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可见光诱导的新型官能化芳基异腈化合物的二氟烷基化环化反应

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摘要 报道了一种新设计的功能化芳基异腈化合物与市售 CF_2 前体的可见光催化的二氟烷基化反应. 在温和的条件下, 通过串联的自由基加成/环化过程, 构建了一系列含 CF_2 的吲哚-1,2-稠二氮杂环酮. 该反应不仅生成了一类多环吲哚稠七元氮杂环, 而且拓宽了官能化异腈化合物的反应类型.

关键词 官能化芳基异腈; 自由基环化; 二氟烷基化; 吲哚稠七元氮杂环

Visible-Light-Induced Difluoroalkylated Cyclization of Novel Functionalized Aromatic Isocyanides

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Abstract In this study, a visible-light photoredox-catalyzed difluoroalkylation of newly designed functionalized aromatic isocyanides with commercially available CF_2 precursors was reported. A series of CF_2-containing indole-1,2-fused diazepanones were constructed in cascade reaction through a sequence of radical addition/cyclization processes under mild conditions. This reaction not only generated a class of polycyclic indole fused seven-membered nitrogen heterocycles but also expanded the reactions of functionalized isocyanides.

Keywords functionalized aromatic isocyanides; radical cyclization; difluoroalkylation; indole fused seven-membered nitrogen heterocycles

1 Introduction

The polycyclic indole fused seven-membered nitrogen heterocycles represent an intriguing structural motif that widely exists in numerous pharmaceutical molecules and natural products.[1] As shown in Figure 1, these compounds have been reported to show antihypertensive, antiallergic, anti-hepatitis C virus and antitumor activities.[2] Undoubtedly, the development of synthetic methods is of great significance in medicinal chemistry and drug discovery. However, the construction of these fascinating frameworks has rarely been reported,[3] which is possibly due to their unfavorable transannular interactions.[4] Therefore, the development of novel strategies for the efficient synthesis of these polycyclic indole scaffolds is in strong demand.

Isocyanides, with unique structures and reactivities, have been applied as versatile synthons to construct various *N*-heterocycles via multicomponent,[5] transition-metal-catalyzed annulations,[6] and radical cyclization reactions.[7] Notably, as an excellent radical acceptor, functionalized isocyanides can be utilized to easily construct *N*-heterocycles because of the high reactivity of imidoyl radicals formed *in situ*, which promotes subsequent cascade reactions. Given the diversity of products and reactions, Ogawa,[8] Chatani,[9] Studer,[10] Alabugin,[11] Zhu,[12] Yu,[13] Xu,[14] Ji,[15] and others[16] have designed and prepared various functionalized aromatic isocyanides for the construction of *N*-heterocycles. Though the new functionalized isocyanides have been widely employed in the construction of five- and six-membered *N*-heterocycles, few

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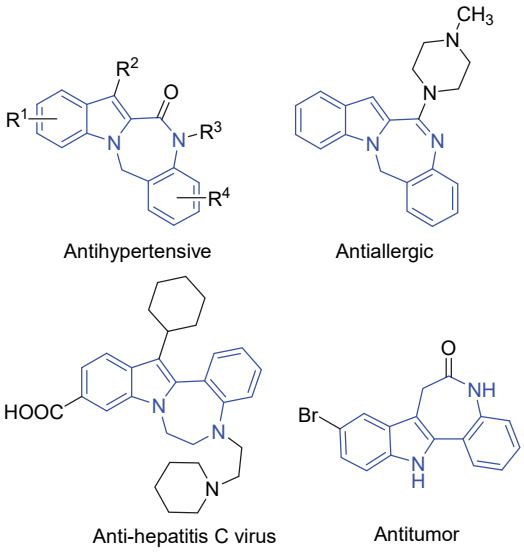
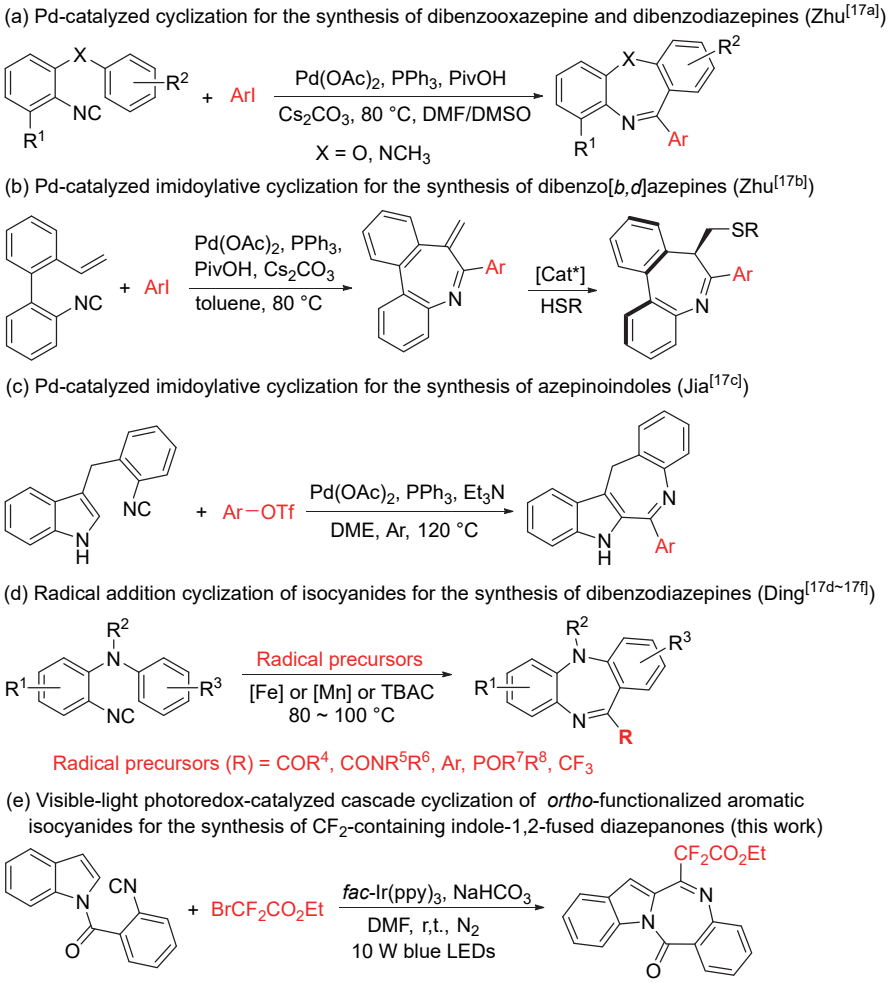


Figure 1 Representative bioactive molecules containing indole-fused seven-membered nitrogen heterocyclic skeletons

studies have been carried out on the synthesis of seven-membered *N*-heterocycles by the cascade cyclization of isocyanides.[17] Zhu group[17a-17b] developed Pd-catalyzed C(sp^2)—H imidoylative annulation of aryl iodides and 1-isocyano-2-phenoxybenzene, 2-isocyano-*N*-methyl-*N*-phenylaniline and 2-isocyano-2'-vinyl-1,1'-biphenyl to construct dibenzooxazepine, dibenzodiazepine and dibenzo[*b*,*d*]azepine skeletons (Schemes 1a, 1b). Notably, 7-methylene-6-aryl-7*H*-dibenzo[*b*,*d*]azepines as Michael acceptors reacted with aryl thiols to generate 7-[(arylthio)-methyl]-7*H*-dibenzo[*b*,*d*]azepines with good to excellent *ee* via chiral phosphoric acid (CPA) catalysis.[17b] Jia and coworkers[17c] disclosed the Pd-catalyzed C—H imidoylative cross-coupling process of 3-(2-isocyanobenzyl)-1*H*-indol and aryl trifluoromethanesulfonates to provide benzazepinoindoles (Scheme 1c). Recently, Ding's group[17d-17f] reported a general and practical synthesis of 11-functionalized dibenzodiazepines via radical cascade cyclization of functionalized isocyanides (Scheme 1d). These reports have inspired us to develop new functionalized isocyanides for the synthesis of seven-membered *N*-heterocycles.

The introduction of difluoromethyl groups into organic molecules leads to dramatic changes in their physicochemical properties, thereby enhancing their metabolic stability, lipophilicity, and biopotency.[18] In particular, difluoromethylation reactions for the structural modifica-



Scheme 1 Synthesis of seven-membered nitrogen heterocycles from functionalized isocyanides

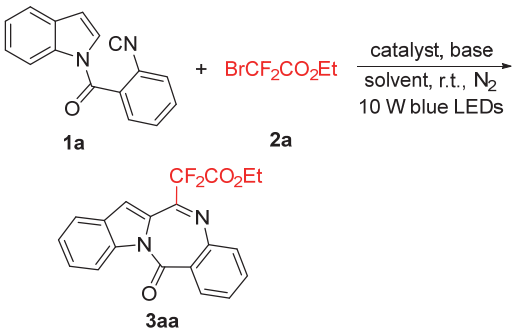
tion of *N*-heterocycles have attracted great attention in the field of pharmaceutical, agrochemical, and material sciences.[19] Among these difluorinated reagents, ethyl 2-bromo-2,2-difluoroacetate ($BrCF_2CO_2Et$) is an extremely appealing difluoroalkyl radical precursor, which is due to its commercial availability, low toxicity, and inexpensive cost. As part of our interest in difluoroalkylation reactions,[20] the synthesis of a newly designed class of functionalized aromatic isocyanides and their radical cascade cyclization with $BrCF_2CO_2Et$ were described to effectively construct CF_2-containing indole-1,2-fused diazepanones via visible-light photoredox catalysis (Scheme 1e).

