d, J = 8 Hz, 1H), 6.44−6.43 (d, J = 4 Hz, 1H), 6.39−6.37 (dd, J = 8 Hz, 1H), 2.79 (s, 3H), 2.20 (s, 3H), 2.15 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 147.7, 137.3, 130.3, 125.3, 114.4, 110.0, 31.2, 20.1, 18.7; Ms (EI, 70 eV): *m*/*z* = 134, 120, 91, 77.

3,4-dimethoxy-N-methylaniline (1q): yellow liquid, 58% yield (194 mg); IR (KBr, cm^{-1}) 2934, 2830, 1617, 1516, 1463, 1297, 1233, 1160, 1128, 1024, 918, 826, 762,

632; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.77−6.75 (d, J = 8 Hz, 1H), 6.24 (s, 1H), 6.16−6.14 (dd, J = 8 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 2.80 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 150.1, 144.4, 141.5, 113.4, 103.1, 98.6, 56.8, 55.7, 31.5; Ms (EI, 70 eV): m/z = 167, 152, 124, 109, 94; HRMS (ESI) calcd for $C_9H_{14}NO_2$ [M + H]$^+$ m/z 168.1019; found m/z 168.1027.

N-methylbenzo[d][1,3]dioxol-5-amine (1t):[21] yellow liquid, 53% yield (160 mg); IR (KBr, cm^{-1}) 2883, 2810, 1634, 1504, 1445, 1356, 1296, 1205, 1145, 1038, 937, 812, 791; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.68−6.66 (d, J = 8 Hz, 1H), 6.24 (s, 1H), 6.05−6.03 (dd, J = 8 Hz, 1H), 5.84 (s, 2H), 2.77 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 148.4, 145.2, 139.6, 108.6, 103.8, 100.6, 95.6, 31.6; Ms (EI, 70 eV): m/z = 151, 136, 122, 93, 78.

General Procedure for the Synthesis of Indoles.

A solution of *N*-methylanilines (0.10 mmol), diethyl but-2-ynedioates (17 mg, 0.10 mmol), perfluorobutyl iodides (51.8 mg, 0.15 mmol), and Et_3N (10 mg, 0.10 mmol, 1.0 equiv) was stirred at 23 ^{o}C in CH_3CN (1.0 mL) under 10 W UV (365 nm) LED irradiation for 12 h in the open air. After completion of the reaction monitored by TLC, the solution was concentrated in vacuum. The residue was then purified by flash chromatography on silica gel to afford the desired products **3** (using the mixture of petroleum ether and ethyl acetate (5:1) as eluent).

For the gram scale synthesis of **3a**: *N*-methylanilines **1a** (3.0 mmol, 0.321 g), diethyl but-2-ynedioates **2a** (3.0 mmol, 0.510 g), perfluorobutyl iodides (4.5 mmol, 1.552 g), Et_3N (0.303 g, 3 mmol, 1.0 equiv) and CH_3CN (4.0 mL) were added

subsequently into a 25 mL dry quartz flask. The mixture was irradiated by a 10 W 365 nm LEDs performed on the photoreaction instrument for 12 h at 23 °C in the open air. The photoreaction was monitored by TLC. Subsequently, water (10 mL) was added, and the resulting mixture was extracted with ethyl acetate. The collected organic phase was dried over $MgSO_4$, filtered, and then concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography using the mixture of petroleum ether/ethyl acetate (PE/EA = 5/1) as eluent to afford the target compound **3a** (0.463 g, yield of 56%).

Diethyl 1-methyl-1H-indole-2,3-dicarboxylate(3a):[22] yellow liquid, 70% yield (19 mg); IR (KBr, cm^{-1}) 3055, 2982, 2816, 1704, 1613, 1532, 1469, 1411, 1336, 1246, 1157, 1106, 1035, 922, 860, 787, 753, 620; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.15−8.13 (d, J = 8 Hz, 1H), 7.37−7.35 (m, 2H), 7.33−7.27 (m, 1H), 4.51−4.46 (q, J = 8 Hz, 2H), 4.41−4.36 (q, J = 8 Hz, 2H), 3.82 (s, 3H), 1.45−1.42 (t, J = 8 Hz, 3H), 1.41−1.39 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.2, 162.9, 136.8, 135.0, 125.4, 124.3, 122.5, 122.3, 110.1, 108.0, 62.3, 60.2, 31.3, 14.4, 14.1; MS (EI, 70 eV): m/z = 275, 243, 216, 185, 159, 129, 102, 77.

Diethyl 5-fluoro-1-methyl-1H-indole-2,3-dicarboxylate (3b): red solid, 62% yield (18 mg); mp 78-80 °C. IR (KBr, cm^{-1}) 2983, 2870, 1705, 1625, 1530, 1481, 1412, 1380, 1303, 1240, 1174, 1104, 1031, 949, 865, 799, 694; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.81−7.78 (dd, J = 8 Hz, 1H), 7.31−7.28 (m, 1H), 7.13−7.08 (m, 1H), 4.52−4.46 (q, J = 8 Hz, 2H), 4.41−4.35 (q, J = 8 Hz, 2H), 3.82 (s, 3H), 1.45−1.42 (t, J = 8 Hz, 3H), 1.42−1.39 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ

163.7, 162.5, 159.5 (d, J = 240.0 Hz) , 136.5, 133.3, 126.1 (d, J = 10.0 Hz), 113.3 (d, J = 30.0 Hz), 111.1 (d, J = 10.0 Hz), 107.8, 107.5 (d, J = 30.0 Hz), 62.5, 60.3, 31.6, 14.4, 14.1; MS (EI, 70 eV): m/z = 293, 248, 220, 175, 148; HRMS (ESI) calcd for $C_{15}H_{16}FNO_4Na$ $[M + Na]^+$ m/z 316.0956, found m/z 316.0959.

Diethyl 5-chloro-1-methyl-1H-indole-2,3-dicarboxylate (3c): yellow liquid, 78% yield (21 mg); IR (KBr, cm^{-1}) 2981, 1736, 1603, 1531, 1493, 1410, 1374, 1206, 1097, 1029, 936, 858, 817, 769, 713, 647, 618; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.13−8.12 (m, 1H), 7.31−7.30 (m, 2H), 4.52−4.47 (q, J = 8 Hz, 2H), 4.41−4.36 (q, J = 8 Hz, 2H), 3.82 (s, 3H), 1.46−1.43 (t, J = 8 Hz, 3H), 1.42−1.39 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.6, 162.5, 136.2, 135.1, 128.5, 126.3, 124.8, 121.9, 111.2, 107.5, 62.5, 60.4, 31.6, 14.4, 14.0; MS (EI, 70 eV): m/z = 309, 264, 236, 209, 191; HRMS (ESI) calcd for $C_{15}H_{17}ClNO_4$ $[M + H]^+$ m/z 310.0841; found m/z 310.0844.

Diethyl 5-bromo-1-methyl-1H-indole-2,3-dicarboxylate (3d): yellow liquid, 56% yield (20 mg); IR (KBr, cm^{-1}) 2981, 1710, 1597, 1526, 1476, 1409, 1383, 1229, 1098, 1023, 861, 788, 753, 618; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.29−8.28 (d, J = 4 Hz, 1H), 7.46−7.43 (dd, J = 8 Hz, 1H), 7.25−7.23 (m, 1H), 4.52−4.46 (q, J = 8 Hz, 2H), 4.41−4.36 (q, J = 8 Hz, 2H), 3.81 (s, 3H), 1.45−1.43 (t, J = 4 Hz, 3H), 1.42−1.39 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.6, 162.4, 136.0, 135.4, 127.4, 126.9, 125.0, 116.2, 111.6, 107.4, 62.5, 60.4, 31.5, 14.4, 14.1; MS (EI, 70 eV): m/z = 353, 309, 280, 253,237, 209; HRMS (ESI) calcd for $C_{15}H_{17}BrNO_4$ $[M + H]^+$ m/z 354.0335; found m/z 354.0341.

