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Synthesis of substituted tetrahydron-1*H*-carbazol-1-one and analogs via PhI(OCOCF$_3$)$_2$-mediated oxidative C–C bond formation

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ABSTRACT

A variety of tetrahydro-1*H*-carbazol-1-ones and analogs were conveniently synthesized from the reaction of the corresponding 2-(phenylamino)cyclohex-2-enone with hypervalent iodine reagent PhI(OCOCF$_3$)$_2$ (PIFA), through a direct intramolecular oxidative C(sp^2)–C(sp^2) bond formation. This approach realized the construction of the biologically important tetrahydro-1*H*-carbazol-1-one and tetrahydrocyclohepta[*b*]indol-6(5*H*)-one skeletons. The mechanism of the process was proposed and briefly discussed.

1. Introduction

Nitrogen-containing heterocycles are structural constituents of many natural products and medicinally important agents. Among them, tetrahydro-1*H*-carbazol-1-one and its analogs have been widely identified in many anti-virus and anti-cancer prodrugs. For example, diketo acid **I** can act as an HIV integrase inhibitor by specifically inhibiting the strand transfer step.[1] Compound **II** was found to be an active anti-prion agent by obstructing the accumulation of PrPSc.[2] Besides, significant activities against bacteria have been observed in dispirooxindolopyrrolizidine **III**.[3] What is common for the above compounds **I**–**III** is that they all bear a tetrahydro-1*H*-carbazole-1-one skeleton in their respective structure. Furthermore, the *R*,*R*-diastereomer of compound **IV**, derived from 4-Br-tetrahydro-1*H*-carbazole-1-one was proven to be active against HPV (human papillomaviruses) with low cytotoxicity and suitable pharmacokinetic profile.[4] Besides, tetrahydrocyclohepta[*b*]indol-6(5*H*)-one, an analog of tetrahydro-1*H*-carbazol-1-one, can also act as useful building blocks for the construction of some biologically important pharmaceutical agents. For example, pentacycle **V** represents a new class of aurora kinase inhibitors with excellent oral availability and high potency against tumor (Fig. 1).[5]

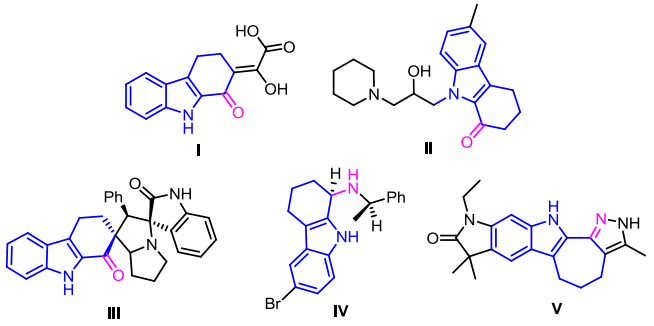

Fig. 1. Biologically important pharmaceutical agents derived from tetrahydro-1*H*-carbazol-1-ones or its analogs.

Owing to the significant biological activities, many methods have been developed for the construction of tetrahydro-1*H*-carbazol-1-one skeletons. To the best of our knowledge, the existing methods can generally be assorted into three categories, including the well-known Fischer indole synthesis (Fig. 2, path a),[6] oxidation of the corresponding tetrahydro-1*H*-carbazol[1,7] (Fig. 2, path b), and intramolecular condensation through Friedel–Crafts reaction (Fig. 2, path c).[8] It is worth noting that in 2012, Bautista et al.[9] tried to synthesize tetrahydro-1*H*-carbazol-1-one **2b** from 2-(phenylamino)cyclohex-2-enone **1b** through the classical Pd-mediated

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C–H activation/C–C bond forming strategy. Unfortunately, what they obtained was the aromatized product **3** rather than the desired tetrahydro-1*H*-carbazol-1-one **2b** (Scheme 1).

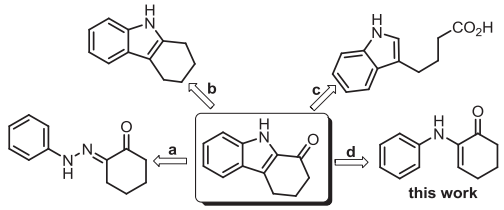
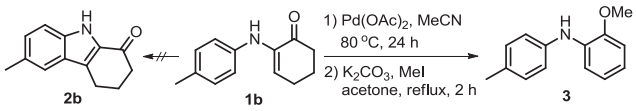


Fig. 2. Synthetic strategies for the construction of tetrahydro-1*H*-carbazol-1-one skeletons.



Scheme 1. Pd-mediated aromatization of compound **1b** rather than the expected oxidative C–C formation by Bautista.

In 2009, we succeeded in the construction of indole product **B** from *N*-aryl enamine **A** through $PhI(OAc)_2$-mediated oxidative C–C bond formation (Fig. 3, Eq. 1).[10] Later on, when we applied the method as an attempt for the synthesis of carbozolone **C** by subjecting the cyclic enamine substrate **D** to the same reaction conditions, only the α-iodinated *N*-arylated product **E** was obtained (Fig. 3, Eq. 2).[11] In our continuation of search for new applications of metal-free oxidative C–C bond formation, we were intrigued to explore the possibility of forming the biologically important tetrahydro-1*H*-carbazol-1-one compound **2** via ring-closure reaction of **1** mediated by a hypervalent iodine reagent.

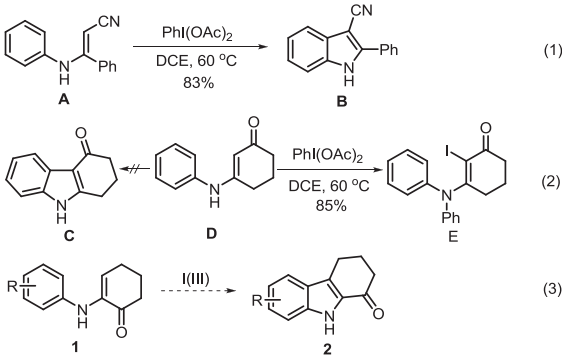
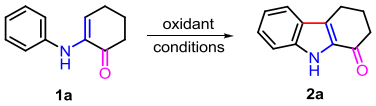


Fig. 3. Hypervalent iodine-mediated oxidations of different *N*-aryl enamine substrates.

