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Palladium-Catalyzed Amination/Dearomatization Reaction of Indoles and Benzofurans

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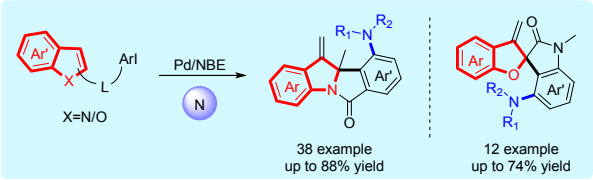
ABSTRACT: This report describes a palladium-catalyzed dearomatization and amination tandem reaction of 2,3-disubstituted indoles and benzofurans via a Catellani strategy. This reaction provides a new method for the construction of amino-substituted indoline fused cyclic and benzofuran spiro compounds in good yields. The reaction has broad functional group compatibility and substrate scope.



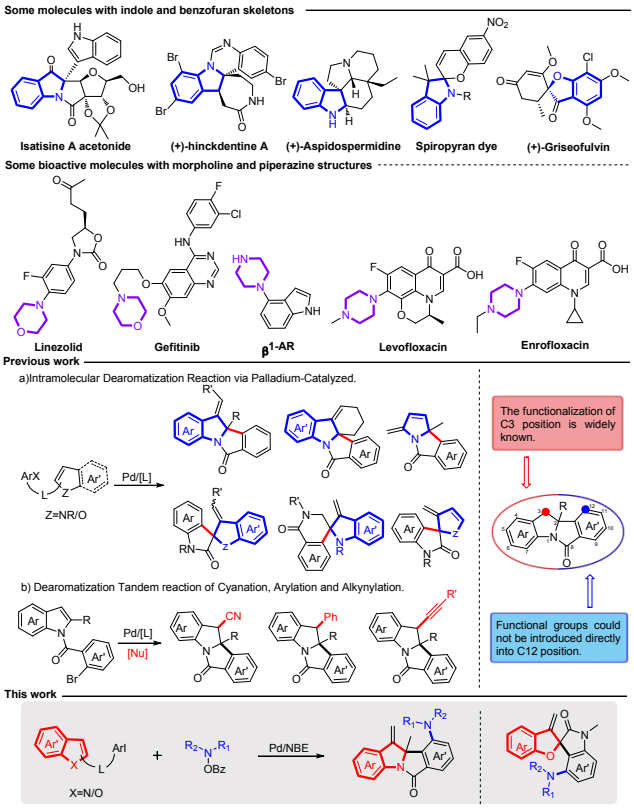
1. INTRODUCTION

Indoline derivatives and benzofuran derivatives are important heterocyclic aromatic compounds that exist widely in natural products and have important applications in medicine and materials science.[1] Isatisine A acetonide is separated from *Folium isatidis* and exhibits anti-HIV-1 activity. The screw-shaped alkaloid (+)-hinckdentine A was isolated from the marine bryozoan *Hincksinoflustra denticulata* in 1987. These two natural products offer great potential for drug development and attract the interest of many synthetic researchers.[2] In addition, (+)-aspidospermidine, a natureproduct with significant respiratory stimulation and antibiotic activity, is an alkaloid extracted from Aspidosperma.[3] Spiropyran dye can be used to make photochromic functional materials.[4] (+)-Griseofulvin is a selective antifungal agent used to treat skin infections in animals and humans. Recently, it has been reported that griseofulvin exhibits both antitumor and antiviral activities in mammals.[5] Due to the low natural abundance, the synthesis of these skeletons has attracted much attention.

Aromatics can now be rapidly transformed into spiro or fused cyclic compounds with complex structures by dearomatization reactions.[6] The dearomatization reactions of indole, benzofuran, pyrrole and furan derivatives and other compounds were carried out by Yao, Jia and Luan.[7] Pyrrole has an electrophilic property after the dearomatization occurs. The selective C-H functionalizations of the cyanation, arylation and alkynylation of indole at the C3 position have been successfully achieved at the same time as dearomatization. These works were implemented by Lautens, Jia, our group and other research groups.[8] Some achievements in the dearomatization reactions of benzofuran derivatives have also been obtained by Yin, Yamaguchi and others.[9] In these studies, the tandem reactions are usually completed by nucleophilic reagents combined with specific sites, while the tandem reactions with electrophilic reagents are less common.

After Catellani discovered the Pd/NBE cooperative catalytic reaction system in 1997, Lautens introduced phosphine ligands to make the reaction system more compatible and established the palladium/norbornene cooperative catalysis reaction system.[10] In past studies, ortho-alkylation, ortho-arylation, ortho-carbonylation and ortho-amination reactions have been developed by Catellani, Lautens, Dong, Bach, Gu and others.[11] Among them, ortho-amination was first realized by the Dong group in 2013.[12] Although the reaction system has ma de some gratifying achievements, its application in the rapid construction of complex structures, especially in the construction of natural products and drug skeletons, still faces great challenges.