Diethyl 1,5-dimethyl-1H-indole-2,3-dicarboxylate (3e): yellow liquid, 44% yield (13 mg); IR (KBr, cm^{-1}) 2981, 2934, 2864, 1703, 1529, 1485, 1411, 1378, 1223, 1152, 1107, 1035, 946, 859, 791, 700; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.92−7.92 (m, 1H), 7.24 (s, 1H), 7.19−7.17 (m, 1H), 4.50−4.45 (q, J = 8 Hz, 2H), 4.41−4.36 (q, J = 8 Hz, 2H), 3.81 (s, 3H), 2.48 (s, 3H), 1.45−1.42 (t, J = 8 Hz, 3H), 1.41−1.39 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.3, 162.9, 135.3, 134.7, 132.1, 126.1, 125.7, 121.8, 109.7, 107.6, 62.2, 60.1, 31.4, 21.6, 14.4, 14.1; MS (EI, 70 eV): *m/z* = 289, 244, 216, 189, 171, 145; HRMS (ESI) calcd for $C_{16}H_{20}NO_4$ $[M + H]^+$ *m/z* 290.1387; found *m/z* 290.1390.

Diethyl 5-methoxy-1-methyl-1H-indole-2,3-dicarboxylate (3f): yellow liquid, 63% yield (19 mg); IR (KBr, cm^{-1}) 2924, 2853, 1719, 1701, 1623, 1524, 1459, 1382, 1251, 1196, 1103, 1040, 951, 848, 806, 779; ^1H NMR (400 MHz, d^6-DMSO, ppm) δ 7.58−7.56 (d, J = 8 Hz, 1H), 7.46−7.45 (d, J = 4 Hz, 1H), 7.04−7.01 (dd, J = 8 Hz, 1H), 4.44−4.38 (q, J = 8 Hz, 2H), 4.29−4.24 (q, J = 8 Hz, 2H), 3.81 (s, 3H), 3.79 (s, 3H), 1.37−1.33 (t, J = 8 Hz, 3H), 1.33−1.29 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.3, 162.8, 156.2, 134.9, 131.9, 126.3, 115.4, 111.0, 107.3, 102.9, 62.2, 60.1, 55.7, 31.5, 14.4, 14.1; MS (EI, 70 eV): *m/z* = 305, 290, 260, 232, 218, 187; HRMS (ESI) calcd for $C_{16}H_{20}NO_5$ $[M + H]^+$ *m/z* 306.1336; found *m/z* 306.1331.

Diethyl 4-fluoro-1-methyl-1H-indole-2,3-dicarboxylate (3ga): yellow liquid, 40% yield (12 mg); IR (KBr, cm^{-1}) 2928, 2867, 1719, 1625, 1576, 1528, 1462, 1378, 1217, 1154, 1107, 1063, 733, 646, 624; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.32−7.28 (m,

1H), 7.17−7.15 (d, J = 8 Hz, 1H), 6.91−6.86 (m, 1H), 4.44−4.38 (m, 4H), 3.97 (s, 3H), 1.42−1.38 (t, J = 8 Hz, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.9, 161.3, 156.7 (d, J = 251.0 Hz), 139.9 (d, J = 10.0 Hz), 129.3, 125.7 (d, J = 8.0 Hz), 113.7 (d, J = 21.0 Hz), 111.5 (d, J = 3.0 Hz), 107.1 (d, J = 20.0 Hz), 106.3 (d, J = 4.0 Hz), 61.8, 61.3, 32.1, 14.1, 14.0; MS (EI, 70 eV): m/z = 293, 247, 220, 176, 148; HRMS (ESI) calcd for $C_{15}H_{16}FNO_4Na$ $[M + Na]^+$ m/z 316.0956; found m/z 316.0948.

Diethyl 6-fluoro-1-methyl-1H-indole-2,3-dicarboxylate (3gb): yellow liquid, 43% yield (13 mg); IR (KBr, cm^{-1}) 2928, 2858, 1708, 1622, 1536, 1468, 1382, 1252, 1221, 1177, 1092, 1032, 938, 828, 734, 613; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.08−8.05 (m, 1H), 7.07−7.02 (m, 2H), 4.50−4.45 (q, J = 8 Hz, 2H), 4.41−4.35 (q, J = 8 Hz, 2H), 3.79 (s, 3H), 1.45−1.42 (t, J = 8 Hz, 3H), 1.41−1.38 (t, J = 8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.9, 162.5, 161.0 (d, J = 241.0 Hz), 137.1 (d, J = 12.0 Hz), 135.2 (d, J = 3.0 Hz), 123.7 (d, J = 10.0 Hz), 121.8, 111.7, 111.5, 108.5, 96.5 (d, J = 26.0 Hz), 62.3, 60.4, 31.5, 14.4, 14.0; MS (EI, 70 eV): m/z = 293, 248, 220, 176, 148; HRMS (ESI) calcd for $C_{15}H_{17}FNO_4$ $[M + H]^+$ m/z 294.1136; found m/z 294.1140.

Diethyl 4-chloro-1-methyl-1H-indole-2,3-dicarboxylate (3ha): yellow solid, 25% yield (8 mg); mp 92-94 ^{o}C; IR (KBr, cm^{-1}) 2922, 2847, 1718, 1634, 1527, 1461, 1410, 1371, 1248, 1222, 1189, 1123, 1029, 938, 831, 777, 735; ^{1}H NMR (400 MHz, d^6-DMSO, ppm) δ 7.69−7.67 (m, 1H), 7.41−7.37 (m, 1H), 7.29−7.27 (m, 1H), 4.35−4.30 (m, 4H), 4.02 (s, 3H), 1.33−1.28 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, d^6-DMSO, ppm) δ 165.5, 160.5, 139.0, 127.1, 126.5, 125.8, 122.4, 121.0, 114.9,

111.2, 61.9, 61.6, 32.7, 14.3, 14.2; MS (EI, 70 eV): *m/z* = 309, 264, 236, 209, 191, 164; HRMS (ESI) calcd for $C_{15}H_{16}ClNO_4Na$ $[M + Na]^+$ *m/z* 332.0660; found *m/z* 332.0656.

Diethyl 6-chloro-1-methyl-1H-indole-2,3-dicarboxylate (3hb): yellow liquid, 23% yield (7 mg); IR (KBr, cm^{-1}) 2969, 2927, 2856, 1729, 1608, 1542, 1476, 1419, 1380, 1321, 1268, 1221, 1188, 1130, 1029, 991, 879, 837, 776, 731, 649; ^1H NMR (400 MHz, d^6-DMSO, ppm) δ 8.00−7.97 (d, J = 12 Hz, 1H), 7.85−7.84 (d, J = 4 Hz, 1H), 7.34−7.31 (dd, J = 8 Hz, 1H), 4.45−4.40 (q, J = 8 Hz, 2H), 4.31−4.26 (q, J = 8 Hz, 2H), 3.82 (s, 3H), 1.37−1.33 (t, J = 8 Hz, 3H), 1.32−1.29 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.7, 162.4, 137.2, 135.5, 130.5, 124.0, 123.5, 123.4, 110.2, 108.3, 62.4, 60.4, 31.5, 14.4, 14.1; MS (EI, 70 eV): *m/z* = 309, 264, 236, 209, 192, 164; HRMS (ESI) calcd for $C_{15}H_{16}ClNO_4Na$ $[M + Na]^+$ *m/z* 332.0660; found *m/z* 332.0664.

Diethyl 4-bromo-1-methyl-1H-indole-2,3-dicarboxylate (3ia): yellow solid, 35% yield (12 mg); mp 109-111 ^oC; IR (KBr, cm^{-1}) 2924, 2856, 1704, 1604, 1527, 1461, 1389, 1246, 1211, 1110, 1033, 910, 826, 730; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.39−7.34 (m, 2H), 7.23−7.19 (t, J = 8 Hz, 1H), 4.47−4.42 (q, J = 8 Hz, 2H), 4.41−4.36 (q, J = 8 Hz, 2H), 4.05 (s, 3H), 1.45−1.42 (t, J = 8 Hz, 3H), 1.41−1.37 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 166.2, 160.7, 138.9, 126.2, 126.1, 125.5, 123.1, 116.9, 115.3, 109.7, 61.8, 61.5, 32.2, 14.1, 14.0; MS (EI, 70 eV): *m/z* = 353, 310, 280, 253, 236, 209; HRMS (ESI) calcd for $C_{15}H_{17}BrNO_4$ $[M + H]^+$ *m/z* 354.0335; found *m/z* 354.0341.