2. Results and discussion

To begin with, 2-(phenylamino)cyclohex-2-enone **1a**, which can be easily prepared by the known methods from the commercially available cyclohexane-1,2-dione in two steps,[12,13] was selected as the model substrate to test the feasibility of the proposed transformation. We were pleased to find that the reaction of **1a** with PIFA in DCE (0.1 M) indeed led to the expected tetrahydro-1*H*-carbazol-1-one **2a** in 45% yield, although the reactions with $PhI(OAc)_2$ (PIDA),[14] PhIO, and IBX were unsuccessful (Table 1, entries 1–4). When the concentration of **1a** in DCE was lowered to 0.05 M from 0.1 M, an improved yield was achieved (Table 1, entry 5). Further solvent screening showed that MeOH, DMF, and dioxane were not effective for the reaction, while CH_3CN and TFE were equally eligible as solvents as DCE (Table 1, entries 5–10). Considering that the free-NH moiety in product **2a** was liable to further oxidization in the presence of PIFA, we implemented two strategies: (a) by carrying out the reaction at a lower temperature for the sake of hindering possible side reactions; (b) switching the solvent to Ac_2O for the reason that the generated **2a** could be simultaneously protected by an acyl group. As expected, the reaction in TFE at −30 °C greatly improved the yield to 75% (Table 1, entry 11). And to our contentment, the same reaction run in Ac_2O was found to give product **2a** in a satisfactory 86% yield, with no formation of the *N*-acylated product (Table 1, entry 12). Further screening showed that operating the reaction in this solvent at lower temperature was not necessary (Table 1, entry 13).

Table 1
Optimization of reaction conditions[a]



Entry	Oxidant (1.1 equiv)	Solvent	Concn (mol/L)	*t* (°C)	Time	Yield[b] (%)
1	PIDA	DCE	0.1	rt	12 h	Trace[c]
2	PIFA	DCE	0.1	rt	10 min	45
3	PhIO	DCE	0.1	rt	12 h	NR
4	IBX	DMSO	0.1	rt	12 h	NR
5	PIFA	DCE	0.05	rt	10 min	55
6	PIFA	TFE	0.05	rt	10 min	56
7	PIFA	MeOH	0.05	rt	10 min	trace
8	PIFA	DMF	0.05	rt	10 min	ND
9	PIFA	Dioxane	0.05	rt	10 min	ND
10	PIFA	CH_3CN	0.05	rt	10 min	49
11	PIFA	TFE	0.05	−30	10 min	75
12	*PIFA*	*Ac_2O*	*0.05*	*rt*	*10 min*	*86*
13	PIFA	Ac_2O	0.05	−30	20 min	84

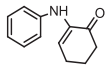
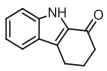
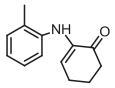
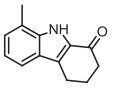
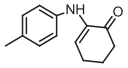
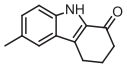
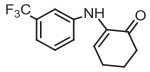
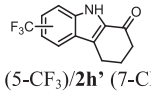
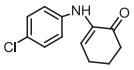
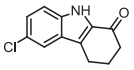
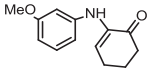
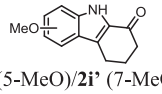
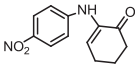
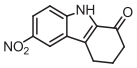
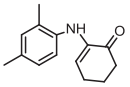
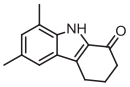
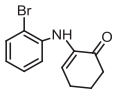
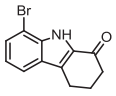
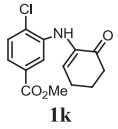
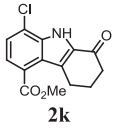
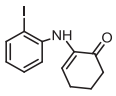
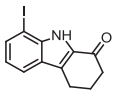
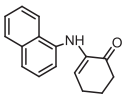
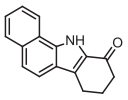
[a] General condition: (1) for entries 1–4, **1a** (0.6 mmol), oxidant (0.66 mmol) in solvent (6 mL); for entries 5–13, **1a** (0.6 mmol), oxidant (0.66 mmol) in solvent (12 mL).
[b] Isolated yields.
[c] Compound **1a** was 60% recovered.

With the optimal reaction conditions established (Table 1, entry 12), the scope and limitation of the method were explored by testing out on the variously substituted anilines. The result indicated that this method could be well applied to various *N*-aryl enaminones bearing either electron-donating or electron-withdrawing substituents (Table 2, entries 2–12). Notably, the presence of *para*-nitro group in the phenyl ring of the substrate did not prevent the occurrence of the cyclization, albeit a lower yield of the desired product was obtained (Table 2, entry 4). *meta*-Substituted substrates have the possibility of producing two regioisomers. For the reaction regarding *N*-aryl enaminone **1h**, bearing a *meta*-CF_3 group, two inseparable regioisomers were generated. Comparably, the reaction of the substrate with a *meta*-MeO group gave two separable isomers in relatively higher yield. When applying this method to some other substrates such as those bearing two substituents or having the phenyl ring replaced by a naphthyl ring, the desired products were also achieved (Table 2, entries 10–12).

Encouraged by the above results, we proceeded to investigate whether the method was applicable to the analogous substrates where the cyclohexene ring in **1** is turned into a cycloheptene ring. However, when substrate **3a** was subjected to the identical conditions, only less than 5% yield of the desired product was isolated. The low yield was mainly attributed to the fact that the enamine substrate was unstable under the reaction conditions. It quickly decomposed into aniline, which underwent a rapid acetylation and led to the unexpected acetyl aniline (isolated in 51% yield). Inspired by Boger's work,[15] we incorporated triethylamine (TEA) in the reaction as a stabilizer of the sensitive substrates. To our satisfaction, the desired product **4a** was achieved in 60% yield after treating **3a** with 1.5 equiv of PIFA in the presence of 10 equiv of TEA in TFE

Table 2
Synthesis of substituted tetrahydro-1*H*-carbazol-1-ones by PIFA[a]

1 **2**

Entry	Substrate	Product	Yield[b] (%)	Entry	Substrate	Product	Yield[b] (%)
1	 **1a**	 **2a**	86	7	 **1g**	 **2g**	55
2	 **1b**	 **2b**	63	8	 **1h**	 **2h** (5-CF_3)/**2h'** (7-CF_3)	55[c]
3	 **1c**	 **2c**	51	9	 **1i**	 **2i** (5-MeO)/**2i'** (7-MeO)	65[d]
4	 **1d**	 **2d**	36	10	 **1j**	 **2j**	71
5	 **1e**	 **2e**	67	11	 **1k**	 **2k**	46
6	 **1f**	 **2f**	30	12	 **1l**	 **2l**	36

[a] Reaction conditions: **1** (0.6 mmol), PIFA (0.66 mmol) in Ac_2O (12 mL).
[b] Isolated yields.
[c] An inseparable mixture, **2h**/**2h**′=0.45:0.55, the ratio was determined by ^1H NMR.
[d] Separable regioisomers, **2i**: 26%, **2i**′: 39%.