2 Results and discussion

To begin our study, (1*H*-indol-1-yl)(2-isocyanophenyl)-methanone (**1a**) was selected to react with ethyl 2-bromo-2,2-difluoroacetate (**2a**) to optimize the reaction conditions (Table 1). Satisfyingly, desired product **3aa** was obtained in 51% yield in the presence of *fac*-Ir(ppy)$_3$ and Na_2HPO_4 in *N*,*N*-dimethylformamide (DMF) in a N_2 atmosphere under irradiation with 10 W blue LEDs (Entry 1). Next, other inorganic bases were tested such as $NaHCO_3$, $KHCO_3$, Na_2CO_3 and Cs_2CO_3. $NaHCO_3$ was proven to be the best choice for this reaction in 62% yield (Entries 2～5). Organic bases, such as Et_3N, 2,6-lutidine, or 1,5-dizzabicyclo[5.4.0]undecen-5-ene (DBU), were used but failed to improve the yield (Entries 6～8). Subsequently, the effect of various solvents, such as dichloromethane (DCM), CH_3CN, *N*,*N*-dimethylacetamide (DMAc), dimethyl sulfoxide (DMSO), tetrahydrofuran (THF), and toluene, was also evaluated in the reaction (Entries 9～14). The results indicated that DMF remained the best one. Based on the optimal bases and solvents, attention was then turned to the investigation of photocatalysts including $Ru(bpy)_3Cl_2•6H_2O$, 4CzIPN, Eosin Y, and methylene blue (Entries 15～18), and it was found that *fac*-Ir(ppy)$_3$ was the optimal catalyst for this reaction. The yield decreased dramatically to 24% and 8% in the absence of base or photocatalyst, which indicated that they played an important role in photoredox catalysis (Entries 19～20). Desired product **3aa** cannot be obtained without light (Entry 21), suggesting that light irradiation was essential to the reaction. Given a little material remained, the effect of the reaction time was then explored, and reaction for 12 h or longer 18 h gave lower yields (Entries 22～23).

With the optimized reaction conditions in hand, the scope and limitation of functionalized aromatic isocyanides **1** in the radical cascade cyclization were investigated (Table 2). The introduction of electron-donating (Me) and electron-withdrawing (CO_2Me) groups at the 3-positions of the indole ring (R^2) in substrate **1** reacted smoothly, and the desired products **3ba**～**3ca** were obtained in 67% and 55% yields, respectively. Next, various substituents at the 4-, 5- and 7-positions of the indole ring (R^1) were examined, and this transformation proceeded smoothly with 44%～74% yields (**3da**～**3ga**). In addition, for substrates

Table 1 Optimization of the reaction conditions[a]



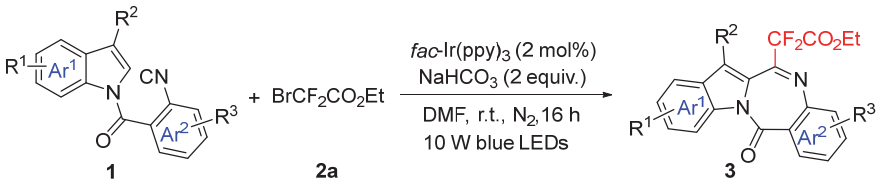
Entry	Catalyst	Base	Solvent	Yield[b]/%
1	*fac*-Ir(ppy)$_3$	Na_2HPO_4	DMF	51
2	*fac*-Ir(ppy)$_3$	$NaHCO_3$	DMF	62
3	*fac*-Ir(ppy)$_3$	$KHCO_3$	DMF	42
4	*fac*-Ir(ppy)$_3$	Na_2CO_3	DMF	32
5	*fac*-Ir(ppy)$_3$	Cs_2CO_3	DMF	26
6	*fac*-Ir(ppy)$_3$	Et_3N	DMF	27
7	*fac*-Ir(ppy)$_3$	2,6-Lutidine	DMF	53
8	*fac*-Ir(ppy)$_3$	DBU	DMF	7
9	*fac*-Ir(ppy)$_3$	$NaHCO_3$	DCM	19
10	*fac*-Ir(ppy)$_3$	$NaHCO_3$	CH_3CN	14
11	*fac*-Ir(ppy)$_3$	$NaHCO_3$	DMAc	47
12	*fac*-Ir(ppy)$_3$	$NaHCO_3$	DMSO	27
13	*fac*-Ir(ppy)$_3$	$NaHCO_3$	THF	45
14	*fac*-Ir(ppy)$_3$	$NaHCO_3$	Toluene	42
15	$Ru(bpy)_3Cl_2•6H_2O$	$NaHCO_3$	DMF	8
16	4CzIPN	$NaHCO_3$	DMF	22
17	Eosin Y	$NaHCO_3$	DMF	Trace
18	Methylene Blue	$NaHCO_3$	DMF	10
19	*fac*-Ir(ppy)$_3$	—	DMF	24
20	—	$NaHCO_3$	DMF	8
21[c]	*fac*-Ir(ppy)$_3$	$NaHCO_3$	DMF	0
22[d]	*fac*-Ir(ppy)$_3$	$NaHCO_3$	DMF	50
23[e]	*fac*-Ir(ppy)$_3$	$NaHCO_3$	DMF	43

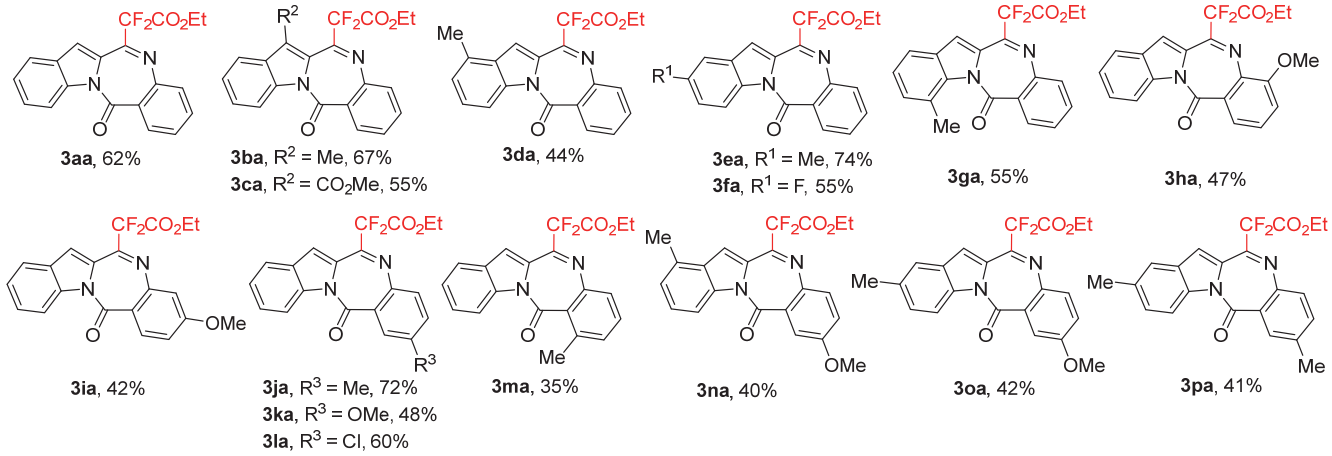
[a] Reactions were carried out using **1a** (0.2 mmol), **2a** (0.4 mmol), catalyst (2 mol%), base (0.4 mmol) and solvent (1 mL) at room temperature for 16 h under a N_2 atmosphere. [b] Isolated yield. [c] In the dark. [d] Reaction for 12 h. [e] Reaction for 18 h.

with various substituents (Me, OMe, Cl) at different positions on the Ar^2 ring (R^3), the corresponding products were obtained in 35%～72% yields (**3ha**～**3ma**). Substrate **1** bearing a substituent simultaneously on the indole ring (R^1) and the Ar^2 ring (R^3), was also compatible with this radical cascade process, generating the desired products **3na**～**3pa** in 40%～42% yields.

Given the biological significance of the difluoromethylene group, the scope of bromodifluorinated reagents in this radical cascade cyclization reaction with (2-isocyanophenyl)(5-methyl-1*H*-indol-1-yl)methanone (**1e**) as a radical acceptor was investigated (Table 3). Various amino moieties of the *N*,*N*-disubstituted bromo-difluoroacetamides, including diethylamine, pyrrolidine, piperidine, morpholine, and piperazine were employed to generate the corresponding products in 35%～60% yields (**3eb**～**3eg**).

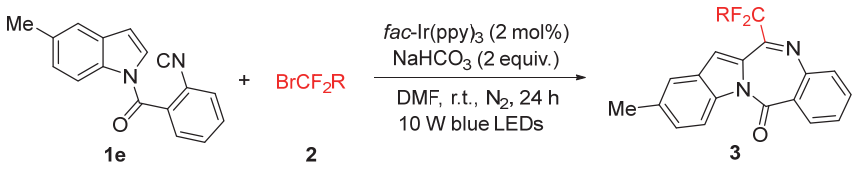
Table 2 Scope of functionalized aromatic isocyanides[a,b]

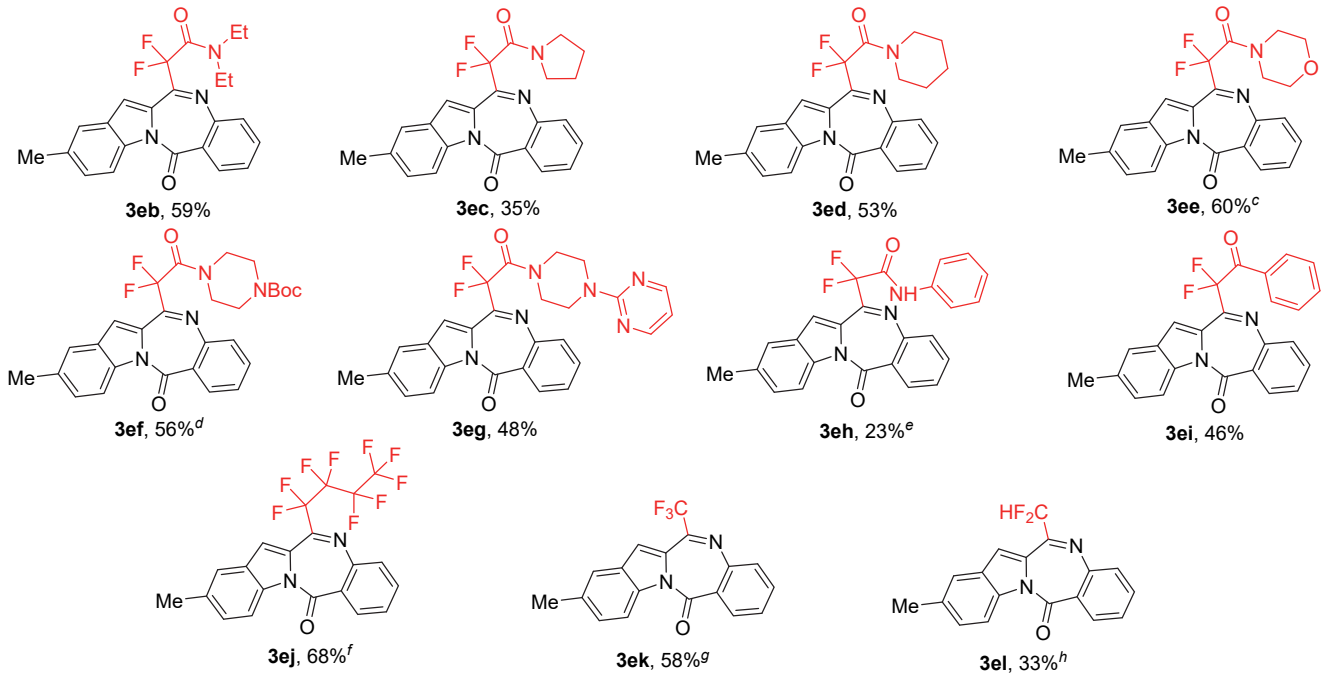




[a] Reactions were carried out using **1** (0.2 mmol), **2a** (0.4 mmol), *fac*-Ir(ppy)$_3$ (2 mol%), $NaHCO_3$ (0.4 mmol) and DMF (1 mL) at room temperature for 16 h under a N_2 atmosphere. [b] Isolated yield.