Diethyl 6-bromo-1-methyl-1H-indole-2,3-dicarboxylate (3ib): yellow solid, 30% yield (11 mg); mp 101-103 ^{o}C; IR (KBr, cm^{-1}) 2976, 2927, 1717, 1594, 1528, 1459, 1411, 1383, 1223, 1187, 1111, 1028, 876, 773, 734; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.00−7.98 (d, J = 8 Hz, 1H), 7.54−7.53 (d, J = 4 Hz, 1H), 7.40−7.37 (dd, J = 8 Hz, 1H), 4.51−4.46 (q, J = 8 Hz, 2H), 4.40−4.35 (q, J = 8 Hz, 2H), 3.80 (s, 3H), 1.45−1.38 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 163.7, 162.4, 137.5, 135.4, 125.9, 124.2, 123.7, 118.0, 113.2, 108.2, 62.5, 60.4, 31.5, 14.4, 14.0; MS (EI, 70 eV): m/z = 353, 328, 280, 253, 236, 209; HRMS (ESI) calcd for $C_{15}H_{17}BrNO_4$ [M + H]$^{+}$ m/z 354.0335; found m/z 354.0337.

Diethyl 1,4-dimethyl-1H-indole-2,3-dicarboxylate (3ja): yellow liquid, 38% yield (11 mg); IR (KBr, cm^{-1}) 2987, 2928, 2855, 1712, 1605, 1527, 1466, 1409, 1372, 1243, 1208, 1157, 1053, 946, 859, 775, 745, 601; ^{1}H NMR (400 MHz, d^6-DMSO, ppm) δ 7.49−7.46 (d, J = 12 Hz, 1H), 7.31−7.27 (t, J = 8 Hz, 1H), 7.00−6.98 (d, J = 8 Hz, 1H), 4.35−4.28 (m, 4H), 3.96 (s, 3H), 2.45 (s, 3H), 1.33−1.28 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, d^6-DMSO, ppm) δ 166.7, 161.2, 138.1, 131.4, 127.3, 125.8, 123.2, 122.8, 114.7, 109.6, 61.7, 61.4, 32.2, 19.5, 14.4, 14.3; MS (EI, 70 eV): m/z = 289, 243, 216, 187, 171, 143; HRMS (ESI) calcd for $C_{16}H_{20}NO_4$ [M + H]$^{+}$ m/z 290.1387; found m/z 290.1393.

Diethyl 1,6-dimethyl-1H-indole-2,3-dicarboxylate (3jb): yellow liquid, 35% yield (10 mg); IR (KBr, cm^{-1}) 2980, 2929, 2856, 1711, 1528, 1466, 1409, 1383, 1244, 1211, 1155, 1101, 1053, 864, 812, 778, 746; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.00−7.98 (d, J = 8 Hz, 1H), 7.15 (s, 1H), 7.13−7.11 (d, J = 8 Hz, 1H), 4.50−4.44 (q, J = 8 Hz,

2H), 4.40−4.35 (q, *J* = 8 Hz, 2H), 3.81 (s, 3H), 2.51 (s, 3H), 1.45−1.42 (t, *J* = 8 Hz, 3H), 1.41−1.38 (t, *J* = 8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.3, 162.9, 137.3, 134.5, 134.1, 124.5, 123.3, 122.0, 109.9, 108.3, 62.2, 60.2, 31.3, 22.0, 14.4, 14.1; MS (EI, 70 eV): *m/z* = 289, 244, 216, 187, 171, 143; HRMS (ESI) calcd for $C_{16}H_{20}NO_4$ $[M + H]^+$ *m/z* 290.1387; found *m/z* 290.1389.

Diethyl 4-chloro-1,5-dimethyl-1H-indole-2,3-dicarboxylate (3ka): yellow solid, 23% yield (7 mg); mp 102-104 °C; IR (KBr, cm^{-1}) 2924, 2858, 1717, 1631, 1526, 1459, 1382, 1228, 1198, 1123, 1022, 868, 789, 699, 620; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.21−7.19 (d, *J* = 8 Hz, 1H), 7.17−7.15 (d, *J* = 8 Hz, 1H), 4.46−4.41 (q, *J* = 8 Hz, 2H), 4.40−4.34 (q, *J* = 8 Hz, 2H), 4.00 (s, 3H), 2.43 (s, 3H), 1.44−1.40 (t, *J* = 8 Hz, 3H), 1.40−1.36 (t, *J* = 8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 166.7, 160.8, 137.6, 128.6, 128.5, 125.9, 125.6, 122.1, 115.6, 108.6, 100.0, 61.7, 61.3, 32.0, 19.4, 14.1, 14.0; MS (EI, 70 eV): *m/z* = 323, 278, 250, 223, 205; HRMS (ESI) calcd for $C_{16}H_{19}ClNO_4$ $[M + H]^+$ *m/z* 324.0997; found *m/z* 324.0990.

Diethyl 6-chloro-1,5-dimethyl-1H-indole-2,3-dicarboxylate (3kb): yellow liquid, 20% yield (7 mg); IR (KBr, cm^{-1}) 2982, 2870, 1736, 1615, 1578, 1532, 1472, 1409, 1305, 1254, 1114, 1042, 952, 862, 791, 702, 610; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.98 (s, 1H), 7.38 (s, 1H), 4.50−4.45 (q, *J* = 8 Hz, 2H), 4.40−4.35 (q, *J* = 8 Hz, 2H), 3.78 (s, 3H), 2.49 (s, 3H), 1.45−1.38 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.9, 162.5, 135.8, 135.2, 131.3, 130.4, 124.3, 123.4, 110.4, 107.6, 62.4, 60.3, 31.5, 20.5, 14.4, 14.0; MS (EI, 70 eV): *m/z* = 323, 278, 250, 223, 205; HRMS (ESI) calcd for $C_{16}H_{19}ClNO_4$ $[M + H]^+$ *m/z* 324.0997; found *m/z* 324.1003.

Diethyl 4-bromo-1,5-dimethyl-1H-indole-2,3-dicarboxylate (3la): yellow solid, 27% yield (10 mg); mp 120-122 °C; IR (KBr, cm^{-1}) 2974, 2940, 1714, 1631, 1534, 1412, 1381, 1227, 1196, 1116, 1055, 885, 785, 696; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.24 (s, 1H), 7.24 (s, 1H), 4.47−4.42 (q, J = 8 Hz, 2H), 4.40−4.35 (q, J = 8 Hz, 2H), 4.03 (s, 3H), 2.48 (s, 3H), 1.45−1.41 (t, J = 8 Hz, 3H), 1.40−1.37 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 166.7, 160.8, 137.4, 131.1, 128.3, 125.7, 123.7, 116.8, 116.5, 109.4, 61.8, 61.4, 32.1, 22.5, 14.1, 14.0; MS (EI, 70 eV): *m/z* = 367, 322, 294, 251, 223, 83; HRMS (ESI) calcd for $C_{16}H_{19}BrNO_4$ $[M + H]^+$ *m/z* 368.0492; found *m/z* 368.0498.

Diethyl 6-bromo-1,5-dimethyl-1H-indole-2,3-dicarboxylate (3lb): yellow liquid, 24% yield (9 mg); IR (KBr, cm^{-1}) 2922, 2847, 1705, 1632, 1531, 1467, 1408, 1382, 1251, 1223, 1112, 1039, 904, 792, 703, 618; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.98 (s, 1H), 7.57 (s, 1H), 4.50−4.45 (q, J = 8 Hz, 2H), 4.40−4.35 (q, J = 8 Hz, 2H), 3.77 (s, 3H), 2.51 (s, 3H), 1.45−1.38 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.8, 162.5, 136.1, 135.2, 131.8, 124.9, 123.2, 121.3, 113.7, 107.5, 62.4, 60.3, 31.5, 23.3, 14.4, 14.1; MS (EI, 70 eV): *m/z* = 367, 322, 294, 251, 223, 183; HRMS (ESI) calcd for $C_{16}H_{19}BrNO_4$ $[M + H]^+$ *m/z* 368.0492; found *m/z* 368.0494.

Diethyl 6-cyano-1,5-dimethyl-1H-indole-2,3-dicarboxylate (3mb): yellow solid, 52% yield (16 mg); mp 86-88 °C; IR (KBr, cm^{-1}) 2926, 2855, 1738, 1708, 1627, 1530, 1476, 1381, 1298, 1249, 1180, 1101, 1022, 861, 787, 697; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.07 (s, 1H), 7.86 (s, 1H), 4.53−4.48 (q, J = 8 Hz, 2H), 4.40−4.36 (q, J = 8 Hz, 2H), 3.83 (s, 3H), 2.65 (s, 3H), 1.46−1.39 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz,

$CDCl_3$, ppm) δ 163.3, 162.1, 138.4, 134.4, 134.2, 128.8, 123.4, 118.9, 115.2, 108.4, 107.5, 62.7, 60.5, 31.6, 20.6, 14.4, 14.0; MS (EI, 70 eV): *m/z* = 314, 269, 241, 214, 196, 168; HRMS (ESI) calcd for $C_{17}H_{19}N_2O_4$ $[M + H]^+$ *m/z* 315.1339; found *m/z* 315.1339.