(trifluoroethanol) as the solvent.[16] Similarly, various substituted 7,8,9,10-tetrahydrocyclohepta[*b*]indol-6(5*H*)-ones bearing either an electron-donating or electron-withdrawing substituent in the phenyl ring were realized through this method (Table 3, entries 1–6). Although only moderate yields of the desired product were obtained, the presented method serves as a more convenient access to the various 7,8,9,10-tetrahydrocyclohepta[*b*]indol-6(5*H*)-ones while compared with the existing approaches, such as the well-known Fischer indole synthesis,[5,6e,17] oxidation of the corresponding 5,6,7,8,9,10-hexahydrocyclohepta[*b*]in-dole,[7b] and condensation through Friedel–Crafts reaction.[18]

In our previous work, we found the reaction between the cyclic enamine substrate **D** and PIDA could only lead to the α-iodinated *N*-arylated product **E** (Fig. 3, Eq. 2).[11] A reasonable explanation for the formation of the C–I bond during the process is that the hypervalent iodine reagent reacts first with the double bond of the enamine substrate.[19] Based on this, we proposed in path a that the intermediate iminium salt **F** was first afforded after the nucleophilic attack on the iodine center of PIFA by the nucleophilic enamine, with the loss of one trifluoroacetate anion. With the abstraction of one proton, the iminium salt **F** was converted to α-iodo enamine **G**. Next, an intramolecular electrophilic aromatic substitution reaction, facilitated by the electron-donating property of the amino moiety and the electron-withdrawing effect of the carbonyl moiety, took place, which resulted in iminium salt **I** via intermediate **H** and the release of a PhI and a trifluoroacetic acid molecules. At the abstraction of a proton from **I**, aromatization was realized and the desired indole skeleton **2a** was achieved (Scheme 2, path a).

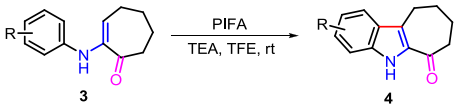
The reaction may also adopt an alternative pathway b. Initially, the nucleophilic attack of the N atom on the iodine center[20] of PIFA afforded ammonium salt **J**, which was converted to enamine **K** via proton transfer. Then **K** underwent electrocyclic ring-closure to give iminium salt **L**, which was converted to **M** by loss of a proton. Next, the release of one molecule of PhI and CF_3CO_2H from **M** resulted in the formation of imine **N**. The final tautomerization of **N** provided the title product **2a** (Scheme 2, path b).

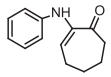
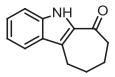
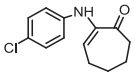
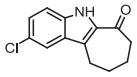
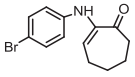
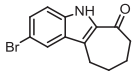
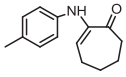
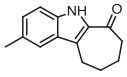
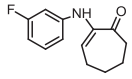
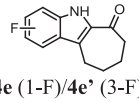
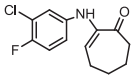
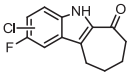
To gain further insight into the reaction mechanism, we carried out a control experiment using 2-(methyl(phenyl)amino) cyclohex-2-enone (**1**′) as substrate, in which a methyl group was substituted on the N atom. However, the reaction of **1**′ under the identical conditions provided no desired cyclized product **2**′ (Scheme 3), which clearly implied that the N–H moiety in the cyclic enamine substrate is important for the cyclization to occur. In this regard, our preliminary experiments show that the reaction might adopt the mechanistic pathway described in path b. Further investigation on the reaction mechanism is still in progress in our lab.

3. Conclusion

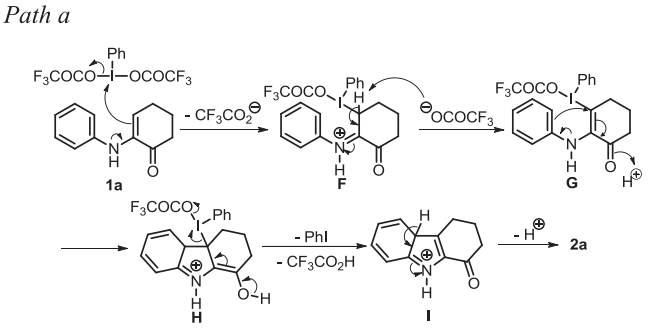
In summary, we have demonstrated the first synthesis of tetrahydro-1*H*-carbazol-1-ones and 7,8,9,10-tetrahydrocyclohep-ta[*b*]

Table 3
Synthesis of substituted 7,8,9,10-tetrahydrocyclohepta[*b*]-indol-6(5*H*)-ones via PIFA-mediated C–C oxidative coupling[a]

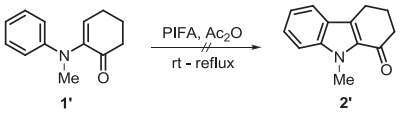


Entry	Substrate	Product	Yield[b] (%)
1	 **3a**	 **4a**	60
2	 **3b**	 **4b**	45
3	 **3c**	 **4c**	47
4	 **3d**	 **4d**	42
5	 **3e**	 **4e** (1-F)/**4e'** (3-F)	51[c]
6	 **3f**	 **4f** (1-Cl)/**4f'** (3-Cl)	48[c]

[a] Reaction condition: **1** (0.5 mmol), PIFA (0.75 mmol), TEA (5 mmol) in TFE (10 mL).
[b] Isolated yields.
[c] Inseparable isomers, **4e**/**4e'**=0.55:0.45, **4f**/**4f'**=0.45:0.55, the ratios were determined by ^{1}H NMR.



Scheme 2. Proposed mechanistic pathways.



Scheme 3. Further probe into the reaction mechanism.

indol-6(5*H*)-ones through a metal-free oxidative C–C bond coupling reaction mediated by PIFA, which has not been realized by any of the well-known transition metal-mediated oxidation annulation strategy. This general reaction tolerates a wide range of function groups and can be conveniently and effectively applied to the construction of the biologically important tetrahydro-1*H*-carbazol-1-one and 7,8,9,10-tetrahydrocyclohepta-[*b*]indol-6(5*H*)-one skeletons.