Table 3 Scope of bromodifluorinated reagents[a,b]





[a] Reactions were carried out using **1e** (0.2 mmol), **2** (0.4 mmol), *fac*-Ir(ppy)$_3$ (2 mol%), $NaHCO_3$ (0.4 mmol) and DMF (1 mL) at room temperature for 24 h under a N_2 atmosphere. [b] Isolated yield. [c] Reaction for 20 h. [d] Reaction for 16 h. [e] Reaction for 48 h. [f] $BrCF_2CO_2Et$ was replaced by $^nC_4F_9I$ and reaction for 16 h. [g] $BrCF_2CO_2Et$ was replaced by Togni Reagent II and reaction for 3 h. [h] $BrCF_2CO_2Et$ was replaced by $[Ph_3PCF_2H]^+Br^-$ and reaction for 16 h.

Bromodifluoroacetamide bearing an N-H group, afforded product **3eh** in a low yield, indicating that the presence of a free N—H bond had a significant impact on this radical reaction. In addition, 2-bromo-2,2-difluoro-1-phenylethan-1-one was also applicable to the radical reaction in 46% yield (**3ei**). Notably, other fluoroalkyl reagents were also suitable for the delivery of fluoroalkylated indole-1,2-fused diazepanone products **3ej**, **3el** and **3ek** in 68%, 58%, 33% yields, respectively.

To examine the scalability of this protocol, a gram-scale reaction of **1a** and **2a** under the irradiation of 2×12 W blue LEDs was performed. The reaction proceeded smoothly, yielding product **3aa** in 55% yield (Scheme 2a). A control experiment was carried out to gain insights into the possible pathway of this reaction. The reaction was inhibited with a dramatic decrease in yield when 2 equiv. of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 2,6-di-*tert*-butyl-4-methylphenol (BHT) as radical scavengers were added under the standard conditions. Corresponding radical trapping adduct **4aa** was isolated in 77% yield (Scheme 2b). Radical trapping experiments indicated the involvement of a radical mechanism. Furthermore, light on/off experiments were also carried out, and the results suggested that continuous light irradiation was essential for the radical cascade reaction (Figure 2).

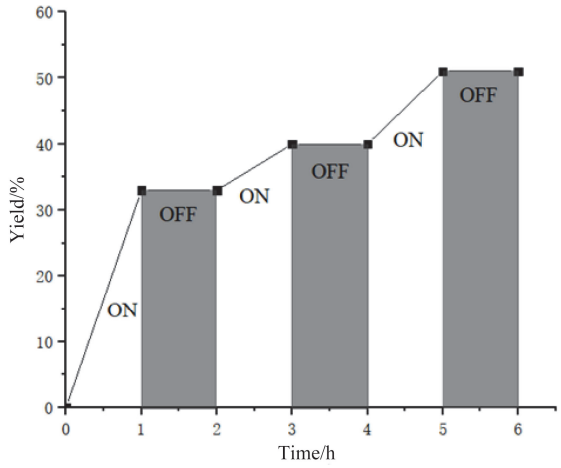
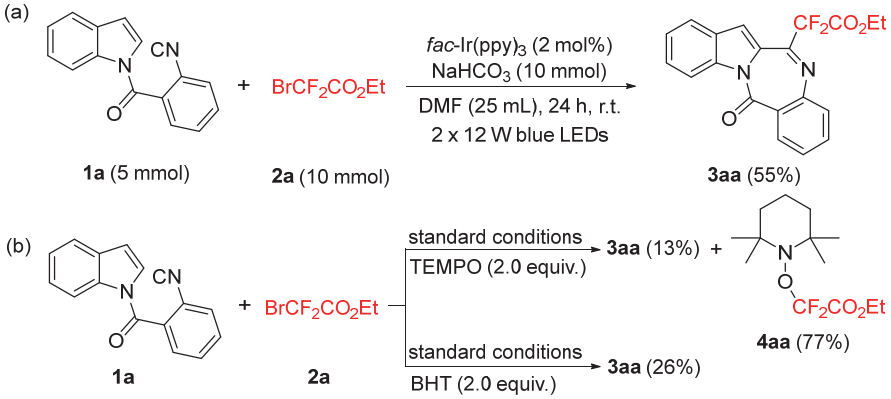
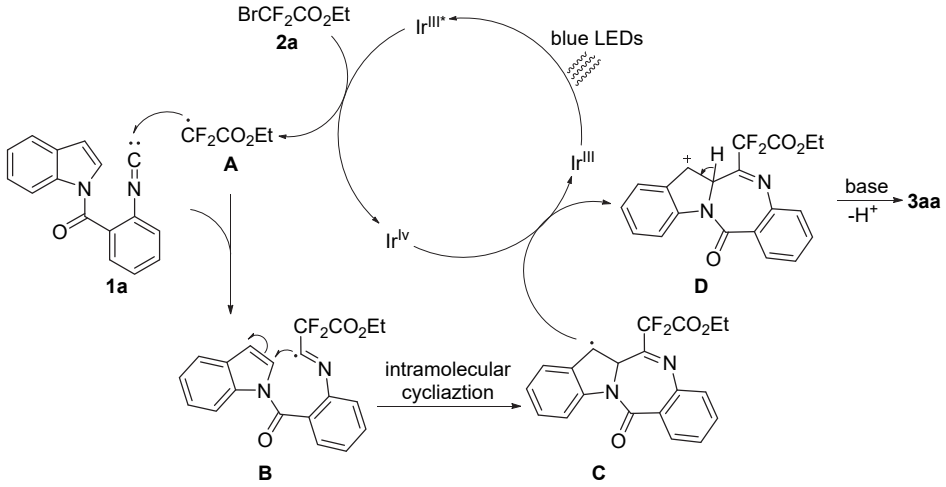


Figure 2 Light on/off experiments

Based on the above experiments and related reports,[13,16c,20] a plausible mechanism was proposed (Scheme 3), in which the photoexcitation of *fac*-Ir(III)(ppy)$_3$ generated the exicted-state *fac*-Ir(III)(ppy)$_3$*, and $BrCF_2CO_2Et$ was reduced to $\bullet CF_2CO_2Et$ radical **A** and the [*fac*-$Ir^{IV}(ppy)_3]^+$ complex. Then, radical **A** attacked isonitrile, giving corresponding imidoyl radical **B**. Subsequently,



Scheme 2 Gram-scale reaction and control experiments



Scheme 3 Plausible mechanism

radical **B** underwent intramolecular addition to the 2-position of the indole ring chemoselectively to provide radical intermediate **C**. Following a single electron oxidation process, carbocation intermediate **D** was produced with the regeneration of the photoredox catalytic cycle. Finally, the desired product **3aa** was obtained by the deprotonation of intermediate **D** in the presence of a base.

3 Conclusions

In summary, a visible-light photoredox protocol for the facile synthesis of CF_2-containing indole-1,2-fused diazepanones under mild conditions was successfully developed. A newly designed class of functionalized aromatic isocyanides was prepared, and their radical cascade cyclization with bromodifluorinated reagents was firstly disclosed. This method features advantages, such as mild reaction conditions, broad substrate scope, good functional group compatibility, easy scale-up and commercially available CF_2 precursors. The present protocol offers novel access to polycyclic indole-fused seven-membered nitrogen heterocycle scaffolds with biological importance.

4 Experimental section

4.1 Instruments and reagents

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker AVANCE 400 spectrometer in $CDCl_3$ with TMS as the internal standard. High-resolution mass spectra (HRMS) were obtained using a waters UPLC G2-XS focus spectrometer (ESI). Column chromatography was performed on silica gel (300～400 mesh) with ethyl acetate (EA)/petroleum ether (PE) or acetone (AC)/petroleum ether (PE). The photocatalytic reactions were performed on WATTCAS Parallel Light Reactor (WP-TEC-1020HSL) with 10 W blue COD LED (455～460 nm). All chemicals were obtained from commercial sources and used as received unless otherwise noted.

4.2 General procedure for the synthesis of 1

In a 50 mL Schlenk tube was added (2-aminophenyl)-(1*H*-indol-1-yl)methanone (0.708 g, 3.0 mmol) and THF (10.0 mL) under N_2 atmosphere and cooled to 0 ℃ in an ice-bath. Acetic formic anhydride, which was prepared from the reaction of acetic anhydride (2.4 mL) with formic acid (1.2 mL) in an oil bath at 55 ℃ for 2 h, was added dropwise to a solution of (2-aminophenyl)(1*H*-indol-1-yl)methanone in an ice bath at 0 ℃. After the addition was completed, the mixture was warmed to room temperature and stirred for 2 h. Then, the mixture was quenched by saturated $NaHCO_3$ solution and extracted with DCM three times. The combined organic layers were dried with Na_2SO_4, and concentrated under reduced pressure to give *N*-(2-(1*H*-indole-1-carbonyl)phenyl)formamide as a pale white solid (The product was used without further purification in the next step).