Diethyl 5-chloro-1,4-dimethyl-1H-indole-2,3-dicarboxylate (3na): yellow liquid, 30% yield (10 mg); IR (KBr, cm^{-1}) 2924, 2855, 1716, 1640, 1526, 1458, 1410, 1383, 1247, 1209, 1108, 1049, 1012, 906, 782, 700; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.36−7.34 (d, *J* = 8 Hz, 1H), 7.17−7.15 (d, *J* = 8 Hz, 1H), 4.45−4.35 (m, 4H), 4.01 (s, 3H), 2.55 (s, 3H), 1.43−1.40 (t, *J* = 8 Hz, 3H), 1.39−1.37 (t, *J* = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 167.3, 161.0, 136.7, 129.2, 127.3, 126.9, 124.0, 116.0, 109.1, 100.0, 61.6, 61.4, 31.9, 15.8, 14.1, 14.1; MS (EI, 70 eV): *m/z* = 323, 277, 250, 223, 221, 192; HRMS (ESI) calcd for $C_{16}H_{19}ClNO_4$ $[M + H]^+$ *m/z* 324.0997; found *m/z* 324.1000.

Diethyl 5-chloro-1,6-dimethyl-1H-indole-2,3-dicarboxylate (3nb): yellow liquid, 27% yield (9 mg); IR (KBr, cm^{-1}) 2925, 2855, 1704, 1656, 1529, 1464, 1381, 1218, 1181, 1102, 1043, 941, 869, 782, 734, 700; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.10 (s, 1H), 7.21 (s, 1H), 4.50−4.45 (q, *J* = 8 Hz, 2H), 4.41−4.35 (q, *J* = 8 Hz, 2H), 3.79 (s, 3H), 2.51 (s, 3H), 1.45−1.39 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.7, 162.6, 135.7, 135.3, 132.5, 129.6, 124.6, 122.2, 111.5, 107.6, 62.4, 60.3, 31.5, 21.1, 14.5, 14.1; MS (EI, 70 eV): *m/z* = 323, 278, 250, 223, 205; HRMS (ESI) calcd for $C_{16}H_{18}ClNO_4Na$ $[M + Na]^+$ *m/z* 346.0817; found *m/z* 346.0820.

Diethyl 5-bromo-1,4-dimethyl-1H-indole-2,3-dicarboxylate (3oa): yellow liquid,

30% yield (11 mg); IR (KBr, cm^{-1}) 2921, 2845, 1715, 1632, 1520, 1466, 1410, 1383, 1245, 1209, 1110, 1047, 1012, 886, 771, 678; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.52−7.50 (d, J = 8 Hz, 1H), 7.11−7.09 (d, J = 8 Hz, 1H), 4.45−4.35 (m, 4H), 4.01 (s, 3H), 2.59 (s, 3H), 1.43−1.40 (t, J = 8 Hz, 3H), 1.40−1.37 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 167.4, 160.9, 137.1, 131.2, 129.8, 126.4, 124.1, 117.7, 116.1, 109.5, 61.7, 61.4, 32.0, 18.9, 14.1, 14.1; MS (EI, 70 eV): m/z = 367, 323, 294, 251, 238, 214; HRMS (ESI) calcd for $C_{16}H_{19}BrNO_4$ $[M + H]^+$ m/z 368.0492; found m/z 368.0492.

Diethyl 5-bromo-1,6-dimethyl-1H-indole-2,3-dicarboxylate (3ob): yellow liquid, 26% yield (10 mg); IR (KBr, cm^{-1}) 2919, 2847, 1705, 1627, 1529, 1463, 1375, 1216, 1102, 1041, 907, 793, 737; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.30 (s, 1H), 7.22 (s, 1H), 4.50−4.45 (q, J = 8 Hz, 2H), 4.41−4.35 (q, J = 8 Hz, 2H), 3.79 (s, 3H), 2.54 (s, 3H), 1.45−1.39 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.7, 162.6, 136.2, 135.2, 133.8, 125.5, 125.0, 119.6, 111.4, 107.3, 62.4, 60.4, 31.5, 23.9, 14.4, 14.1; MS (EI, 70 eV): m/z = 367, 323, 294, 251, 238, 214; HRMS (ESI) calcd for $C_{16}H_{19}BrNO_4$ $[M + H]^+$ m/z 368.0492; found m/z 368.0488.

Diethyl 1,4,5-trimethyl-1H-indole-2,3-dicarboxylate (3pa): red solid, 34% yield (10 mg); mp 82-84 ^oC; IR (KBr, cm^{-1}) 2977, 2924, 2858, 1710, 1653, 1531, 1457, 1380, 1210, 1101, 1052, 906, 865, 798, 734; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.19−7.17 (d, J = 8 Hz, 1H), 7.12−7.10 (d, J = 8 Hz, 1H), 4.44−4.39 (q, J = 8 Hz, 2H), 4.39−4.34 (q, J = 8 Hz, 2H), 3.99 (s, 3H), 2.41 (s, 3H), 2.36 (s, 3H), 1.43−1.40 (t, J = 8 Hz, 3H), 1.39−1.36 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ

168.3, 161.3, 137.3, 129.2, 128.8, 128.7, 125.4, 123.6, 115.8, 107.5, 61.4, 61.1, 31.7, 19.6, 15.1, 14.2, 14.1; MS (EI, 70 eV): *m/z* = 303, 257, 228, 201, 185, 172; HRMS (ESI) calcd for $C_{17}H_{22}NO_4$ $[M + H]^+$ *m/z* 304.1543; found *m/z* 304.1547.

Diethyl 1,5,6-trimethyl-1H-indole-2,3-dicarboxylate (3pb): yellow liquid, 32% yield (10 mg); IR (KBr, cm^{-1}) 2928, 2855, 1709, 1582, 1526, 1460, 1408, 1372, 1229, 1153, 1096, 1024, 872, 795, 761; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.86 (s, 1H), 7.13 (s, 1H), 4.49−4.43 (q, *J* = 8 Hz, 2H), 4.40−4.35 (q, *J* = 8 Hz, 2H), 3.80 (s, 3H), 2.40 (s, 3H), 2.38 (s, 3H), 1.44−1.42 (t, *J* = 8 Hz, 3H), 1.40−1.38 (t, *J* = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.4, 163.0, 135.9, 133.9, 133.6, 131.6, 123.8, 122.1, 110.2, 107.9, 62.0, 60.1, 31.3, 20.7, 20.2, 14.4, 14.1; MS (EI, 70 eV): *m/z* = 303, 258, 230, 203, 185, 157; HRMS (ESI) calcd for $C_{17}H_{22}NO_4$ $[M + H]^+$ *m/z* 304.1543; found *m/z* 304.1548.

Diethyl 4,5-dimethoxy-1-methyl-1H-indole-2,3-dicarboxylate (3qa): yellow liquid, 33% yield (11 mg); IR (KBr, cm^{-1}) 2928, 2853, 1710, 1622, 1572, 1506, 1464, 1410, 1376, 1311, 1224, 1107, 1026, 966, 865, 784, 688; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.14−7.12 (d, *J* = 8 Hz, 1H), 7.05−7.03 (d, *J* = 8 Hz, 1H), 4.45−4.40 (q, *J* = 8 Hz, 2H), 4.39−4.34 (q, *J* = 8 Hz, 2H), 3.98 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H), 1.44−1.40 (t, *J* = 8 Hz, 3H), 1.39−1.36 (t, *J* = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 167.0, 161.0, 146.1, 142.4, 135.3, 125.8, 119.5, 116.3, 114.3, 105.6, 61.4, 61.2, 61.1, 58.2, 31.9, 14.2, 14.0; MS (EI, 70 eV): *m/z* = 335, 320, 290, 262, 246, 218; HRMS (ESI) calcd for $C_{17}H_{21}NO_6Na$ $[M + Na]^+$ *m/z* 358.1261; found *m/z* 358.1258.