4. Experimental section

4.1. General information

Unless otherwise noted, all the reagents were purchased from commercial suppliers, used without further purification and all the reaction mixtures were stirred magnetically without precaution of contact with air. ^{1}H and ^{13}C NMR spectra were recorded on a 600 MHz NMR instrument (150 MHz for ^{13}C NMR) at 25 °C. The chemical shifts were recorded in parts per million (ppm) and referred as the internal standard to TMS: 0.00 ppm. The multiplicities are defined as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; and td, triplet of doublets. The coupling constants *J* are reported in hertz (Hz). High resolution mass spectra (HRMS) were obtained on a Q-TOF micro-spectrometer. Melting points were determined with a micro melting-point apparatus without correction. Unless otherwise noted, flash column chromatography was performed over silica gel 200–300 mesh, and the eluent was a mixture of petroleum ether (PE) and ethyl acetate (EA).

4.2. General procedure for the synthesis of 2-(substituted phenylamino)cyclohex-2-enone 1

A mixture of substituted aniline (1.5 mmol), 2-morpholinocyclohex-2-enone[12] (1.5 mmol), and *p*-toluenesulfonic acid monohydrate (1.5 mmol) in toluene (10 mL) was heated at 50 °C under N_2 for 2 h, during which time the solution became homogeneous. The mixture was cooled down to room temperature, diluted with EtOAc (30 mL), and washed with saturated aqueous $NaHCO_3$ (10 mL×3). The separated organic layer was dried with Na_2SO_4, filtered, and concentrated under vacuum. Purification of the crude residue by column chromatography using a mixture of PE and EA as eluent gave compounds **1a**–**l**.

Following the general procedure, the known compounds **1a**,[21] **1b**,[9] **1c**,[22] **1g**,[22] and **1i**,[9] were prepared in 95%, 68%, 58%, 55% and 74% yields, respectively. The properties and ^{1}H NMR data of **1a**, **1b**, **1c**, **1g**, and **1i** were consistent with those in the literature. The novel compounds **1d**–**f**, **1h**, and **1j**–**l** thus obtained were characterized as follows:

*4.2.1. 2-((4-Nitrophenyl)amino)cyclohex-2-enone (**1d**).* Following the general procedure, **1d** was purified by silica gel chromatography (20% EA/PE). Yield: 226 mg, 65%, orange solid, mp 119–121 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, *J*=9.0 Hz, 2H), 7.01 (d, *J*=9.0 Hz, 2H), 6.93 (s, 1H), 6.71 (t, *J*=4.8 Hz, 1H), 2.62–2.55 (m, 4H), 2.11–2.05 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.0, 148.2, 140.1, 134.4, 125.9,

123.7, 115.2, 37.4, 24.8, 22.4. HRMS (ESI): calculated for $[M+H]^+$ $C_{12}H_{13}N_2O_3^+$ 233.0921; found 233.0921.

*4.2.2. 2-((2-Bromophenyl)amino)cyclohex-2-enone (**1e**).* Following the general procedure, **1e** was purified by silica gel chromatography (10% EA/PE). Yield: 196 mg, 49%, yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (dd, J=7.8, 1.2 Hz, 1H), 7.26 (dd, J=7.8, 1.2 Hz, 1H), 7.20 (td, J=7.2, 1.2 Hz, 1H), 6.75 (td, J=7.8, 1.2 Hz, 2H), 6.43 (t, J=4.8 Hz, 1H), 2.60–2.56 (m, 2H), 2.49–2.45 (m, 2H), 2.06–2.01 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.1, 139.8, 135.7, 133.2, 127.9, 121.6, 118.8, 117.7, 114.3, 37.7, 24.7, 22.8. HRMS (ESI): calculated for $[M+H]^+$ $C_{12}H_{13}BrNO^+$ 266.0175; found 266.0176.

*4.2.3. 2-((2-Iodophenyl)amino)cyclohex-2-enone (**1f**).* Following the general procedure, **1f** was purified by silica gel chromatography (10% EA/PE). Yield: 379 mg, 81%, yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (dd, J=7.8, 1.2 Hz, 1H), 7.26–7.20 (m, 2H), 6.64 (td, J=8.4, 1.8 Hz, 1H), 6.54 (br s, 1H), 6.35 (t, J=4.8 Hz, 2H), 2.60–2.57 (m, 2H), 2.47–2.44 (m, 2H), 2.06–2.01 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.1, 142.4, 139.8, 136.1, 128.8, 122.7, 118.3, 118.1, 91.2, 37.7, 24.6, 22.9. HRMS (ESI): calculated for $[M+H]^+$ $C_{12}H_{13}INO^+$ 314.0036; found 314.0035.

*4.2.4. 2-((3-(Trifluoromethyl)phenyl)amino)cyclohex-2-enone (**1h**).* Following the general procedure, **1h** was purified by silica gel chromatography (10% EA/PE). Yield: 230 mg, 60%, white solid, mp 79–83 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (t, J=8.4 Hz, 1H), 7.26 (s, 1H), 7.16 (dd, J=7.8, 1.8 Hz, 1H), 7.13 (d, J=7.2 Hz, 1H), 6.52 (br s, 1H), 6.46 (t, J=4.8 Hz, 1H), 2.59–2.56 (m, 2H), 2.51–2.48 (m, 2H), 2.07–2.02 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.3, 142.6, 135.6, 131.6 (q, J_{F-C}=32 Hz), 129.8, 124.0 (q, J_{F-C}=270 Hz), 121.2, 118.2, 117.2 (q, J_{F-C}=4 Hz), 114.2 (q, J_{F-C}=4 Hz), 37.6, 24.6, 22.8. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{13}F_3NO^+$ 256.0944; found 256.0944.

*4.2.5. 2-((2,4-Dimethylphenyl)amino)cyclohex-2-enone (**1j**).* Following the general procedure, **1j** was purified by silica gel chromatography (10% EA/PE). Yield: 271 mg, 84%, yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.04 (d, J=7.8 Hz, 1H), 6.99 (s, 1H), 6.95 (d, J=7.8 Hz, 1H), 5.95 (br s, 1H), 5.92 (t, J=4.8 Hz, 1H), 2.57–2.54 (m, 2H), 2.40–2.36 (m, 2H), 2.27 (s, 3H), 2.17 (s, 3H), 2.02–1.97 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.7, 137.5, 137.3, 132.2, 131.6, 130.3, 127.1, 121.2, 115.0, 37.8, 24.5, 23.2, 20.7, 17.7. HRMS (ESI): calculated for $[M+H]^+$ $C_{14}H_{18}NO^+$ 216.1383; found 216.1382.