In a 50 mL Schlenk tube was added THF (10.0 mL), NEt_3 (2.0 mL, 14.5 mmol, 5.0 equiv) and the *N*-(2-(1*H*-indole-1-carbonyl)phenyl)formamide (0.753 g, 2.9 mmol) under N_2 atmosphere and cooled to 0 ℃ in an ice-bath. $POCl_3$ (0.674 g, 4.4 mmol, 1.5 equiv.) was added dropwise, and the mixture was stirred for 2 h at 0 ℃ after the addition was completed (monitored by TLC). Then, the mixture was quenched by saturated $NaHCO_3$ solution and extracted with DCM three times. The combined organic layers were dried with Na_2SO_4. Subsequently, the solvent was evaporated under vacuum. The crude residue was purified by silica gel column chromatography [*V*(petroleum ether)∶*V*(ethyl acetate)＝10∶1] to afford (1*H*-indol-1-yl)(2-isocyanophenyl)methanone (**1a**) 556.6 mg, yield 74% (2 steps). White solid, m.p. 105～106 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.39 (d, *J*＝7.6 Hz, 1H), 7.61～7.51 (m, 5H), 7.41～7.37 (m, 1H), 7.33 (td, *J*＝7.6, 1.2 Hz, 1H), 6.99 (d, *J*＝4.0 Hz, 1H), 6.64 (d, *J*＝3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 169.8, 164.4, 135.6, 132.6, 131.8, 131.0, 129.7, 128.9, 127.8, 126.2, 125.5, 124.6, 124.2, 121.2, 116.5, 110.4; HRMS (ESI-TOF) calcd for $C_{16}H_{10}N_2NaO$ $[M+Na]^+$ 269.0688, found 269.0691.

(2-Isocyanophenyl)(3-methyl-1*H*-indol-1-yl)methanone (**1b**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)＝10∶1, 491.6 mg, yield 63% (2 steps). Yellow solid, m.p. 108～110 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.36 (s, 1H), 7.60～7.49 (m, 5H), 7.41～7.33 (m, 2H), 6.75 (s, 1H), 2.22 (d, *J*＝1.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 169.5, 164.0, 135.9, 133.0, 132.1, 131.5, 129.6, 128.7, 127.7, 125.5, 124.4, 124.1, 122.8, 119.7, 119.1, 116.6, 9.7; HRMS (ESI-TOF) calcd for $C_{17}H_{12}N_2NaO$ $[M+Na]^+$ 283.0845, found 283.0847.

Methyl 1-(2-isocyanobenzoyl)-1*H*-indole-3-carboxylate (**1c**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)＝10∶1, 492.6 mg, yield 54% (2 steps). White solid, m.p. 132～135 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 8.46～8.41 (m, 1H), 8.20～8.16 (m, 1H), 7.69～7.65 (m, 2H), 7.62～7.57 (m, 3H), 7.49～7.43 (m, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 170.4, 164.7, 164.1, 136.0, 132.4, 132.0, 131.4, 129.8, 129.1, 128.1, 127.8. 126.3, 125.7, 124.4, 121.9, 116.4, 115.1, 51.7; HRMS (ESI-TOF) calcd for $C_{18}H_{12}N_2NaO_3$ $[M+Na]^+$ 327.0749, found 327.0746.

(2-Isocyanophenyl)(4-methyl-1*H*-indol-1-yl)methanone (**1d**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)＝10∶1, 476.0 mg, yield 61% (2 steps). Green solid, m.p. 114～126 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.21 (d, *J*＝8.0 Hz, 1H), 7.63～7.53 (m, 4H), 7.29 (t, *J*＝8.0 Hz, 1H), 7.14 (t, *J*＝7.6 Hz, 1H), 7.00 (d, *J*＝4.0 Hz, 1H), 6.68 (d, *J*＝3.6 Hz, 1H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 169.7, 164.4, 135.4, 132.8, 131.7, 130.6, 130.5, 129.6, 128.9, 127.8, 125.5, 125.1, 124.2, 114.0, 108.8, 18.5; HRMS (ESI-TOF) calcd for $C_{17}H_{12}N_2NaO$ $[M+Na]^+$ 283.0849, found 283.0847.

(2-Isocyanophenyl)(5-methyl-1*H*-indol-1-yl)methanone (**1e**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)＝10∶1, 546.2 mg, yield 70% (2 steps). Green solid, m.p. 104～106 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 8.25 (s, 1H), 7.61～7.51 (m, 4H), 7.37 (s, 1H), 7.21 (d, *J*＝8.0 Hz, 1H), 6.95 (d, *J*＝3.6 Hz, 1H), 6.57 (d, *J*＝3.6 Hz, 1H), 2.46 (s, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.7, 164.2, 134.3, 133.8, 132.7, 131.7, 131.2, 129.6, 128.9, 127.8, 126.7, 126.2, 124.2, 121.1, 116.1, 110.2, 21.5; HRMS (ESI-TOF) calcd for $C_{17}H_{12}N_2NaO$ $[M+Na]^+$ 283.0844, found 283.0847.

(5-Fluoro-1*H*-indol-1-yl)(2-isocyanophenyl)methanone (**1f**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 507.0 mg, yield 64% (2 steps). White solid, m.p. 121～123 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.43～8.39 (m, 1H), 7.65～7.54 (m, 4H), 7.26～7.23 (m, 1H), 7.12 (td, *J*=8.8, 2.4 Hz, 1H), 7.02 (d, *J*=3.6 Hz, 1H), 6.61 (d, *J*=3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.8, 164.2, 160.2 (d, *J*=240.0 Hz), 132.2, 132.1 (d, *J*=10.0 Hz), 132.0, 131.9, 129.7, 128.9, 127.8, 127.7, 124.2, 117.7 (d, *J*=9.1 Hz), 113.2 (d, *J*=24.7 Hz), 110.0 (d, *J*=3.8 Hz), 106.9 (d, *J*=23.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ: −117.82; HRMS (ESI-TOF) calcd for $C_{16}H_9FN_2NaO$ $[M+Na]^+$ 287.0598, found 287.0597.

(2-Isocyanophenyl)(7-methyl-1*H*-indol-1-yl)methanone (**1g**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 491.6 mg, yield 63% (2 steps). Yellow solid, m.p. 110～112 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 7.74～7.71 (m, 1H), 7.66～7.60 (m, 1H), 7.58～7.53 (m, 2H), 7.44 (d, *J*=7.6 Hz, 1H), 7.29～7.25 (m, 1H), 7.21 (d, *J*=7.2 Hz, 1H), 6.94 (d, *J*=3.6 Hz, 1H), 6.62 (d, *J*=3.6 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.2, 163.6, 135.3, 132.5, 132.4, 132.3, 130.3, 129.6, 128.3, 128.2, 127.5, 126.6, 124.8, 118.8, 109.8, 22.1; HRMS (ESI-TOF) calcd for $C_{17}H_{12}N_2NaO$ $[M+Ma]^+$ 283.0851, found 283.0847.

(1*H*-Indol-1-yl)(2-isocyano-3-methoxyphenyl)methanone (**1h**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 579.8 mg, yield 70% (2 steps). White solid, m.p. 130～132 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.42 (s, 1H), 7.59 (d, *J*=7.6 Hz, 1H), 7.51～7.47 (m, 1H), 7.42～7.38 (m, 1H), 7.33 (td, *J*=7.6, 1.2 Hz, 1H), 7.15 (d, *J*=8.4 Hz, 1H), 7.13～7.10 (m, 1H), 7.01 (d, *J*=7.6 Hz, 1H), 6.63 (d, *J*=3.6 Hz, 1H), 4.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.2, 164.3, 155.5, 135.6, 133.8, 131.0, 130.5, 126.3, 126.2, 125.4, 124.6, 121.1, 119.7, 116.6, 113.7, 110.2, 56.5; HRMS (ESI-TOF) calcd for $C_{17}H_{13}N_2O_2$ $[M+H]^+$ 277.0979, found 277.0977.

(1*H*-Indol-1-yl)(2-isocyano-4-methoxyphenyl)methanone (**1i**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 521.8 mg, yield 63% (2 steps). Yellow solid, m.p. 123～126 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.35 (d, *J*=8.4 Hz, 1H), 7.59 (d, *J*=7.2 Hz, 1H), 7.51 (d, *J*=8.4 Hz, 1H), 7.38 (td, *J*=7.6, 1.6 Hz, 1H), 7.32 (td, *J*=7.2, 1.2 Hz, 1H), 7.08～7.02 (m, 3H), 6.64 (d, *J*=3.2 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.6, 164.4, 161.9, 135.7, 131.0, 130.8, 126.4, 125.7, 125.3, 124.6, 124.4, 121.1, 116.4, 115.5, 113.2, 109.8, 56.0; HRMS (ESI-TOF) calcd for $C_{17}H_{12}N_2NaO_2$ $[M+Na]^+$ 299.0800, found 299.0796.

(1*H*-Indol-1-yl)(2-isocyano-5-methylphenyl)methanone (**1j**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 444.8 mg, yield 57% (2 steps). White solid, m.p. 144～145 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 8.39 (d, *J*=8.0 Hz, 1H), 7.59 (d, *J*=7.6 Hz, 1H), 7.43～7.31 (m, 5H), 7.01 (d, *J*=4.0 Hz, 1H), 6.64 (d, *J*=4.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.9, 164.6, 140.5, 135.6, 132.5, 132.3, 131.0, 129.3, 127.5, 126.2, 125.4, 124.6, 121.7, 121.1, 116.5, 110.3, 21.3; HRMS (ESI-TOF) calcd for $C_{17}H_{13}N_2O$ $[M+H]^+$ 261.1023, found 261.1028.

(1*H*-Indol-1-yl)(2-isocyano-5-methoxyphenyl)methanone (**1k**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 588.1 mg, yield 71% (2 steps). White solid, m.p. 117～119 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 8.40 (s, 1H), 7.60～7.58 (m, 1H), 7.47～7.44 (m, 1H), 7.42～7.38 (m, 1H), 7.33 (td, *J*=7.6, 1.2 Hz, 1H), 7.08～7.03 (m, 3H), 6.65 (d, *J*=4.0 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.0, 164.3, 159.9, 135.6, 134.0, 131.0, 129.2, 126.2, 125.5, 124.6, 121.1, 117.3, 116.5, 113.8, 110.4, 56.0; HRMS (ESI-TOF) calcd for $C_{17}H_{12}N_2NaO_2$ $[M+Na]^+$ 299.0798, found 299.0796.