Diethyl 5,6-dimethoxy-1-methyl-1H-indole-2,3-dicarboxylate (3qb): yellow solid,

35% yield (12 mg); mp 113-115 °C; IR (KBr, cm^{-1}) 2927, 2856, 1730, 1699, 1533, 1486, 1309, 1238, 1165, 1101, 1015, 951, 856, 783; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.55 (s, 1H), 6.77 (s, 1H), 4.47−4.42 (q, J = 8 Hz, 2H), 4.40−4.35 (q, J = 8 Hz, 2H), 3.97 (s, 3H), 3.97 (s, 3H), 3.83 (s, 3H), 1.44−1.42 (t, J = 8 Hz, 3H), 1.40−1.38 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.5, 162.7, 149.1, 147.3, 131.9, 131.7, 118.8, 108.6, 102.8, 92.5, 61.9, 60.2, 56.2, 56.2, 31.7, 14.4, 14.1; MS (EI, 70 eV): m/z = 335, 320, 290, 262, 246, 218; HRMS (ESI) calcd for $C_{17}H_{22}NO_6$ $[M + H]^+$ m/z 336.1442; found m/z 336.1448.

Diethyl 5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline-1,2-dicarboxylate (3r): yellow liquid, 50% yield (15 mg); IR (KBr, cm^{-1}) 2980, 2895, 1745, 1701, 1571, 1494, 1378, 1218, 1151, 1047, 1021, 938, 861, 794, 754, 671; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.86−7.84 (d, J = 8 Hz, 1H), 7.20−7.16 (t, J = 8 Hz, 1H), 7.06 −7.04 (d, J = 8 Hz, 1H), 4.49−4.44 (q, J = 8 Hz, 2H), 4.42−4.36 (q, J = 8 Hz, 2H), 4.30−4.28 (t, J = 4 Hz, 2H), 3.01−2.98 (t, J = 8 Hz, 2H), 2.27−2.22 (m, 2H), 1.44−1.39 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.5, 162.4, 134.1, 132.1, 124.0, 122.8, 122.8, 121.5, 119.8, 109.0, 62.0, 60.2, 43.9, 24.5, 22.7, 14.5, 14.1; MS (EI, 70 eV): m/z = 301, 255, 228, 200, 183, 155; HRMS (ESI) calcd for $C_{17}H_{20}NO_4$ $[M + H]^+$ m/z 302.1387; found m/z 302.1389.

Diethyl 8-methyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline-1,2-dicarboxylate (3s): yellow liquid, 28% yield (9 mg); IR (KBr, cm^{-1}) 2925, 2854, 1705, 1644, 1515, 1429, 1379, 1277, 1222, 1121, 1024, 862, 761, 694; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.63 (s, 1H), 6.89 (s, 1H), 4.48−4.42 (q, J = 8 Hz, 2H), 4.41−4.36 (q, J = 8 Hz, 2H),

4.29−4.26 (t, *J* = 8 Hz, 2H), 2.96−2.93 (t, *J* = 8 Hz, 2H), 2.45 (s, 3H), 2.25−2.19 (m, 2H), 1.44−1.39 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.6, 162.4, 132.6, 132.4, 131.7, 123.4, 122.5, 119.0, 108.5, 61.9, 60.1, 43.9, 24.4, 22.9, 21.9, 14.5, 14.1; MS (EI, 70 eV): *m*/*z* = 315, 269, 242, 214, 197, 169; HRMS (ESI) calcd for $C_{18}H_{21}NO_4Na$ $[M + Na]^+$ *m/z* 338.1363; found *m/z* 338.1369.

Diethyl 5-methyl-5H-[1,3]dioxolo[4,5-f]indole-6,7-dicarboxylate (3t): yellow liquid, 65% yield (21 mg); IR (KBr, cm^{-1}) 2927, 2856, 1701, 1523, 1473, 1407, 1309, 1231, 1182, 1081, 1037, 941, 859, 782, 721; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.47 (s, 1H), 6.78 (s, 1H), 6.00 (s, 2H), 4.47−4.41 (q, *J* = 8 Hz, 2H), 4.39−4.34 (q, *J* = 8 Hz, 2H), 3.78 (s, 3H), 1.43−1.37 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.3, 162.5, 147.1, 145.3, 132.6, 132.2, 119.9, 109.4, 101.2, 100.4, 90.5, 62.0, 60.3, 31.8, 14.4, 14.1; MS (EI, 70 eV): *m*/*z* = 319, 274, 246, 219, 172; HRMS (ESI) calcd for $C_{16}H_{17}NO_6Na$ $[M + Na]^+$ *m/z* 342.0948; found *m/z* 342.0956.

Diethyl 1-methyl-1H-pyrrolo[3,2-b]pyridine-2,3-dicarboxylate (3u): yellow liquid, 36% yield (10 mg); IR (KBr, cm^{-1}) 2974, 2922, 2852, 1735, 1631, 1523, 1460, 1383, 1301, 1093, 1049, 877, 718, 620; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.86 (s, 1H), 8.45−8.44 (d, *J* = 4 Hz, 1H), 8.02−8.01 (d, *J* = 4 Hz, 1H), 4.55−4.50 (q, *J* = 8 Hz, 2H), 4.42−4.37 (q, *J* = 8 Hz, 2H), 3.93 (s, 3H), 1.47−1.40 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.1, 162.1, 141.4, 138.4, 133.8, 130.5, 116.3, 107.1, 100.0, 62.8, 60.5, 31.7, 14.4, 14.0; MS (EI, 70 eV): *m*/*z* = 276, 231, 203, 176, 158; HRMS (ESI) calcd for $C_{14}H_{17}N_2O_4$ $[M + H]^+$ *m/z* 277.1183; found *m/z* 277.1184.

Diethyl 1-ethyl-1H-indole-2,3-dicarboxylate (3v): yellow liquid, 57% yield (17

mg); IR (KBr, cm^{-1}) 3065, 2982, 2875, 1754, 1702, 1534, 1427, 1377, 1345, 1259, 1204, 1157, 1107, 1037, 949, 856, 788, 753, 628; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.16−8.14 (m, 1H), 7.40−7.38 (m, 1H), 7.36−7.32 (m, 1H), 7.31−7.27 (m, 1H), 4.51−4.46 (q, J = 8 Hz, 2H), 4.41−4.36 (q, J = 8 Hz, 2H), 4.30−4.25 (q, J = 8 Hz, 2H), 1.45−1.39 (m, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.2, 163.0, 135.6, 134.7, 125.6, 124.2, 122.5, 122.5, 110.2, 107.7, 62.3, 60.2, 40.2, 15.5, 14.5, 14.1; MS (EI, 70 eV): *m*/*z* = 289, 244, 214, 170, 143, 114; HRMS (ESI) calcd for $C_{16}H_{20}NO_4$ $[M + H]^+$ *m/z* 290.1387; found *m/z* 290.1391.

Diethyl 1-isopropyl-1H-indole-2,3-dicarboxylate (3w): yellow liquid, 25% yield (8 mg); IR (KBr, cm^{-1}) 2979, 2927, 2854, 1735, 1703, 1533, 1426, 1373, 1349, 1203, 1107, 1077, 1019, 864, 790, 753; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.21−8.18 (m, 1H), 7.54−7.52 (m, 1H), 7.32−7.27 (m, 2H), 4.73−4.66 (m, 1H), 4.52−4.46 (q, J = 8 Hz, 2H), 4.40−4.34 (q, J = 8 Hz, 2H), 1.67 (s, 3H), 1.65 (s, 3H), 1.45−1.38 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 166.6, 164.1, 164.0, 136.0, 134.7, 126.2, 123.5, 122.6, 122.2, 111.9, 62.4, 60.0, 50.2, 21.6, 14.4, 14.0; MS (EI, 70 eV): *m*/*z* = 303, 258, 228, 211, 188, 170; HRMS (ESI) calcd for $C_{17}H_{22}NO_4$ $[M + H]^+$ *m/z* 304.1543; found *m/z* 304.1543.

Diethyl 1-ethyl-4-methyl-1H-indole-2,3-dicarboxylate (3xa): yellow liquid, 30% yield (9 mg); IR (KBr, cm^{-1}) 2980, 2923, 2870, 1713, 1616, 1528, 1467, 1374, 1278, 1205, 1158, 1057, 941, 862, 776, 747, 610; ^1H NMR (400 MHz, d^6-DMSO, ppm) δ 7.52−7.50 (d, J = 8 Hz, 1H), 7.30−7.27 (m, 1H), 7.00−6.98 (d, J = 8 Hz, 1H), 4.53−4.48 (q, J = 8 Hz, 2H), 4.36−4.28 (m, 4H), 2.44 (s, 3H), 1.33−1.28 (m, 9H);

$^{13}C\{^{1}H\}$ NMR (100 MHz, d^6-DMSO, ppm) δ 166.7, 161.1, 137.0, 131.6, 126.5, 125.9, 123.2, 123.0, 115.0, 109.4, 61.7, 61.4, 29.5, 19.5, 15.9, 14.4, 14.3; MS (EI, 70 eV): *m/z* = 303, 257, 228, 210, 184, 157; HRMS (ESI) calcd for $C_{17}H_{22}NO_4$ $[M + H]^+$ *m/z* 304.1543; found *m/z* 304.1548.