*4.2.6. Methyl 4-chloro-3-((6-oxocyclohex-1-enyl)amino)-benzoate (**1k**).* Following the general procedure, **1k** was purified by silica gel chromatography (10% EA/PE). Yield: 325 mg, 77%, white solid, mp 43–46 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, J=1.8 Hz, 1H), 7.46 (dd, J=7.8, 1.8 Hz, 1H), 7.40 (d, J=8.4 Hz, 1H), 6.91 (br s, 1H), 6.56 (t, J=4.8 Hz, 1H), 3.91 (s, 3H), 2.62–2.58 (m, 2H), 2.55–2.51 (m, 2H), 2.09–2.04 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.0, 166.5, 138.8, 135.1, 129.9, 129.3, 127.9, 121.6, 120.2, 117.3, 52.3, 37.6, 24.7, 22.7. HRMS (ESI): calculated for $[M+H]^+$ $C_{14}H_{15}ClNO_3^+$ 280.0735; found 280.0735.

*4.2.7. 2-(Naphthalen-1-ylamino)cyclohex-2-enone (**1l**).* Following the general procedure, **1l** was purified by silica gel chromatography (10% EA/PE). Yield: 265 mg, 74%, yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98–7.95 (m, 1H), 7.84–7.81 (m, 1H), 7.53 (d, J=7.8 Hz, 1H), 7.49–7.45 (m, 1H), 7.39 (t, J=7.2 Hz, 1H), 7.30 (dd, J=7.2, 1.2 Hz, 1H), 6.70 (s, 1H), 6.10 (t, J=4.8 Hz, 1H), 2.62–2.59 (m, 2H), 2.40–2.36 (m, 2H), 2.05–2.00 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.7, 137.7, 137.6, 134.7, 128.5, 128.0, 126.1, 125.8, 125.6, 123.1, 122.0, 116.9, 116.6, 37.8, 24.5, 23.2. HRMS (ESI): calculated for $[M+H]^+$ $C_{16}H_{16}NO^+$ 238.1226; found 238.1227.

4.3. General procedure for the synthesis of substituted tetrahydro-1*H*-carbazol-1-one 2

To a solution of 2-(substituted phenylamino)cyclohex-2-enone **1** (0.6 mmol) in Ac_2O (10 mL) was added a solution of PIFA (0.66 mmol) in Ac_2O (2 mL) in a dropwise manner. The reaction mixture was stirred at room temperature for 10 min, monitored by TLC. Then the solution was poured into saturated $NaHCO_3$ solution (50 mL) and $NaHCO_3$ (solid) was added portionwise while the mixture was stirred vigorously until no more CO_2 emerged. The mixture was extracted with EA (20 mL×3), and the combined organic layer was washed by brine (20 mL), dried with $NaSO_4$, filtered, and concentrated under vacuum. Purification of the crude residue by column chromatography using PE and EA as eluent gave compounds **2a**–**l**.

*4.3.1. 2,3,4,9-Tetrahydro-1H-carbazol-1-one[23] (**2a**).* Following the general procedure, **2a** was purified by silica gel chromatography (20% EA/PE). Yield: 96 mg, 86%, white solid, mp 165–168 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.58 (s, 1H), 7.66 (d, J=7.8 Hz, 1H), 7.40 (d, J=8.4 Hz, 1H), 7.30 (t, J=7.8 Hz, 1H), 7.08 (t, J=7.2 Hz, 1H), 2.96–2.93 (m, 2H), 2.57–2.55 (m, 2H), 2.17–2.14 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.3.2. 6-Methyl-2,3,4,9-tetrahydro-1H-carbazol-1-one[24] (**2b**).* Following the general procedure, **2b** was purified by silica gel chromatography (20% EA/PE). Yield: 75 mg, 63%, white solid, mp 189–191 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.43 (s, 1H), 7.43 (s, 1H), 7.28 (d, J=8.4 Hz, 1H), 7.13 (d, J=8.4 Hz, 1H), 2.93–2.90 (m, 2H), 2.55–2.52 (m, 2H), 2.37 (s, 3H), 2.16–2.11 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.3.3. 6-Chloro-2,3,4,9-tetrahydro-1H-carbazol-1-one[1] (**2c**).* Following the general procedure, **2c** was purified by silica gel chromatography (20% EA/PE). Yield: 67 mg, 51%, yellowish solid, mp 220–223 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.01 (s, 1H), 7.63 (s, 1H), 7.36 (d, J=9.0 Hz, 1H), 7.31 (d, J=8.4 Hz, 1H), 2.99–2.96 (m, 2H), 2.68–2.65 (m, 2H), 2.30–2.25 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.3.4. 6-Nitro-2,3,4,9-tetrahydro-1H-carbazol-1-one[24] (**2d**).* Following the general procedure, **2d** was purified by silica gel chromatography (20% EA/PE). Yield: 50 mg, 36%, orange solid, mp 252–255 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.68 (s, 1H), 8.26 (dd, J=9.0, 1.8 Hz, 1H), 7.50 (d, J=9.0 Hz, 1H), 3.09–3.07 (m, 2H), 2.74–2.71 (m, 2H), 2.36–2.31 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.3.5. 8-Bromo-2,3,4,9-tetrahydro-1H-carbazol-1-one[24] (**2e**).* Following the general procedure, **2e** was purified by silica gel chromatography (20% EA/PE). Yield: 106 mg, 67%, white solid, mp 154–156 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.71 (s, 1H), 7.70 (dd, J=10.8, 8.4 Hz, 1H), 7.54 (dd, J=7.2, 4.8 Hz, 1H), 7.03 (dd, J=14.4, 7.8 Hz, 1H), 2.97–2.93 (m, 2H), 2.60–2.57 (m, 2H), 2.18–2.14 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.3.6. 8-Iodo-2,3,4,9-tetrahydro-1H-carbazol-1-one (**2f**).* Following the general procedure, **2f** was purified by silica gel chromatography (20% EA/PE). Yield: 56 mg, 30%, white solid, mp 133–135 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.73 (d, J=7.8 Hz, 1H), 7.64 (d, J=8.4 Hz, 1H), 6.93 (t, J=7.8 Hz, 1H), 3.01–2.99 (m, 2H), 2.69–2.66 (m, 2H), 2.31–2.26 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 190.1,

139.9, 135.6, 131.7, 129.4, 125.9, 121.5, 121.2, 77.8, 38.4, 24.4, 21.0. HRMS (ESI): calculated for $[M+H]^+$ $C_{12}H_{11}INO^+$ 311.9880; found 311.9880.