(5-Chloro-2-isocyanophenyl)(1*H*-indol-1-yl)methanone (**1l**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 436.9 mg, yield 52% (2 steps). Green solid, m.p. 148～151 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 8.40 (s, 1H), 7.60～7.56 (m, 3H), 7.50～7.47 (m, 1H), 7.42 (t, *J*=7.2 Hz, 1H), 7.35 (d, *J*=7.6 Hz, 1H), 6.98 (d, *J*=3.6 Hz, 1H), 6.68 (d, *J*=3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.2, 162.9, 135.9, 135.5, 134.0, 131.9, 131.0, 129.0, 128.9, 125.72, 125.71, 124.9, 121.3, 116.5, 111.0; HRMS (ESI-TOF) calcd for $C_{16}H_9ClN_2NaO$ $[M+Na]^+$ 303.0303, found 303.0301.

(1*H*-Indol-1-yl)(2-isocyano-6-methylphenyl)methanone (**1m**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 554.0 mg, yield 71% (2 steps). Blue solid, m.p. 121～122 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 8.69～8.65 (m, 1H), 7.60 (d, *J*=8.0 Hz, 1H), 7.48～7.42 (m, 2H), 7.39～7.34 (m, 3H), 6.79～6.77 (m, 1H), 6.64～6.62 (m, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.8, 164.8, 137.2, 135.4, 132.9, 131.2, 131.0, 130.7, 125.7, 125.3, 124.8, 124.6, 121.1, 117.0, 110.8, 19.3; HRMS (ESI-TOF) calcd for $C_{17}H_{12}N_2NaO$ $[M+Na]^+$ 283.0850, found 283.0847.

(2-Isocyano-5-methoxyphenyl)(4-methyl-1*H*-indol-1-yl)methanone (**1n**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 452.6 mg, yield 52% (2 steps). White solid, m.p. 128～129 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 8.21 (s, 1H), 7.46～7.43 (m, 1H), 7.29 (t, *J*=7.6 Hz, 1H), 7.13 (d, *J*=7.6 Hz, 1H), 7.07～7.02 (m, 3H), 6.68 (d, *J*=3.6 Hz, 1H), 3.85 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.0, 164.3, 159.9, 135.4, 134.1, 130.59, 130.57, 129.1, 125.6, 125.5, 125.1, 117.2, 116.8, 114.0, 113.8, 108.8, 56.0, 18.5; HRMS (ESI-TOF) calcd for $C_{18}H_{14}N_2NaO_2$ $[M+Na]^+$ 313.0955, found 313.0953.

(2-Isocyano-5-methoxyphenyl)(5-methyl-1*H*-indol-1-yl)methanone (**1o**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 644.0 mg, yield 74% (2 steps). Yellow solid, m.p. 123～125 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 8.25 (s, 1H), 7.45～7.42 (m, 1H), 7.37 (s, 1H), 7.21 (d, *J*=8.4 Hz, 1H), 7.07～7.04 (m, 2H), 6.98 (d, *J*=3.2 Hz, 1H), 6.57 (d, *J*=3.6 Hz, 1H), 3.85 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.0, 164.1, 159.8, 134.3,

134.0, 133.7, 131.3, 129.1, 126.7, 126.2, 121.1, 117.2, 116.8, 116.1, 113.7, 110.3, 56.0, 21.5; HRMS (ESI-TOF) calcd for $C_{18}H_{14}N_2NaO_2$ $[M+Na]^+$ 313.0949, found 313.0953.

(2-Isocyano-5-methylphenyl)(5-methyl-1*H*-indol-1-yl)methanone (**1p**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=10∶1, 509.8 mg, yield 62% (2 steps). Yellow solid, m.p. 147～149 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) 8.24 (s, 1H), 7.42～7.36 (m, 4H), 7.20 (d, *J*=8.4 Hz, 1H), 6.97 (d, *J*=4.0 Hz, 1H), 6.57 (d, *J*=3.6 Hz, 1H), 2.46 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.8, 164.4, 140.4, 134.2, 133.8, 132.6, 132.2, 131.2, 129.3, 127.5, 126.7, 126.3, 121.1, 116.1, 110.1, 21.4, 21.3; HRMS (ESI-TOF) calcd for $C_{18}H_{14}N_2NaO$ $[M+Na]^+$ 297.1003, found 297.1004.

4.3 General procedure for the synthesis of 3

In a 25 mL Schlenk tube was added **1a** (0.2 mmol, 49.2 mg), **2a** (0.4 mmol, 81.2 mg) and $NaHCO_3$ (0.4 mmol, 33.6 mg) in the presence of 0.02 equiv. *fac*-Ir(ppy)$_3$ in DMF (1.0 mL) under N_2 atmosphere and stirred in 10 W blue LEDs for 16 h. After the reaction was completed, the solvent was removed under reduced pressure. The crude residue was purified by silica gel column chromatography [*V*(ethyl acetate)∶*V*(petroleum ether)=1∶30] to afford ethyl 2,2-difluoro-2-(6-oxo-6*H*-benzo[5,6][1,4]diazepino-[1,2-*a*]indol-12-yl)-acetate (**3aa**) 45.3 mg, yield 62%. Yellow solid, m.p. 160～164 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.75～8.72 (m, 1H), 8.49 (dd, *J*=8.0, 2.0 Hz, 1H), 7.81 (d, *J*=7.6 Hz, 1H), 7.66 (t, *J*=2.8 Hz, 1H), 7.62～7.68 (m, 1H), 7.61～7.51 (m, 3H), 7.61～7.52 (m, 1H), 4.48 (q, *J*=7.2 Hz, 2H), 1.42 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 164.3, 163.0 (t, *J*=30.9 Hz), 148.6 (t, *J*=29.7 Hz), 141.7, 137.9, 134.1, 133.1, 132.8, 129.7, 128.4, 128.2, 126.9 (t, *J*=3.3 Hz), 125.3, 125.0, 122.5, 117.8, 117.3 (t, *J*=6.0 Hz), 115.2 (t, *J*=257.8 Hz), 63.0, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) *δ*: −101.03; HRMS (ESI-TOF) calcd for $C_{20}H_{14}F_2N_2NaO_3$ $[M+Na]^+$ 391.0873, found 391.0870.

Ethyl 2,2-difluoro-2-(13-methyl-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3ba**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 50.9 mg, yield 67%. Yellow solid, m.p. 143～146 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.57～8.56 (m, 1H), 8.14 (dd, *J*=7.6, 1.2 Hz, 1H), 7.73 (d, *J*=8.0 Hz, 1H), 7.64～7.55 (m, 2H), 7.48～7.40 (m, 3H), 4.36 (q, *J*=6.8 Hz, 2H), 2.64 (q, *J*=2.4 Hz, 3H), 1.29 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.4, 162.8 (t, *J*=32.3 Hz), 152.9 (t, *J*=31.5 Hz), 141.9, 136.8, 133.3, 131.3, 129.8, 128.9, 128.7, 128.5, 127.1, 125.9, 124.7, 121.2 (t, *J*=2.1 Hz), 120.2, 115.7, 113.0 (t, *J*=258.2 Hz), 63.1, 14.0, 11.1; ^{19}F NMR (376 MHz, $CDCl_3$) *δ*: −100.98; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2N_2NaO_3$ $[M+Na]^+$ 405.1028, found 405.1027.

Methyl 12-(2-ethoxy-1,1-difluoro-2-oxoethyl)-6-oxo-6*H*-benzo[5,6][1,4]diazepino-[1,2-*a*]indole-13-carboxylate (**3ca**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 46.5 mg, yield 55%. Yellow solid, m.p. 139～140 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.47 (d, *J*=8.4 Hz, 1H), 8.26 (d, *J*=8.0 Hz, 1H), 8.07 (dd, *J*=8.0, 1.6 Hz, 1H), 7.71～7.67 (m, 1H), 7.62～7.57 (m, 2H), 7.53～7.45 (m, 2H), 4.30 (q, *J*=6.8 Hz, 2H), 3.98 (s, 3H), 1.23 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.2, 163.7, 162.4 (t, *J*=33.6 Hz), 153.4 (t, *J*=29.3 Hz), 142.2, 136.3, 133.8, 131.0, 128.9, 128.53, 128.48, 126.1, 125.9, 124.7, 122.3, 118.8 (t, *J*=1.5 Hz), 114.7, 110.2 (t, *J*=259.1 Hz), 63.4, 52.2, 13.9; ^{19}F NMR (376 MHz, $CDCl_3$) *δ*: −103.37; HRMS (ESI-TOF) calcd for $C_{22}H_{17}F_2N_2O_5$ $[M+H]^+$ 427.1105, found 427.1106.

Ethyl 2,2-difluoro-2-(1-methyl-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3da**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 33.5 mg, yield 44%. Yellow solid, m.p. 168～171 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.55 (d, *J*=8.8 Hz, 1H), 8.49 (dd, *J*=8.0, 1.6 Hz, 1H), 7.78 (t, *J*=3.2 Hz, 1H), 7.69 (td, *J*=7.6, 1.6 Hz, 1H), 7.59 (dd, *J*=8.0, 1.2 Hz, 1H), 7.56～7.52 (m, 1H), 7.49～7.45 (m, 1H), 7.25～7.23 (m, 1H), 4.38 (q, *J*=7.2 Hz, 2H), 2.65 (s, 3H), 1.42 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 164.4, 163.0 (t, *J*=31.0 Hz), 148.7 (t, *J*=24.7 Hz), 141.7, 137.9, 134.1, 133.0, 132.7, 132.3, 129.6, 128.6, 128.2, 125.4, 125.1, 115.7 (t, *J*=6.0 Hz), 115.3 (t, *J*=285.5 Hz), 115.2, 63.0, 18.5, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) *δ*: −100.92; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2N_2NaO_3$ $[M+Na]^+$ 405.1021, found 405.1027.