Diethyl 1-ethyl-6-methyl-1H-indole-2,3-dicarboxylate (3xb): yellow liquid, 33% yield (10 mg); IR (KBr, cm^{-1}) 3054, 2981, 2866, 2742, 1712, 1606, 1529, 1427, 1374, 1203, 1155, 1117, 962, 814, 778, 747; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01−7.99 (d, *J* = 8 Hz, 1H), 7.16 (s, 1H), 7.12−7.10 (d, *J* = 8 Hz, 1H), 4.50−4.44 (q, *J* = 8 Hz, 2H), 4.40−4.35 (q, *J* = 8 Hz, 2H), 4.27−4.22 (q, *J* = 8 Hz, 2H), 2.50 (s, 3H), 1.44−1.38 (m, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.3, 163.0, 136.1, 134.3, 133.7, 124.3, 123.5, 122.1, 109.9, 108.0, 62.1, 60.1, 40.0, 21.9, 15.4, 14.4, 14.0; MS (EI, 70 eV): *m/z* = 303, 257, 228, 210, 184, 157; HRMS (ESI) calcd for $C_{17}H_{22}NO_4$ $[M + H]^+$ *m/z* 304.1543; found *m/z* 304.1545.

Diethyl 1-allyl-1H-indole-2,3-dicarboxylate (3y): yellow liquid, 38% yield (11 mg); IR (KBr, cm^{-1}) 2981, 2870, 1739, 1694, 1572, 1496, 1379, 1232, 1152, 1049, 927, 862, 793, 753, 698, 618; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.16−8.13 (m, 1H), 7.35−7.28 (m, 3H), 5.99−5.90 (m, 1H), 5.21−5.18 (m, 1H), 5.07−5.02 (m, 1H), 4.88−4.86 (m, 2H), 4.48−4.42 (q, *J* = 8 Hz, 2H), 4.42−4.36 (q, *J* = 8 Hz, 2H), 1.43−1.39 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.1, 162.8, 136.2, 134.6, 132.3, 125.5, 124.4, 122.6, 122.4, 117.7, 110.5, 62.3, 60.3, 47.2, 14.4, 14.0; MS (EI, 70 eV): *m/z* = 301, 255, 228, 210, 182, 154; HRMS (ESI) calcd for $C_{17}H_{19}NO_4Na$ $[M + Na]^+$ *m/z* 324.1206; found *m/z* 324.1203.

Dimethyl 1-methyl-1H-indole-2,3-dicarboxylate (3z): yellow liquid, 57% yield (14 mg); IR (KBr, cm^{-1}) 3001, 2950, 2845, 1703, 1608, 1532, 1470, 1378, 1249, 1217, 1158, 1107, 1025, 928, 840, 789, 753, 636; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.13−8.11 (d, J = 8 Hz, 1H), 7.38−7.36 (m, 2H), 7.32−7.28 (m, 1H), 4.02 (s, 3H), 3.93 (s, 3H), 3.84 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.6, 163.3, 136.8, 134.7, 125.3, 124.5, 122.6, 122.4, 110.2, 108.1, 53.0, 51.5, 31.4; MS (EI, 70 eV): m/z = 247, 216, 186, 157, 129; HRMS (ESI) calcd for $C_{13}H_{13}NO_4Na$ $[M + Na]^+$ m/z 270.0737; found m/z 270.0743.

Diethyl 2-(methyl(phenyl)amino)maleate (A): yellow liquid; IR (KBr, cm^{-1}) 2985, 2926, 2853, 1741, 1656, 1597, 1462, 1376, 1248, 1184, 1101, 1046, 1028, 859, 809, 702, 615; ^1H NMR (400 MHz, d^6-DMSO, ppm) δ 7.42−7.37 (m, 2H), 7.31−7.27 (m, 1H), 7.23−7.20 (m, 2H), 4.78 (s, 1H), 4.01−3.93 (m, 4H), 3.18 (s, 3H), 1.16−1.13 (t, J = 8 Hz, 3H), 1.00−0.96 (t, J = 8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 167.3, 164.7, 154.2, 144.7, 129.3, 127.4, 126.8, 88.5, 61.7, 59.4, 40.8, 14.4, 13.6; MS (EI, 70 eV): m/z = 277, 232, 204, 176, 158, 131; HRMS (ESI) calcd for $C_{15}H_{20}NO_4$ $[M + H]^+$ m/z 278.1387; found m/z 278.1391.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.

^1H and ^{13}C spectra of all synthesized compounds (PDF)

AUTHOR INFORMATION

Corresponding Author

* E-mail: guoweigw@126.com

* E-mail: fanxl2008@gnnu.edu.cn

* E-mail: zhenglvyin@126.com

Author Contributions

† Wei Guo and Kailiang Tao contributed equally.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (21602031, 21662002 and 21867001), and the Jiangxi Natural Science Foundation (20171BAB203010).

REFERENCES

(1) (a) Lima, C. G. S.; Lima, T. de M.; Duarte, M.; Jurberg, I. D.; Paixao, M. W. Organic Synthesis Enabled by Light-Irradiation of EDA Complexes: Theoretical Background and Synthetic Applications. *ACS Catal.* **2016**, *6*, 1389–1407. (b) Rosokha, S. V.; Kochi, J. K. Fresh Look at Electron-Transfer Mechanisms via the Donor/Acceptor Bindings in the Critical Encounter Complex. A*cc. Chem. Res.* **2008,**

41, 641–653. (c) Fernández-Alvarez, V. M.; Nappi, M.; Melchiorre, P.; Maseras, F. Computational Study with DFT and Kinetic Models on the Mechanism of Photoinitiated Aromatic Perfluoroalkylations. *Org. Lett.* **2015**, *17*, 2676–2679. (d) Lin, L.; Bai, X.; Ye, X.; Zhao, X.; Tan, C.-H.; Jiang, Z. Organocatalytic Enantioselective Protonation for Photoreduction of Activated Ketones and Ketimines Induced by Visible Light. *Angew. Chem. Int. Ed.* **2017**, *56*, 13842–13846. (e) Spell, M. L.; Deveaux, K.; Bresnahan, C. G.; Bernard, B. L.; Sheffield, W.; Kumar, R.; Ragains, J. R. A Visible-Light-Promoted O-Glycosylation with a Thioglycoside Donor. *Angew. Chem. Int. Ed.* **2016,** *55*, 6515–6519.

(2) (a) Nappi, M.; Bergonzini, G.; Melchiorre, P. Metal-Free Photochemical Aromatic Perfluoroalkylation of a-Cyano Arylacetates. *Angew. Chem., Int. Ed.* **2014**, *53*, 4921–4925. (b) Arceo, E.; Bahamonde, A.; Bergonzini, G.; Melchiorre, P. Enantioselective direct α-alkylation of cyclic ketones by means of photo-organocatalysis. Ch*em. Sci.* **2014**, *5*, 2438–2442. (c) Tobisu, M.; Furukawa, T.; Chatani, N. Visible Light-mediated Direct Arylation of Arenes and Heteroarenes Using Diaryliodonium Salts in the Presence and Absence of a Photocatalyst. *Chem. Lett.* **2013,** *42*, 1203–1205. (d) Jiang, H.; He, Y.; Cheng, Y.; Yu, S. Radical Alkynyltrifluoromethylation of Alkenes Initiated by an Electron Donor−Acceptor Complex. *Org. Lett.* **2017**, *19*, 1240–1243. (e) Hu, R.-B.; Sun, S.; Su, Y. Visible-Light-Induced Carbo-2-pyridylation of Electron-Deficient Alkenes with Pyridinium Salts. *Angew. Chem., Int. Ed.* **2017**, *56*, 10877–10880.