4.3.7. 8-Methyl-2,3,4,9-tetrahydro-1H-carbazol-1-one[24] (***2g***). Following the general procedure, **2g** was purified by silica gel chromatography (20% EA/PE). Yield: 66 mg, 55%, white solid, mp 156–160 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.48 (s, 1H), 7.48 (d, J=7.8 Hz, 1H), 7.09 (d, J=6.6 Hz, 1H), 6.99 (t, J=7.8 Hz, 1H), 2.95–2.92 (m, 2H), 2.58–2.55 (m, 2H), 2.48 (s, 3H), 2.17–2.12 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.3.8. 5-(Trifluoromethyl)-2,3,4,9-tetrahydro-1H-carbazol-1-one (**2h**)/7-(trifluoromethyl)-2,3,4,9-tetrahydro-1H-carbazol-1-one (**2h′**).* Following the general procedure, **2h**/**2h′** was purified by silica gel chromatography (10% EA/PE). Yield: 78 mg, 51%, white solid, mp 160–164 °C. ^{1}H NMR (600 MHz, $CDCl_3$) isomer **2h** δ 9.34 (s, 1H), 7.70 (d, J=8.4 Hz, 1H), 7.50 (d, J=7.2 Hz, 1H), 7,40 (t, J=7.8 Hz, 1H), 3.14–3.12 (m, 2H), 2.75–2.70 (m, 2H), 2.34–2.27 (m, 2H); Isomer **2h′** δ 9.86 (s, 1H), 7.78 (s, 1H), 7.76 (d, J=8.4 Hz, 1H), 7.37 (d, J=8.4 Hz, 1H), 3.06–3.03 (m, 2H), 2.75–2.70 (m, 2H), 2.34–2.27 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.4, 191.9, 138.4, 136.7, 133.1, 132.5, 129.0, 128.7(q, J_{F-C}=32 Hz), 127.9, 127.2, 125.5, 125.3, 125.2, 123.7, 123.7, 123.5, 123.4, 122.1, 121.4, 118.8 (q, J_{F-C}=6 Hz), 117.0, 116.8, 110.4 (q, J_{F-C}=5 Hz), 38.3, 37.9, 24.9, 24.8, 22.7, 21.3. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{11}F_3NO^+$ 254.0787; found 254.0787.

4.3.9. 5-Methoxy-2,3,4,9-tetrahydro-1H-carbazol-1-one[6h] (***2i***). Following the general procedure, **2i** was purified by silica gel chromatography (20% EA/PE). Yield: 33 mg, 26%, yellow solid, mp 150–152 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.24 (t, J=7.8 Hz, 1H), 6.99 (d, J=8.4 Hz, 1H), 6.45 (d, J=7.8 Hz, 1H), 3.23–3.20 (m, 2H), 2.63–2.60 (m, 2H), 2.25–2.20 (m, 2H). The ^{1}H NMR data was consistent with that in the literature.

4.3.9.1. 7-Methoxy-2,3,4,9-tetrahydro-1H-carbazol-1-one[6h] (***2i′***). Following the general procedure, **2i′** was purified by silica gel chromatography (20% EA/PE). Yield: 50 mg, 39%, yellow solid, mp 139–142 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.04 (s, 1H), 6.83–6.79 (m, 2H), 3.87 (s, 1H), 2.98–2.95 (m, 2H), 2.65–2.62 (m, 2H), 2.27–2.22 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

4.3.10. 6,8-Dimethyl-2,3,4,9-tetrahydro-1H-carbazol-1-one[6h] (***2j***). Following the general procedure, **2j** was purified by silica gel chromatography (10% EA/PE). Yield: 91 mg, 71%, yellow solid, mp 190–193 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.27 (s, 1H), 7.01 (s, 1H), 2.99–2.96 (m, 2H), 2.66–2.63 (m, 2H), 2.45 (s, 3H), 2.42 (s, 3H), 2.28–2.23 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.3.11. Methyl 8-chloro-1-oxo-2,3,4,9-tetrahydro-1H-carbazole-5-carboxylate (**2k**).* Following the general procedure, **2k** was purified by silica gel chromatography (10% EA/PE). Yield: 77 mg, 46%, white solid, mp 109–112 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.71 (d, J=8.4 Hz, 1H), 7.37 (d, J=8.4 Hz, 1H), 3.97 (s, 3H), 3.26–3.23 (m, 2H), 2.67–2.65 (m, 2H), 2.26–2.21 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.9, 167.0, 135.5, 133.2, 129.3, 125.4, 124.8, 124.7, 124.6, 122.7, 52.2, 37.8, 24.8, 24.7. HRMS (ESI): calculated for $[M+H]^+$ $C_{14}H_{13}ClNO_3^+$ 278.0578; found 278.0578.

*4.3.12. 8,9-Dihydro-7H-benzo[a]carbazol-10(11H)-one (**2l**).* Following the general procedure, **2l** was purified by silica gel chromatography (10% EA/PE). Yield: 51 mg, 36%, white solid, mp 230–232 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.57 (s, 1H), 8.69 (d, J=8.4 Hz, 1H), 7.94 (d, J=7.8 Hz, 1H), 7.69 (d, J=8.4 Hz, 1H), 7.58–7.50 (m, 3H), 3.04–3.01 (m, 2H), 2.61–2.58 (m, 2H), 2.21–2.16 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 189.5, 134.0, 132.3, 130.3, 129.5, 128.5, 125.9, 122.4, 122.3, 121.1, 120.9, 119.8, 99.5, 38.1, 24.7, 20.9. HRMS (ESI): calculated for $[M+H]^+$ $C_{16}H_{14}NO^+$ 236.1070; found 236.1069.

4.4. General procedure for the synthesis of 2-(substituted phenylamino)cyclohept-2-enone 3

A solution of cycloheptane-1,2-dione (2.4 mmol) and substituted aniline (2 mmol) in toluene (5 mL) was heated to reflux with a water condenser and Dean–Stark trap under N_2 for 5 h. The solvent was removed under vacuum. Purification of the crude residue by column chromatography using TEA (triethylamine) and PE as eluent gave compounds **3a**–**f**. The 2-(substituted phenylamino)cyclohept-2-enone **3** was unstable and characterized shortly after being obtained.