Ethyl 2,2-difluoro-2-(2-methyl-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3ea**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 56.5 mg, yield 74%. Yellow solid, m.p. 175～177 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.62 (d, *J*=8.8 Hz, 1H), 8.51 (dd, *J*=8.4, 1.6 Hz, 1H), 7.72～7.67 (m, 2H), 7.61～7.52 (m, 3H), 7.39 (dd, *J*=8.8, 1.6 Hz, 1H), 4.48 (q, *J*=6.8 Hz, 2H), 2.49 (s, 3H), 1.42 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 164.1, 163.0 (t, *J*=30.8 Hz), 148.5 (t, *J*=29.4 Hz), 141.7 (t, *J*=1.8 Hz), 136.3, 135.2, 134.0, 133.1, 132.9, 130.2, 129.6, 128.5, 126.0 (t, *J*=3.4 Hz), 124.9, 122.0, 117.5, 117.2 (t, *J*=6.2 Hz), 115.3 (t, *J*=258.4 Hz), 63.0, 21.4, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) *δ*: −100.97; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2N_2NaO_3$ $[M+Na]^+$ 405.1022, found 405.1027.

Ethyl 2,2-difluoro-2-(2-fluoro-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3fa**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 42.4 mg, yield 55%. Yellow solid, m.p. 169～171 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.72 (dd, *J*=9.2, 4.8 Hz, 1H), 8.49 (dd, *J*=8.0, 1.6 Hz, 1H), 7.74～7.70 (m, 2H), 7.61 (dd, *J*=8.0, 1.2 Hz, 1H), 7.58～7.54 (m, 1H), 7.43 (dd, *J*=8.4, 2.8 Hz, 1H), 7.28 (td, *J*=8.8, 2.4 Hz, 1H), 4.49 (q, *J*=7.2 Hz, 2H), 1.42 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 163.9, 162.8 (t, *J*=30.8 Hz), 160.1 (d, *J*=242.8 Hz), 148.2 (t, *J*=29.8 Hz), 141.5 (t, *J*=1.9 Hz), 134.3, 133.1, 133.0, 130.0, 129.1 (d, *J*=10.4 Hz), 127.0 (t, *J*=3.3 Hz), 124.7, 119.4 (d, *J*=8.7 Hz), 116.9, 116.7, 116.6 (t, *J*=5.2 Hz), 115.2 (t, *J*=258.5 Hz), 107.2 (d, *J*=23.5

Hz), 63.1, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −101.04, −115.86; HRMS (ESI-TOF) calcd for $C_{20}H_{13}F_3N_2NaO_3$ $[M+Na]^+$ 409.0781, found 409.0776.

Ethyl 2,2-difluoro-2-(4-methyl-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3ga**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 42.3 mg, yield 55%. Yellow solid, m.p. 179～180 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.13 (dd, *J*=7.6, 1.6 Hz, 1H), 7.69～7.64 (m, 3H), 7.58 (dd, *J*=8.0, 1.2 Hz, 1H), 7.52 (td, *J*=7.6, 1.2 Hz, 1H), 7.37～7.33 (m, 2H), 4.47 (q, *J*=7.2 Hz, 2H), 2.45 (s, 3H), 1.41 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5, 163.0 (t, *J*=30.8 Hz), 148.2 (t, *J*=29.7 Hz), 141.0, 137.1, 133.4, 132.2, 131.1, 130.7, 130.0, 129.6, 127.8 (t, *J*=3.3 Hz), 126.9, 126.7, 125.3, 120.4, 116.0 (t, *J*=5.9 Hz), 115.1 (t, *J*=258.3 Hz), 63.0, 21.8, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −101.29; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2N_2NaO_3$ $[M+Na]^+$ 405.1022, found 405.1027.

Ethyl 2,2-difluoro-2-(10-methoxy-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3ha**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 37.1 mg, yield 47%. Yellow solid, m.p. 148～151 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.68 (d, *J*=8.4 Hz, 1H), 8.04 (dd, *J*=8.0, 1.2 Hz, 1H), 7.81 (d, *J*=8.0 Hz, 1H), 7.73 (t, *J*=2.8 Hz, 1H), 7.59～7.54 (m, 1H), 7.50～7.42 (m, 2H), 7.22 (dd, *J*=8.4, 1.6 Hz, 1H), 4.48 (q, *J*=6.8 Hz, 2H), 3.92 (s, 3H), 1.41 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.5, 163.2 (t, *J*=30.7 Hz), 157.0, 147.0 (t, *J*=30.0 Hz), 137.7, 131.6, 130.5, 128.4, 128.1, 126.5, 126.2 (t, *J*=3.3 Hz), 125.2, 124.2, 122.4, 117.5, 116.6, 116.2 (t, *J*=5.9 Hz), 115.3 (t, *J*=258.3 Hz), 63.0, 56.8, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −101.49; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2N_2NaO_4$ $[M+Na]^+$ 421.0978, found 421.0976.

Ethyl 2,2-difluoro-2-(9-methoxy-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3ia**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 33.2 mg, yield 42%. Yellow solid, m.p. 144～145 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.77 (d, *J*=8.4 Hz, 1H), 8.74 (d, *J*=8.8 Hz, 1H), 7.80 (d, *J*=8.0 Hz, 1H), 7.76 (t, *J*=2.8 Hz, 1H), 7.59～7.54 (m, 1H), 7.45～7.41 (m, 1H), 7.07～7.04 (m, 2H), 4.48 (q, *J*=7.2 Hz, 2H), 3.90 (s, 3H), 1.42 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.0, 163.8, 163.0 (t, *J*=30.9 Hz), 148.8 (t, *J*=29.5 Hz), 143.5, 138.1, 135.2, 128.3, 128.1, 125.9 (t, *J*=3.2 Hz), 125.1, 122.5, 118.1, 117.8, 117.4 (t, *J*=6.0 Hz), 116.4, 116.3, 115.2 (t, *J*=258.5 Hz), 63.0, 55.8, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −100.82; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2N_2NaO_4$ $[M+Na]^+$ 421.0981, found 421.0976.

Ethyl 2,2-difluoro-2-(8-methyl-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3ja**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 55.2 mg, yield 72%. Yellow solid, m.p. 153～156 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.76～8.33 (m, 1H), 8.31 (s, 1H), 7.81 (dt, *J*=8.0, 0.8 Hz, 1H), 7.74 (t, *J*=2.8 Hz, 1H), 7.59～7.55 (m, 1H), 7.50 (t, *J*=1.2 Hz, 2H), 7.47～7.43 (m, 1H), 4.48 (q, *J*=7.2 Hz, 2H), 2.49 (s, 3H), 1.41 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.5, 163.0 (t, *J*=31.0 Hz), 147.6 (t, *J*=29.6 Hz), 140.4, 139.6 (t, *J*=2.1 Hz), 137.9, 135.0, 133.3, 133.0, 128.3, 128.2, 126.1 (t, *J*=3.4 Hz), 125.2, 124.5, 122.4, 117.8, 116.8 (t, *J*=5.9 Hz), 115.4 (t, *J*=258.2 Hz), 63.0, 21.3, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −101.06; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2N_2NaO_3$ $[M+Na]^+$ 405.1029, found 405.1027.

Ethyl 2,2-difluoro-2-(8-methoxy-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3ka**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 38.2 mg, yield 48%. Yellow solid, m.p. 168～172 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.79～8.77 (m, 1H), 8.02 (d, *J*=3.2 Hz, 1H), 7.82 (dt, *J*=8.0, 1.2 Hz, 1H), 7.74 (t, *J*=2.8 Hz, 1H), 7.60～7.54 (m, 2H), 7.48～7.44 (m, 1H), 7.23 (dd, *J*=8.8, 3.2 Hz, 1H), 4.48 (q, *J*=7.2 Hz, 2H), 3.95 (s, 3H), 1.42 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.0, 163.1 (t, *J*=30.9 Hz), 160.4, 145.8 (t, *J*=27.0 Hz), 137.8, 135.7 (t, *J*=1.9 Hz), 135.2, 128.4, 128.0, 126.3 (t, *J*=3.2 Hz), 126.1, 125.3, 122.4, 121.2, 118.0, 116.4 (t, *J*=5.9 Hz), 116.0, 115.6 (t, *J*=258.0 Hz), 63.0, 56.0, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −101.00; HRMS (ESI-TOF) calcd for $C_{21}H_{17}F_2N_2O_4$ $[M+H]^+$ 399.1158, found 399.1156.

Ethyl 2-(8-chloro-6-oxo-6*H*-benzo[5,6][1,4]diazepino-[1,2-*a*]indol-12-yl)-2,2-difluoroacetate (**3la**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 47.9 mg, yield 60%. Yellow solid, m.p. 137～138 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.74 (d, *J*=8.8 Hz, 1H), 8.50 (d, *J*=2.4 Hz, 1H), 7.85～7.82 (m, 1H), 7.81 (t, *J*=3.2 Hz, 1H) 7.66～7.59 (m, 2H), 7.54 (d, *J*=8.4 Hz, 1H), 7.48 (d, *J*=7.6 Hz, 1H), 4.47 (q, *J*=7.2 Hz, 2H), 1.41 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.1, 162.8 (t, *J*=30.8 Hz), 148.8 (t, *J*=30.1 Hz), 140.2 (t, *J*=1.8 Hz), 138.0, 135.7, 134.4, 134.1, 132.7, 128.7, 128.3, 126.0, 125.8 (t, *J*=3.2 Hz), 125.6, 122.7, 118.1 (t, *J*=6.0 Hz), 117.9, 115.1 (t, *J*=258.7 Hz), 63.1, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −100.87; HRMS (ESI-TOF) calcd for $C_{20}H_{13}ClF_2N_2NaO_3$ $[M+Na]^+$ 425.0479, found 425.0480.

Ethyl 2,2-difluoro-2-(7-methyl-6-oxo-6*H*-benzo[5,6]-[1,4]diazepino[1,2-*a*]indol-12-yl)acetate (**3ma**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 26.6 mg, yield 35%. Yellow solid, m.p. 162～164 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.35～8.33 (m, 1H), 7.80 (dt *J*=8.0, 0.8 Hz, 1H), 7.56～7.51 (m, 2H), 7.47 (t, *J*=7.6 Hz, 1H), 7.41～7.33 (m, 3H), 4.45 (q, *J*=7.2 Hz, 2H), 2.70 (s, 3H), 1.38 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.6, 162.8 (t, *J*=30.8 Hz), 149.6 (t, *J*=30.0 Hz), 142.2, 140.8, 136.9, 132.7, 131.8, 128.5, 128.0, 127.8, 125.7, 125.1 (t, *J*=3.0 Hz), 124.6, 122.7, 114.8, 114.4 (t, *J*=5.1 Hz), 114.3 (t, *J*=256.8 Hz), 63.1, 22.8, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −102.64; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2N_2NaO_3$ $[M+Na]^+$ 405.1028, found 405.1027.