(3) (a) Li, Y.; Miao, T.; Li, P.; Wang, L. Photo-Driven Synthesis of

C6-Polyfunctionalized Phenanthridines from Three-Component Reactions of Isocyanides, Alkynes, and Sulfinic Acids by Electron Donor−Acceptor Complex. *Org. Lett.* **2018**, *20*, 1735–1739. (b) Cheng, Y.; Yuan, X.; Ma, J.; Yu, S. Direct Aromatic C-H Trifluoromethylation via an Electron-Donor–Acceptor Complex. *Chem. Eur. J.* **2015**, *21*, 8355–8359.

(4) (a) Arceo, E.; Jurberg, I. D.; Álvarez-Fernández, A.; Melchiorre, P. Photochemical Activity of a Key Donor-acceptor Complex can Drive Stereoselective Catalytic α-Alkylation of Aldehydes. *Nat. Chem.* **2013**, *5*, 750-756. (b) Gualandi, A.; Marchini, M.; Mengozzi, L.; Natali, M.; Lucarini, M.; Ceroni, P.; Cozzi, P. G. Organocatalytic Enantioselective Alkylation of Aldehydes with $[Fe(bpy)_3]Br_2$ Catalyst and Visible Light. *ACS Catal.* **2015**, *5*, 5927–5931. (c) Yang, C.; Zhang, W.; Li, Y.-H.; Xue, X.-S., Li, X.; Cheng, J.-P. Origin of Stereoselectivity of the Photoinduced Asymmetric Phase-Transfer-Catalyzed Perfluoroalkylation of *β*-Ketoesters. *J. Org. Chem.* **2017**, *82*, 9321–9327. (d) Zhu, Y.; Zhang, L.; Luo, S. Asymmetric α-Photoalkylation of β-Ketocarbonyls by Primary Amine Catalysis: Facile Access to Acyclic All-Carbon Quaternary Stereocenters. *J. Am. Chem. Soc.* **2014**, *136*, 14642–14645.

(5) (a) Dadashpour, S.; Emami, S. Indole in the Target-based Design of Anticancer Agents: A Versatile Scaffold with Diverse Mechanism. *Eur. J. Med. Chem.* **2018**, *150*, 9–29. (b) Singh, A. K.; Raj, V.; Saha, S. Indole-fused Azepines and Analogues as Anticancer Lead Molecules: Privileged Dindings and Future Directions. *Eur. J. Med. Chem.* **2017**, *142*, 244–265. (c) Kochanowska-Karamyan, A. J.; Hamann, M. T.

Marine Indole Alkaloids: Potential New Drug Leads for the Control of Depression and Anxiety. *Chem. Rev.* **2010**, *110*, 4489–4497. (d) Lee, C. W.; Lee, J. Y. Above 30% External Quantum Effi ciency in Blue Phosphorescent Organic Light-Emitting Diodes Using Pyrido[2,3-b]indole Derivatives as Host Materials. *Adv. Mater.* **2013**, *25*, 5450–5454. (e) Yang, J.; Wang, C.; Xu, S.; Zhao, J. Ynamide-Mediated Thiopeptide Synthesis. *Angew. Chem., Int. Ed.* **2019**, *58*, 1382–1386.

(6) (a) Ji, X.; Huang, H.; Wu, W.; Li, X.; Jiang, H. Palladium-Catalyzed Oxidative Coupling of Aromatic Primary Amines and Alkenes under Molecular Oxygen: Stereoselective Assembly of (*Z*)-Enamines. *J. Org. Chem.* **2013**, *78*, 11155–11162. (b) Chen, J.; Chang, D.; Xiao, F.; Deng, G.-J. Three-Component Ordered Annulation of Amines, Ketones, and Nitrovinylarenes: Access to Fused Pyrroles and Substituted Indoles under Metal-Free Conditions. *J. Org. Chem.* **2019**, *84*, 568–578. (c) Liu, Y.-Y.; Yu, X.-Y.; Chen, J.-R.; Qiao, M.-M.; Qi, X.; Shi, D.-Q.; Xiao, W.-J. Visible-Light-Driven Aza-ortho-quinone Methide Generation for the Synthesis of Indoles in a Multicomponent Reaction. *Angew. Chem., Int. Ed.* **2017**, *56*, 9527–9531. (d) Lian, X.-L.; Ren, Z.-H.; Wang, Y.-Y.; Guan, Z.-H. Palladium-Catalyzed Oxidative Cyclization of Tertiary Enamines for Synthesis of 1,3,4-Trisubstituted Pyrroles and 1,3-Disubstituted Indoles. *Org. Lett.* **2014**, *16*, 3360–3363. (e) Xia, X.-D.; Xuan, J.; Wang, Q.; Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. Synthesis of 2-Substituted Indoles through Visible Light-Induced Photocatalytic Cyclizations of Styryl Azides. *Adv. Synth. Catal.* **2014**, *356*, 2807–2812.

(7) (a) Hao, W.; Geng, W.; Zhang, W.-X.; Xi, Z. Palladium-Catalyzed One-Pot

Three- or Four-Component Coupling of Aryl Iodides, Alkynes, and Amines through C-N Bond Cleavage: Efficient Synthesis of Indole Derivatives. *Chem. Eur. J.* **2014**, *20*, 2605–2612. (b) Geng, W.; Zhang, W.-X.; Hao, W.; Xi, Z. Cyclopentadiene-Phosphine/Palladium Catalyzed Cleavage of CN Bonds in Secondary Amines: Synthesis of Pyrrole and Indole Derivatives from Secondary Amines and Alkenyl or Aryldibromides. *J. Am. Chem. Soc.* **2012**, *134*, 20230–20233. (c) Youn, S. W.; Ko, T. Y. Metal-Catalyzed Synthesis of Substituted Indoles. *Asian J. Org. Chem.* **2018**, *7*, 1467–1487. (d) Ackermann, L. General and Efficient Indole Syntheses Based on Catalytic Amination Reactions. *Org. Lett.* **2005**, *7*, 439–442. (e) Weng, W.-Z.; Zhang, B. Mild and Efficient Synthesis of Indoles and Isoquinolones via a Nickel-Catalyzed Larock-type Heteroannulation Reaction. *Org. Biomol. Chem.* **2018**, *16*, 3983–3988. (f) Kumar, I.; Kumar, R.; Sharma, U. Recent Advances in the Regioselective Synthesis of Indoles via C–H Activation/Functionalization. *Synthesis* **2018**, *50*, 2655–2677.

(8) (a) Zhang, P.; Xiao, T.; Xiong, S.; Dong, X.; Zhou, L. Synthesis of 3-Acylindoles by Visible-Light Induced Intramolecular Oxidative Cyclization of *o*-Alkynylated N,N-Dialkylamines. *Org. Lett.* **2014**, *16*, 3264–3267. (b) Zhu, S.; Das, A.; Bui, L.; Zhou, H.; Curran, D. P.; Rueping, M. The Oxygen Switch in Visible-Light Photoredox Catalysis: Radical Additions and Cyclizations and Unexpected C-C-Bond Cleavage Reactions. *J. Am. Chem. Soc.* **2013**, *135*, 1823–1829. (c) Kohls, P.; Jadhav, D.; Pandey, G.; Reiser, O. Visible Light Photoredox Catalysis: Generation and Addition of N-Aryltetrahydroisoquinoline-Derived R-Amino Radicals to Michael

Acceptors. *Org. Lett.* **2012**, *14*, 672–675. (d) Yuan, X.; Wu, X.; Dong, S.; Wu, G.; Ye, J. Bronsted Acid Cocatalysis in Photocatalytic Intramolecular Coupling of Tertiary Amines: Efficient Synthesis of 2-Arylindols. *Org. Biomol. Chem.* **2016**, *14*, 7447–7450. (e) Guo, W.; Tan, W.; Zhao, M.; Zheng, L.; Tao, K.; Chen, D.; Fan, X. Direct Photocatalytic S−H Bond Cyanation with Green "CN" Source. *J. Org. Chem.* **2018**, *83*, 6580–6588. (f) Guo, W.; Tao, K.; Tan, W.; Zhao, M.; Zheng, L.; Fan, X. Recent Advances in Photocatalytic C-S/P-S Bonds Formation via the Generation of Sulfur Centered Radicals and Functionalization. *Org. Chem. Front.* **2019**, *6*, 2048–2066. (g) Guo, W.; Tan, W.; Zhao, M.; Tao, K.; Zheng, L.-Y.; Wu, Y.; Chen, D.; Fan, X.-L. Photocatalytic Direct C–S Bond Formation: Facile Access to 3-Sulfenylindoles via Metal-Free C-3 Sulfenylation of Indoles with Thiophenols. *RSC Adv.* **2017**, *7*, 37739–37742. (h) Guo, W.; Zhao, M.; Tan, W.; Zheng, L.; Tao, K.; Fan, X. Developments towards Synthesis of *N*-heterocycles from Amidines via C–N/C–C Bond Formation. *Org. Chem. Front.* **2019**, *6*, 2120–2141.