*4.4.1. 2-(Phenylamino)cyclohept-2-enone (**3a**).* Following the general procedure, **3a** was purified by silica gel chromatography (1% TEA/PE). Yield: 163 mg, 40%, yellow oil. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.15 (t, J=7.8 Hz, 2H), 6.98 (s, 1H), 6.89 (d, J=7.8 Hz, 2H), 6.73 (t, J=7.2 Hz, 1H), 6.39 (t, J=7.2 Hz, 1H), 2.66–2.62 (m, 2H), 2.43–2.38 (m, 2H), 1.75–1.67 (m, 4H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.1, 144.0, 140.1, 128.8, 122.5, 119.0, 116.8, 40.7, 24.8, 24.4, 20.5. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{16}NO^+$ 202.1226; found 202.1223.

*4.4.2. 2-((4-Chlorophenyl)amino)cyclohept-2-enone (**3b**).* Following the general procedure, **3b** was purified by silica gel chromatography (1% TEA/PE). Yield: 193 mg, 41%, yellow oil. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.20 (s, 1H), 7.15 (d, J=9.0 Hz, 2H), 6.87 (d, J=8.4 Hz, 2H), 6.42 (t, J=7.2 Hz, 1H), 2.65–2.62 (m, 2H), 2.44–2.40 (m, 2H), 1.76–1.67 (m, 4H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.0, 143.3, 139.8, 128.5, 124.8, 121.9, 117.7, 40.7, 24.8, 24.5, 20.5. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{15}ClNO^+$ 236.0837; found 236.0836.

*4.4.3. 2-((4-Bromophenyl)amino)cyclohept-2-enone (**3c**).* Following the general procedure, **3c** was purified by silica gel chromatography (1% TEA/PE). Yield: 258 mg, 46%, yellow oil. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.27 (d, J=9.0 Hz, 2H), 7.22 (s, 1H), 6.81 (d, J=9.0 Hz, 2H), 6.43 (t, J=7.2 Hz, 1H), 2.65–2.62 (m, 2H), 2.44–2.40 (m, 2H), 1.75–1.68 (m, 4H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.0, 143.8, 139.7, 131.4, 125.3, 118.1, 109.4, 40.8, 24.8, 24.6, 20.6. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{15}BrNO^+$ 280.0332; found 280.0335.

*4.4.4. 2-(p-Methylamino)cyclohept-2-enone (**3d**).* Following the general procedure, **3d** was purified by silica gel chromatography (1% TEA/PE). Yield: 164 mg, 38%, yellow oil. ^{1}H NMR (600 MHz, DMSO-d_6) δ 6.98 (d, J=8.4 Hz, 2H), 6.83 (d, J=8.4 Hz, 2H), 6.78 (s, 1H), 6.28 (t, J=7.2 Hz, 1H), 2.64–2.61 (m, 2H), 2.40–2.36 (m, 2H), 2.19 (s, 3H), 1.73–1.66 (m, 4H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 199.9, 141.1, 140.5, 129.3, 128.2, 119.5, 117.8, 40.6, 24.8, 24.3, 20.4, 20.2. HRMS (ESI): calculated for $[M+H]^+$ $C_{14}H_{18}NO^+$ 216.1383; found 216.1384.

*4.4.5. 2-((3-Fluorophenyl)amino)cyclohept-2-enone (**3e**).* Following the general procedure, **3e** was purified by silica gel chromatography (1% TEA/PE). Yield: 258 mg, 59%, yellow oil. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.32 (s, 1H), 7.13 (dd, J=7.8, 1.8 Hz, 1H), 6.66 (dd, J=7.8, 1.8 Hz, 1H), 6.59 (d, J=12.6 Hz, 1H), 6.50 (t, J=7.2 Hz, 1H), 6.46 (td, J=8.4, 2.4 Hz, 1H), 2.66–2.63 (m, 2H), 2.46–2.42 (m, 2H), 1.76–1.69 (m, 4H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.0, 163.0 (d,

J_{F-C}=240 Hz), 146.8, 146.7 (d, J_{F-C}=11 Hz), 139.4, 130.2 (d, J_{F-C}=10 Hz), 127.1 (d, J_{F-C}=2 Hz), 111.7, 104.5 (d, J_{F-C}=20 Hz), 102.1 (d, J_{F-C}=25 Hz), 40.8, 24.8, 24.6, 20.6. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{15}FNO^+$ 220.1132; found 220.1131.

*4.4.6. 2-((3-Chloro-4-fluorophenyl)amino)cyclohept-2-enone (**3f**).* Following the general procedure, **3f** was purified by silica gel chromatography (1% TEA/PE). Yield: 318 mg, 63%, yellow solid, mp 57–60 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.23 (s, 1H), 7.17 (t, J=9.0 Hz, 1H), 6.99 (dd, J=6.6, 2.4 Hz, 1H), 6.86–6.82 (m, 1H), 6.43 (t, J=7.2 Hz, 1H), 2.65–2.63 (m, 2H), 2.45–2.41 (m, 2H), 1.75–1.69 (m, 4H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 199.8, 150.0 (d, J_{F-C}=236 Hz), 141.9 (d, J_{F-C}=2 Hz), 139.8, 125.3 (d, J_{F-C}=6 Hz), 119.2 (d, J_{F-C}=5 Hz), 117.3, 116.7 (d, J_{F-C}=22 Hz), 116.3 (d, J_{F-C}=7 Hz), 40.8, 24.8, 24.5, 20.5. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{14}ClFNO^+$ 254.0742; found 254.0742.

4.5. General procedure for the synthesis of substituted 7,8,9,10-tetrahydrocyclohepta[*b*]indol-6(5*H*)-one 4

To a solution of 2-(substituted phenylamino)cyclohept-2-enone **3** (0.5 mmol) in TFE (10 mL) and TEA (5 mmol) was added PIFA (0.75 mmol). The mixture was stirred at room temperature and monitored by TLC. After the starting material was consumed, saturated $NaHCO_3$ solution (10 mL) was added with stirring. The mixture was then extracted with EA (20 mL×3). The combined organic layer was washed with brine (20 mL), dried with $NaSO_4$, filtered, and concentrated under vacuum. Purification of the crude residue by column chromatography using PE and EA as eluent gave compounds **4a**–**f**.