Ethyl 2,2-difluoro-2-(8-methoxy-1-methyl-6-oxo-6*H*-benzo[5,6][1,4]diazepino-[1,2-*a*]indol-12-yl)acetate (**3na**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 32.7 mg, yield 40%. Yellow solid, m.p. 167～168 ℃; ^{1}H NMR

(400 MHz, $CDCl_3$) δ: 8.60 (d, J=8.4 Hz, 1H), 8.00 (d, J=2.8 Hz, 1H), 7.75 (t, J=2.8 Hz, 1H), 7.54 (d, J=8.8 Hz, 1H), 7.50～7.46 (m, 1H), 7.27～7.24 (m, 1H), 7.22(dd, J=8.8, 2.8 Hz, 1H), 4.48 (q, J=7.2 Hz, 2H), 3.96 (s, 3H), 2.66 (s, 3H), 1.42 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.1, 163.2 (t, J=31.1 Hz), 160.4, 145.9 (t, J=29.7 Hz), 137.7, 135.8 (t, J=1.8 Hz), 135.1, 132.1, 128.3, 128.2, 126.2, 125.9 (t, J=3.2 Hz), 125.5, 121.1, 115.9, 115.6 (t, J=257.9 Hz), 115.4, 114.8 (t, J=6.0 Hz), 62.9, 55.9, 18.5, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −100.90; HRMS (ESI-TOF) calcd for $C_{22}H_{18}F_2N_2NaO_4$ $[M+Na]^+$ 435.1137, found 435.1132.

Ethyl 2,2-difluoro-2-(8-methoxy-2-methyl-6-oxo-6*H*-benzo[5,6][1,4]diazepino-[1,2-*a*]indol-12-yl)acetate (**3oa**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 34.6 mg, yield 42%. Yellow solid, m.p. 155～158 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.66 (d, J=8.8 Hz, 1H), 8.02 (d, J=3.2 Hz, 1H), 7.66 (t, J=2.8 Hz, 1H), 7.58～7.57 (m, 1H), 7.54 (d, J=8.8 Hz, 1H), 7.38 (dd, J=8.8, 1.6 Hz, 1H), 7.22 (dd, J=8.8, 3.2 Hz, 1H), 4.78 (q, J=7.2 Hz, 2H), 3.95 (s, 3H), 2.49 (s, 3H), 1.42 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.7, 163.2 (t, J=30.9 Hz), 160.4, 145.7 (t, J=29.6 Hz), 136.1, 135.8 (t, J=1.9 Hz), 135.3, 135.2, 129.8, 128.7, 126.4 (t, J=3.2 Hz), 126.0, 121.8, 120.1, 117.3, 116.3 (t, J=5.9 Hz), 116.0, 115.6 (t, J=258.0 Hz), 62.9, 55.9, 21.4, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: − 100.94; HRMS (ESI-TOF) calcd for $C_{22}H_{18}F_2N_2NaO_4$ $[M+Na]^+$ 435.1128, found 435.1132.

Ethyl-2-(2,8-dimethyl-6-oxo-6*H*-benzo[5,6][1,4]diazepino-[1,2-*a*]indol-12-yl)-2,2-difluoroacetate (**3pa**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=30∶1, 32.5 mg, yield 41%. Yellow solid, m.p. 190～192 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.63 (d, J=8.8 Hz, 1H), 8.33～8.32 (m, 1H), 7.67 (t, J=2.8 Hz, 1H), 7.57～7.56 (m, 1H), 7.49 (d, J=1.2 Hz, 2H), 7.38 (dd, J=8.8, 1.6 Hz, 1H), 4.78 (q, J=7.2 Hz, 2H), 2.49 (s, 6H), 1.41 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.2, 163.1 (t, J=30.8 Hz), 147.5 (t, J=29.6 Hz), 140.3, 139.6, 136.3, 135.1, 134.9, 133.3, 133.0, 130.0, 128.6, 126.1 (t, J=3.4 Hz), 124.4, 121.9, 117.5, 116.7 (t, J=5.9 Hz), 115.4 (t, J=258.2 Hz), 62.9, 21.4, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −101.00; HRMS (ESI-TOF) calcd for $C_{22}H_{18}F_2N_2NaO_3$ $[M+Na]^+$ 419.1180, found 419.1183.

N,*N*-Diethyl-2,2-difluoro-2-(2-methyl-6-oxo-6*H*-benzo-[5,6][1,4]diazepino[1,2-*a*]-indol-12-yl)acetamide (**3eb**): Eluent: *V*(petroleum ether)∶*V*(acetone)=25∶1, 47.9 mg, yield 59%. Yellow solid, m.p. 156～158 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.64 (d, J=8.8 Hz, 1H), 8.52 (dd, J=8.0, 1.6 Hz, 1H), 7.79 (t, J=2.8 Hz, 1H), 7.72～7.68 (m, 1H), 7.63～7.60 (m, 2H), 7.57～7.53 (m, 1H), 7.14 (dd, J=8.8, 2.0 Hz, 1H), 3.51 (q, J=6.8 Hz, 2H), 3.30 (q, J=6.8 Hz, 2H), 2.51 (s, 3H), 1.28 (t, J=6.8 Hz, 3H), 1.13 (t, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.3, 162.2 (t, J=27.1 Hz), 149.2 (t, J=29.4 Hz), 142.0, 136.3, 135.2, 134.1, 133.0, 132.8, 130.2, 129.5, 128.6, 126.2 (t, J=3.0 Hz), 124.8, 122.0, 117.7 (t, J=6.1 Hz), 117.4, 116.0 (t, J=255.8 Hz), 42.3, 41.1, 21.4, 13.9, 12.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −95.35; HRMS (ESI-TOF) calcd for $C_{23}H_{21}F_2N_3NaO_2$ $[M+Na]^+$ 432.1503, found 432.1500.

12-(1,1-Difluoro-2-oxo-2-(pyrrolidin-1-yl)ethyl)-2-methyl-6*H*-benzo[5,6][1,4]diazepino[1,2-*a*]indol-6-one (**3ec**): *V*(petroleum ether)∶*V*(acetone)=30∶1, 28.5 mg, yield 35%. Yellow solid, m.p. 222～224 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.64 (d, J=8.8 Hz, 1H), 8.52 (dd, J=8.0, 1.6 Hz, 1H), 7.79 (t, J=2.8 Hz, 1H), 7.72～7.68 (m, 1H), 7.60～7.52 (m, 3H), 7.41 (dd, J=8.8, 1.6 Hz, 1H), 3.70 (t, J=6.8 Hz, 2H), 3.56 (t, J=5.6 Hz, 2H), 2.51 (s, 3H), 1.94～1.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.2, 161.6 (t, J=28.0 Hz), 148.8 (t, J=29.5 Hz), 141.9 (t, J=1.67 Hz), 136.3, 135.2, 134.1, 133.02, 132.97, 130.2, 129.6, 128.6, 126.4 (t, J=3.0 Hz), 124.8, 122.1, 177.7 (t, J=6.1 Hz), 117.4, 116.0 (t, J=256.5 Hz), 47.5, 47.2 (t, J=4.3 Hz), 26.6, 23.6, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: − 97.67; HRMS (ESI-TOF) calcd for $C_{23}H_{19}F_2N_3NaO_2$ $[M+Na]^+$ 430.1340, found 430.1343.

12-(1,1-Difluoro-2-oxo-2-(piperidin-1-yl)ethyl)-2-methyl-6*H*-benzo[5,6][1,4]-diazepino[1,2-*a*]indol-6-one (**3ed**): Eluent: *V*(petroleum ether)∶*V*(acetone)=25∶1, 45.0 mg, yield 53%. Yellow solid, m.p. 183～185 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.64 (d, J=8.4 Hz, 1H), 8.52 (dd, J=8.4, 1.6 Hz, 1H), 7.80 (t, J=2.8 Hz, 1H), 7.74～7.67 (m, 2H), 7.60 (s, 1H), 7.58～7.53 (m, 1H), 7.42 (dd, J=8.8, 1.6 Hz, 1H), 3.70 (t, J=4.8 Hz, 2H), 3.41 (t, J=5.6 Hz, 2H), 2.52 (s, 3H), 1.68～1.59 (m, 4H), 1.43～1.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.3, 161.3 (t, J=27.0 Hz), 149.1 (t, J=28.7 Hz), 141.9, 136.3, 135.2, 134.2, 133.0, 132.9, 130.2, 129.5, 128.6, 126.1 (t, J=2.8 Hz), 124.8, 122.1, 177.8 (t, J=6.0 Hz), 117.4, 116.1 (t, J=255.8 Hz), 47.5 (t, J=3.8 Hz), 44.3, 25.9, 25.6, 24.4, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −95.06; HRMS (ESI-TOF) calcd for $C_{24}H_{21}F_2N_3NaO_2$ $[M+Na]^+$ 444.1497, found 444.1500.