(9) Sagadevan, A.; Ragupathi, A.; Hwang, K. H. Photoinduced Copper-Catalyzed Regioselective Synthesis of Indoles: Three-Component Coupling of Arylamines, Terminal Alkynes, and Quinones. *Angew. Chem., Int. Ed.* **2015**, *54*, 13896–13901.

(10) Kim, H. J.; Fabry, D. C.; Mader, S.; Rueping, M. Photoredox/Rhodium Catalysis in C–H Activation for the Synthesis of Nitrogen Containing Heterocycles. *Org. Chem. Front.* **2019**, *6*, 2319–2323.

(11) (a) Guo, W.; Tao, K.; Zheng, L.; Zhao, M.; Tan, W.; Cai, L.; Xie, Z.; Chen, D.; Fan, X. Visible Light-Promoted Three-Component Coupling Annulation: Synthesis of

2-Iminothiazolidin-4-ones via in-situ Formed Electron Donor-Acceptor Complexes. *J. Org. Chem.* **2019**, *84*, 6448–6458. (b) Guo, W.; Zhao, M.; Tan, W.; Zheng, L.; Tao, K.; Liu, L.; Wang, X.; Chen, D.; Fan, X. Visible Light-Promoted Three-Component Tandem Annulation for the Synthesis of 2-Iminothiazolidin-4-ones. *J. Org. Chem.* **2018**, *83*, 1402–1413.

(12) (a) Kandukuri, S. R.; Bahamonde, A.; Chatterjee, I.; Jurberg, I. D.; Escudero-Adán, E. C.; Melchiorre, P. Expedient Iron-Catalyzed C-H Allylation/Alkylation by Triazole Assistance with Ample Scope. *Angew. Chem., Int. Ed.* **2015**, *54*, 1485–1489. (b) Dohi, T.; Ito, M.; Yamaoka, N.; Morimoto, K.; Fujioka, H.; Kita, Y. Unusual ipso Substitution of Diaryliodonium Bromides Initiated by a Single-Electron-Transfer Oxidizing Process. *Angew. Chem. Int. Ed.* **2010**, *49*, 3334–3337. (c) Hubig, S. M.; Bockman, T. M.; Kochi, J. K. Optimized Electron Transfer in Charge-Transfer Ion Pairs. Pronounced Inner-Sphere Behavior of Olefin Donors. *J. Am. Chem. Soc.* **1996**, *118*, 3842–3851.

(13) (a) Davies, J.; Booth, S. G.; Essafi, S.; Dryfe, R. A. W.; Leonori, D. Visible-Light-Mediated Generation of Nitrogen-Centered Radicals: Metal-Free Hydroimination and Iminohydroxylation Cyclization Reactions. *Angew. Chem., Int. Ed.* **2015**, *54*, 14017–14021. (b) Silvi, M.; Arceo, E.; Jurberg, I. D.; Cassani, C.; Melchiorre, P. Enantioselective Organocatalytic Alkylation of Aldehydes and Enals Driven by the Direct Photoexcitation of Enamines. *J. Am. Chem. Soc.* **2015**, *137*, 6120–6123. (c) Böhm, A.; Bach, T. Radical Reactions Induced by Visible Light in Dichloromethane Solutions of Henig's Base: Synthetic Applications and Mechanistic

Observations. *Chem. Eur. J.* **2016**, *22*, 15921−15928. (d) Zhu, M.; Zhou, K.; Zhang, X.; You, S.-L. Visible-Light-Promoted Cascade Alkene Trifluoromethylation and Dearomatization of Indole Derivatives via Intermolecular Charge Transfer. *Org. Lett.* **2018**, *20*, 4379–4383. (e) Sun, J.; He, Y.; An, X.-D.; Zhang, X.; Yu, L.; Yu, S. Visible-Light-Induced Iminyl Radical Formation via Electron-Donor Acceptor Complexes: A Photocatalyst-Free Approach to Phenanthridines and Quinolines. *Org. Chem. Front.* **2018**, *5*, 977–981.

(14) (a) Marzo, L.; Wang, S.; König, B. Visible-Light-Mediated Radical Arylation of Anilines with Acceptor-Substituted (Hetero)aryl Halides. *Org. Lett.* **2017**, *19*, 5976–5979. (b) Zhang, H.-H.; Yu, S. Visible-Light-Induced Radical Acylation of Imines with α-Ketoacids Enabled by Electron-Donor-Acceptor Complexes. *Org. Lett.* **2019**, *21*, 3711–3715. (c) Wang, R.; Wang, L.; Xu, Q.; Ren, B.-Y.; Liang, F. Visible-Light-Promoted [5+1] Annulation Initiated by Electron-Donor-Acceptor Complexes: Synthesis of Perfluoroalkyl-s-Triazines. *Org. Lett.* **2019**, *21*, 3072–3076.

(15) (a) Zhang, J.; Li, Y.; Xu, R.; Chen, Y. Donor–Acceptor Complex Enables Alkoxyl Radical Generation for Metal-Free $C(sp^3)$–$C(sp^3)$ Cleavage and Allylation/Alkenylation. *Angew. Chem. Int. Ed.* **2017**, *56*, 12619-12623. (b) Cheng, Y.; Yu, S. Hydrotrifluoromethylation of Unactivated Alkenes and Alkynes Enabled by an Electron-Donor-Acceptor Complex of Togni's Reagent with a Tertiary Amine. *Org. Lett.* **2016**, *18*, 2962–2965.

(16) Wu, C.-J.; Meng, Q.-Y.; Lei, T.; Zhong, J.-J.; Liu, W.-Q.; Zhao, L.-M.; Li, Z.-J.; Chen, B.; Tung, C.-H.; Wu, L.-Z. An Oxidant-Free Strategy for Indole Synthesis via

Intramolecular C-C Bond Construction under Visible Light Irradiation. *ACS Catal.* **2016**, *6*, 4635-4639.

(17) (a) Liu, J.-L.; Zhu, Z.-F.; Liu, F. Oxycyanation of Vinyl Ethers with 2,2,6,6-Tetramethyl-*N*-oxopiperidinium Enabled by Electron Donor-Acceptor Complex. *Org. Lett.* **2018**, *20*, 720–723. (b) Hilinski, E. F.; Masnovi, J. M.; Amatore, C.; Kochi, J. K.; Rentzepis, P. M. Charge-Transfer Excitation of Electron Donor-Acceptor Complexes. Direct Observation of Ion Pairs by Time-Resolved Picosecond Spectroscopy. *J. Am. Chem. Soc.* **1983**, *105*, 6167–6168. (c) Papadopulos, G. N.; Voutyritsa, E.; Kaplaneris, N.; Kokotos, C. G. Green Photo-Organocatalytic C-H Activation of Aldehydes: Selective Hydroacylation of Electron-Deficient Alkenes. *Chem. Eur. J.* **2018**, *24*, 1726−1731. (d) Hsu, C.-W.; Sundén, H. α-Aminoalkyl Radical Addition to Maleimides via Electron Donor-Acceptor Complexes. *Org. Lett.* **2018**, *20*, 2051–2054.

(18) The intermediate **A** was detected by GC-MS. (see the Supporting Information for details)

(19) The intermediate **D** was detected by GC-MS. (see the Supporting Information for details)

(20) Quint, V.; Morlet-Savary, F.; Lohier, J.-F.; Lalevée, J.; Gaumont, A.-C.; Lakhdar, S. Metal-Free, Visible Light-Photocatalyzed Synthesis of Benzo[*b*]phosphole Oxides: Synthetic and Mechanistic Investigations. *J. Am. Chem. Soc.* **2016**, *138*, 7436–7441.

(21) Bruneau-Voisine, A.; Wang, D.; Dorcet, V.; Roisnel, T.; Darcel, C.; Sortais, J.-B. Mono-N-methylation of Anilines with Methanol Catalyzed by a Manganese

Pincer-Complex. *Journal of Catalysis.* **2017**, *347*, 57–62.

(22) Liang, Y.; Ning, J. Cationic Cobalt (III) Catalyzed Indole Synthesis: The RegioselectiveIntermolecular Cyclization of *N*-Nitrosoanilines and Alkynes. *Angew. Chem. Int. Ed.* **2016**, *55*, 4035–4039.