*4.5.1. 7,8,9,10-Tetrahydrocyclohepta[b]indol-6(5H)-one[17b] (**4a**).* Following the general procedure, **4a** was obtained after a reaction for 2 h, purified by silica gel chromatography (10% EA/PE). Yield: 60 mg, 60%, white solid, mp 140–143 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.66 (d, J=8.4 Hz, 1H), 7.37–7.33 (m, 2H), 7.15–7.11 (m, 1H), 3.18–3.15 (m, 2H), 2.86–2.83 (m, 2H), 2.13–2.08 (m, 2H), 2.03–1.98 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.5.2. 2-Chloro-7,8,9,10-tetrahydrocyclohepta[b]indol-6(5H)-one (**4b**).* Following the general procedure, **4b** was obtained after a reaction lasted for 1 h, purified by silica gel chromatography (10% EA/PE). Yield: 53 mg, 45%, white solid, mp 181–184 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.61 (d, J=1.2 Hz, 1H), 7.32–7.25 (m, 2H), 3.10–3.07 (m, 2H), 2.87–2.84 (m, 2H), 2.11–2.06 (m, 2H), 2.02–1.97 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.9, 134.8, 133.7, 128.9, 127.0, 125.7, 123.7, 120.6, 113.1, 42.9, 26.6, 25.7, 22.7. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{13}ClNO^+$ 234.0680; found 234.0680.

*4.5.3. 2-Bromo-7,8,9,10-tetrahydrocyclohepta[b]indol-6(5H)-one[25] (**4c**).* Following the general procedure, **4c** was obtained after a reaction lasted for 10 min, purified by silica gel chromatography (10% EA/PE). Yield: 66 mg, 47%, white solid, mp 180–183 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.79 (d, J=1.2 Hz, 1H), 7.41 (dd, J=8.4, 1.8 Hz, 1H), 7.25 (d, J=9.6 Hz, 1H), 3.11–3.08 (m, 2H), 2.86–2.83 (m, 2H), 2.11–2.07 (m, 2H), 2.02–1.97 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.5.4. 2-Methyl-7,8,9,10-tetrahydrocyclohepta[b]indol-6(5H)-one[17c] (**4d**).* Following the general procedure, **4d** was obtained after a lasted reaction for 5 min, purified by silica gel chromatography (10% EA/PE). Yield: 45 mg, 42%, white solid, mp 177–179 °C.[1] H NMR (600 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.42 (s, 1H), 7.25 (d, J=4.8 Hz, 1H), 7.17 (d, J=8.4 Hz, 1H), 3.13–3.10 (m, 2H), 2.84–2.82 (m, 2H), 2.44 (s, 3H), 2.10–2.05 (m, 2H), 2.01–1.96 (m, 2H). The ^{1}H NMR data were consistent with those in the literature.

*4.5.5. 1-Fluoro-7,8,9,10-tetrahydrocyclohepta[b]indol-6(5H)-one (**4e**)/3-fluoro-7,8,9,10-tetrahydrocyclohepta[b]indol-6(5H)-one (**4e′**).* Following the general procedure, **4e**/**4e′** was obtained after a reaction lasted for 1 h, purified by silica gel chromatography (10% EA/PE). Yield: 55 mg, 51%, white solid, mp 122–128 °C. ^{1}H NMR (600 MHz, $CDCl_3$) isomer **4e** δ 9.46 (s, 1H), 7.56 (dd, J=9.0, 5.4 Hz, 1H), 7.06–7.03 (m, 1H), 6.90–6.86 (m, 1H), 3.12–3.09 (m, 2H), 2.87–2.84 (m, 2H), 2.09–2.05 (m, 2H), 2.01–1.96 (m, 2H); isomer **4e′** δ 9.46 (s, 1H), 7.23–7.19 (m, 1H), 7.16–7.12 (m, 1H), 6.73–6.69 (m, 1H), 3.36–3.33 (m, 2H), 2.87–2.84 (m, 2H), 2.09–2.05 (m, 2H), 2.01–1.96 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.0, 194.6, 162.0 (d, J_{F-C}=242 Hz), 159.0 (d, J_{F-C}=249 Hz), 139.0 (d, J_{F-C}=10 Hz), 137.1 (d, J_{F-C}=13 Hz), 133.4 (d, J_{F-C}=3 Hz), 132.9 (d, J_{F-C}=2 Hz), 127.0 (d, J_{F-C}=7 Hz), 126.9 (d, J_{F-C}=8 Hz), 124.7 (d, J_{F-C}=32 Hz), 123.6 (d, J_{F-C}=4 Hz), 122.6 (d, J_{F-C}=11 Hz), 117.2 (d, J_{F-C}=18 Hz), 109.6 (d, J_{F-C}=25 Hz), 108.1 (d, J_{F-C}=4 Hz), 104.8 (d, J_{F-C}=19 Hz), 97.8 (d, J_{F-C}=26 Hz), 42.8, 42.8, 27.3, 26.8, 26.6, 25.8, 22.8, 22.4. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{13}FNO^+$ 218.0976; found 218.0976.

*4.5.6. 1-Chloro-2-fluoro-7,8,9,10-tetrahydrocyclohepta[b]indol-6(5H)-one (**4f**)/3-chloro-2-fluoro-7,8,9,10-tetrahydrocyclohepta -[b] indol-6(5H)-one (**4f′**).* Following the general procedure, **4f**/**4f′** was obtained after a reaction lasted for 1 h, purified by silica gel chromatography (10% EA/PE). Yield: 61 mg, 48%, white solid, mp 153–157 °C. ^{1}H NMR (600 MHz, $CDCl_3$) isomer **4f** δ 9.51 (s, 1H), 7.23 (dd, J=9.0, 3.6 Hz, 1H), 7.12 (t, J=9.0 Hz, 1H), 3.55–3.52 (m, 2H), 2.88–2.85 (m, 2H), 2.11–1.93 (m, 4H); isomer **4f′** δ 9.41 (s, 1H), 7.42 (d, J=6.0 Hz, 1H), 7.33 (d, J=9.0 Hz, 1H), 3.06–3.03 (m, 2H), 2.88–2.85 (m, 2H), 2.11–1.93 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.3, 194.9, 153.0 (d, J_{F-C}=237 Hz), 152.6 (d, J_{F-C}=239 Hz), 134.8, 134.3, 134.1, 133.0, 126.6 (d, J_{F-C}=8 Hz), 125.3 (d, J_{F-C}=6 Hz), 124.6, 124.3 (d, J_{F-C}=6 Hz), 121.0 (d, J_{F-C}=22 Hz), 115.7 (d, J_{F-C}=27 Hz), 114.2 (d, J_{F-C}=20 Hz), 113.3, 111.3 (d, J_{F-C}=9 Hz), 106.7 (d, J_{F-C}=23 Hz), 42.9, 42.7, 27.02, 26.7, 26.5, 25.7, 22.6, 21.9. HRMS (ESI): calculated for $[M+H]^+$ $C_{13}H_{12}ClFNO^+$ 252.0586; found 252.0585.

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Supplementary data

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