12-(1,1-Difluoro-2-morpholino-2-oxoethyl)-2-methyl-6*H*-benzo[5,6][1,4]diazepino[1,2-*a*]indol-6-one (**3ee**): Eluent: *V*(petroleum ether)∶*V*(acetone)=20∶1, 50.7 mg, yield 60%. Yellow solid, m.p. 217～220 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57 (d, J=8.8 Hz, 1H), 8.46 (dd, J=8.0, 1.6 Hz, 1H), 7.72 (t, J=2.4 Hz, 1H), 7.68～7.64 (m 1H), 7.59 (dd, J=8.0, 1.6 Hz, 1H), 7.52～7.47 (m, 2H), 7.34 (dd, J=8.0, 2.0 Hz, 1H), 3.17 (s, 4H), 3.50～3.48 (m, 2H), 3.44～3.40 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.1, 161.9 (t, J=27.1 Hz), 148.8 (t, J=29.0 Hz), 141.7, 136.4, 135.3, 134.3, 133.2, 133.0, 130.4, 129.8, 128.6, 125.9 (t, J=3.0 Hz), 124.7, 122.1, 178.0 (t, J=6.1 Hz), 117.6, 116.3 (t, J=256.3 Hz), 66.7, 66.3, 47.1, 43.5, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −94.94; HRMS (ESI-TOF) calcd for $C_{23}H_{19}F_2N_3NaO_3$ $[M+Na]^+$ 446.1289, found 446.1292.

tert-Butyl 4-(2,2-difluoro-2-(2-methyl-6-oxo-6*H*-benzo-[5,6][1,4]diazepino[1,2-*a*]-indol-12-yl)acetyl)piperazine-1-carboxylate (**3ef**): Eluent: *V*(petroleum ether)∶*V*(acetone)=20∶1, 58.5 mg, yield 56%. Yellow solid, m.p. 216～218 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.64

(d, J=8.8 Hz, 1H), 8.54 (dd, J=7.6, 1.6 Hz, 1H), 7.80 (t, J=2.8 Hz, 1H), 7.74～7.70 (m, 1H), 7.65～7.55 (m, 3H), 7.42 (dd, J=8.8, 2.0 Hz, 1H), 3.77～3.75 (m, 2H), 3.56～3.53 (m, 2H), 3.48～3.46 (m, 2H), 3.36～3.33 (m, 2H), 2.51 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.0, 161.9 (t, J=21.8 Hz), 154.4, 148.8 (t, J=29.1 Hz), 141.7, 136.4, 135.3, 134.3, 133.2, 132.9, 130.4, 129.8, 128.5, 125.9 (t, J=2.9 Hz), 124.7, 122.1, 118.0 (t, J=6.1 Hz), 117.5, 116.3 (t, J=256.4 Hz), 80.4, 46.4, 43.1, 34.2, 28.3, 22.3, 21.4, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −94.76; HRMS (ESI-TOF) calcd for $C_{28}H_{28}F_2N_4NaO_4$ $[M+Na]^+$ 545.1981, found 545.1976.

12-(1,1-Difluoro-2-oxo-2-(4-(pyrimidin-2-yl)piperazin-1-yl)ethyl)-2-methyl-6*H*-benzo[5,6][1,4]diazepino[1,2-*a*]-indol-6-one (**3eg**): Eluent: *V*(petroleum ether)∶*V*(acetone)=20∶1, 48.1 mg, yield 48%. Yellow solid, m.p. 221～224 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.67 (d, J=8.8 Hz, 1H), 8.54 (dd, J=8.0, 1.2 Hz, 1H), 8.29 (d, J=4.8 Hz, 2H), 7.84 (t, J=2.8 Hz, 1H), 7.72～7.63 (m, 3H), 7.59～7.54 (m, 1H), 7.46～7.23 (m, 1H), 6.52 (t, J=4.8 Hz, 1H), 3.97～3.95 (m, 2H), 3.88～3.45 (m, 2H), 3.77～3.74 (m, 2H), 3.60～3.58 (m, 2H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.1, 162.0 (t, J=28.5 Hz), 161.4, 157.8, 148.8 (t, J=26.0 Hz), 141.7, 136.5, 135.3, 134.3, 133.2, 133.0, 130.4, 129.8, 128.6, 126.0 (t, J=2.6 Hz), 124.7, 122.1, 118.0 (t, J=6.1 Hz), 117.6, 116.3 (t, J=253.9 Hz), 110.6, 46.4, 43.4, 43.3, 43.2, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −94.81; HRMS (ESI-TOF) calcd for $C_{27}H_{22}F_2N_6NaO_2$ $[M+Na]^+$ 523.1672, found 523.1670.

2,2-Difluoro-2-(2-methyl-6-oxo-6*H*-benzo[5,6][1,4]-diazepino[1,2-*a*]indol-12-yl)-*N*-phenylacetamide (**3eh**): Eluent: *V*(petroleum ether)∶*V*(acetone)=15∶1, 19.5 mg, yield 23%. Yellow solid, m.p. 219～222 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.59 (d, J=8.8 Hz, 1H), 8.46 (d, J=8.0 Hz, 1H), 8.14 (s, 1H), 7.71 (t, J=3.2 Hz, 1H), 7.67～7.63 (m, 2H), 7.60 (d, J=7.6 Hz, 1H), 7.55～7.53 (m, 2H), 7.49 (t, J=7.6 Hz, 1H), 7.41～7.37 (m, 3H), 7.21 (t, J=7.2 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.2, 160.8 (t, J=30.2 Hz), 148.8 (t, J=28.7 Hz), 141.7, 136.4, 136.3, 135.2, 134.0, 133.1, 132.9, 130.2, 129.6, 129.3, 128.5, 126.2 (t, J=2.8 Hz), 125.5, 124.8, 122.0, 120.3, 117.5 (t, J=6.2 Hz), 117.4, 115.2 (t, J=255.5 Hz), 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −101.53; HRMS (ESI-TOF) calcd for $C_{25}H_{18}F_2N_3O_2$ $[M+H]^+$ 430.1360, found 430.1367.

12-(1,1-Difluoro-2-oxo-2-phenylethyl)-2-methyl-6*H*-benzo[5,6][1,4]diazepino[1,2-*a*]indol-6-one (**3ei**): Eluent: *V*(petroleum ether)∶*V*(acetone)=35∶1, 38.0 mg, yield 46%. Yellow solid, m.p. 204～205 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.67 (d, J=8.8 Hz, 1H), 8.49 (dd, J=8.0, 2.0 Hz, 1H), 8.04 (d, J=7.6 Hz, 2H), 7.86 (t, J=3.2 Hz, 1H), 7.63～7.62 (m, 1H), 7.58～7.54 (m, 2H), 7.49 (dd, J=7.6, 1.6 Hz, 1H), 7.46～7.41 (m, 3H), 7.27 (dd, J=8.0, 1.6 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 187.9 (t, J=27.2 Hz), 164.1, 150.1 (t, J=29.4 Hz), 141.5, 136.5, 135.3, 134.1, 133.6, 133.3, 133.1, 132.8, 130.4, 130.0 (t, J=2.2 Hz), 129.7, 128.7, 128.5, 126.3 (t, J=3.2 Hz), 124.6, 122.1, 117.7 (t, J=5.9 Hz), 117.6, 116.4 (t, J=259.1 Hz), 21.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −96.81; HRMS (ESI-TOF) calcd for $C_{25}H_{16}F_2N_2NaO_2$ $[M+Na]^+$ 437.1079, found 437.1078.

2-Methyl-12-(perfluorobutyl)-6*H*-benzo[5,6][1,4]diazepino[1,2-*a*]indol-6-one (**3ej**): Eluent: *V*(petroleum ether)∶*V*(acetone)=100∶1, 65.1 mg, yield 68%. Yellow solid, m.p. 102～103 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57 (d, J=8.8 Hz, 1H), 8.48～8.45 (m, 1H), 7.75～7.69 (m, 2H), 7.75～7.53 (m, 3H), 7.38 (dd, J=8.8, 1.6 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.2, 145.3 (t, J=26.7 Hz), 141.3, 136.2, 135.2, 134.1, 132.8, 132.7, 130.3, 129.9, 128.3, 126.1 (t, J=2.4 Hz), 124.9, 121.9, 119.1 (t, J=33.7 Hz), 117.2, 117.1 (t, J=7.6 Hz), 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −80.61, −106.15, −119.10, −123.01; HRMS (ESI-TOF) calcd for $C_{21}H_{12}F_9N_2O$ $[M+H]^+$ 479.0811, found 479.0806.

2-Methyl-12-(trifluoromethyl)-6*H*-benzo[5,6][1,4]diazepino[1,2-*a*]indol-6-one (**3ek**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=100∶1, 38.5 mg, yield 58%. Yellow solid, m.p. 172～173 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.63 (d, J=8.8 Hz, 1H), 8.53 (dd, J=8.0, 1.6 Hz, 1H), 7.81 (dd, J=8.0, 1.6 Hz, 1H), 7.75 (td, J=7.2, 1.6 Hz, 1H), 7.60～7.56 (m, 2H), 7.54～7.52 (m, 1H), 7.42 (dd, J=8.8, 2.0 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.2, 143.6 (d, J=33.7 Hz), 141.6, 136.4, 135.3, 134.2, 133.4, 133.0, 130.3, 129.8, 128.3, 126.0, 124.9, 121.9, 119.3 (d, J=277.7 Hz), 117.4, 117.0 (q, J=4.3 Hz), 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −66.11; HRMS (ESI-TOF) calcd for $C_{18}H_{12}F_3N_2O$ $[M+H]^+$ 329.0905, found 329.0902.

12-(Difluoromethyl)-2-methyl-6*H*-benzo[5,6][1,4]diazepino[1,2-*a*]indol-6-one (**3el**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=100∶1, 20.7 mg, yield 33%. Yellow solid, m.p. 163～166 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.66 (d, J=8.8 Hz, 1H), 8.56～8.53 (m, 1H), 7.76～7.70 (m, 3H), 7.58～7.53 (m, 2H), 7.41 (dd, J=8.8, 1.6 Hz, 1H), 6.58 (t, J=55.2 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.3, 149.4 (t, J=26.9 Hz), 142.7, 136.3, 135.1, 134.1, 133.1, 130.0, 129.3, 128.7, 126.4, 124.8, 121.9, 118.3 (t, J=248.5 Hz), 117.6, 116.8 (t, J=5.4 Hz), 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −113.18; HRMS (ESI-TOF) calcd for $C_{18}H_{13}F_2N_2O$ $[M+H]^+$ 311.100, found 311.0996.

Ethyl 2,2-difluoro-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)acetate (**4aa**): Eluent: *V*(petroleum ether)∶*V*(ethyl acetate)=50∶1, colorless liquid, 85.9 mg, yield 77%. ^{1}H NMR (400 MHz, $CDCl_3$): 4.38～4.33 (q, J=7.2 Hz, 2H), 1.62～1.53 (m, 6H), 1.37 (t, J=7.2 Hz, 3H), 1.20～1.19 (m, 6H), 1.17 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.7 (t, J=42.6 Hz), 115.5 (t, J=269.9 Hz), 63.0, 61.4, 40.2, 33.4 (t, J=4.4 Hz), 20.8, 16.9, 13.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −73.46.

Supporting Information Mechanism study; ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra for compounds **1a**～**1p**,

3aa～**3pa**, **3eb**～**3el**, **4aa**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

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