Scheme 1. Palladium-Catalyzed Amination/Dearomatization Reaction of Indoles and Benzofurans

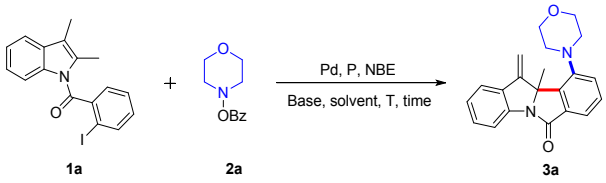


A large number of biologically active molecules in nature have amino functional groups,[13] such as piperidine, piperazine, morpholine and other functional groups.[14] In addition, in pharmaceutical chemistry, antibacterial linezolid[15] and anti-tumor targeted therapy drug gefitinib[16] has morpholine group, hypertension drug β1-AR,[17] antibacterial levofloxacin[18] and wide-spectrum veterinary antibacterial enrofloxacin[19] has piperazine group, etc. These show that the site-selective introduction of amino functional groups is very valuable for drug screening. Due to the limitations of natural extraction, artificial synthesis is particularly important, and the synthesis of these compounds has always been a primary focus of organic synthesis research. However, the domino reaction of selective amination of benzene ring and heterocyclic dearomatization has not been realized. We attempt to use the electrophilic N-(benzoyloxy)amine reagents as the amine source and introduce amines into the construction of fused cyclic compounds containing indole framework or spiro compounds containing benzofuran framework at the same time via Pd/NBE cooperative catalysis. (Scheme 1)

2. RESULTS AND DISCUSSION

For the tandem reaction conditions of dearomatization and amination of indole derivatives, we used morpholine benzoate as the amino source with $Pd(OAc)_2/PPh_3/Cs_2CO_3$ as the starting condition. Fortunately, we detected the presence of the product by GC-MS and successfully separated it to determine the structure. Interestingly, toluene was not the best solvent in the initial solvent selection, and the yield was only 51%. With the decrease of reaction temperature, the advantage of toluene as reaction solvent gradually emerged. When the temperature was reduced to 80 ℃, the yield reached 67% (Entries 1-7). However, the reaction was not complete, and there was a surplus of starting substrate **1a**. Therefore, the reaction time was prolonged, and the conversion rate of the reaction was significantly improved. We finally found that 48 h was the optimal reaction time (Entry 8). After that, we found that phosphine ligands crucially influenced the reaction direction. When trialkylphosphine ligands (such as PCy_3 and P^tBu_3-HBF_4) were used, the dearomatization reaction was more likely to occur without amination. When electron-poor aromatic phosphine ligands were used, the reaction was promoted. Finally, TFP exerted the best effect on the reaction, and the yield reached 84% (Entries 9-12). At last, we screened the base and palladium. We found that when we used another base to replace Cs_2CO_3, the yield decreased or the reaction direction moved towards the product of the dearomatization reaction without amination. Finally, we found that $Pd(OAc)_2$ was the best palladium catalyst. (Entries 13-17) (Table 1)

Table 1. Optimization of the Tandem Reaction Conditions of Dearomatization and Amination of Indole Derivatives [a]



Entry	Solvent	Temperature (℃)	Pd	Ligand	Base	Time (h)	Yield (%)
1	toluene	120	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	18	51
2	1,4-dioxane	120	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	18	66
3	THF	120	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	18	70
4	DCE	120	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	18	62
5	toluene	80	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	18	67
6	toluene	100	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	18	68
7	toluene	140	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	18	46
8	toluene	80	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	48	78
9	toluene	80	$Pd(OAc)_2$	TFP	Cs_2CO_3	18	74
10	toluene	80	$Pd(OAc)_2$	X-Phos	Cs_2CO_3	18	60
11	toluene	80	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	18	trace

12	**toluene**	**80**	**$Pd(OAc)_2$**	**TFP**	**Cs_2CO_3**	**48**	**84**
13	toluene	80	$Pd(OAc)_2$	TFP	Cs_2CO_3	24	81
14	toluene	80	$Pd(PPh_3)_4$	TFP	Cs_2CO_3	24	33
15	toluene	80	$Pd(PPh_3)Cl_2$	TFP	Cs_2CO_3	24	76
16	toluene	80	$Pd(PPh_3)Cl_2$	—	Cs_2CO_3	24	79
17	toluene	80	$Pd(OAc)_2$	TFP	K_2CO_3	24	55

[a] Reaction conditions: substrate **1a** (0.2 mmol), **2a** (0.4 mmol, 2.0 equiv.), $Pd(OAc)_2$ (0.02 mmol, 10 mol %), TFP (0.04 mmol, 20 mol %), norbornene (0.8 mmol, 4.0 equiv.), Cs_2CO_3 (0.8 mmol, 4.0 equiv.), toluene (3.0 mL), 80 °C, 48 h. TFP = Trifurylphosphine, PCy_3 = Tricyclohexylphosphine.

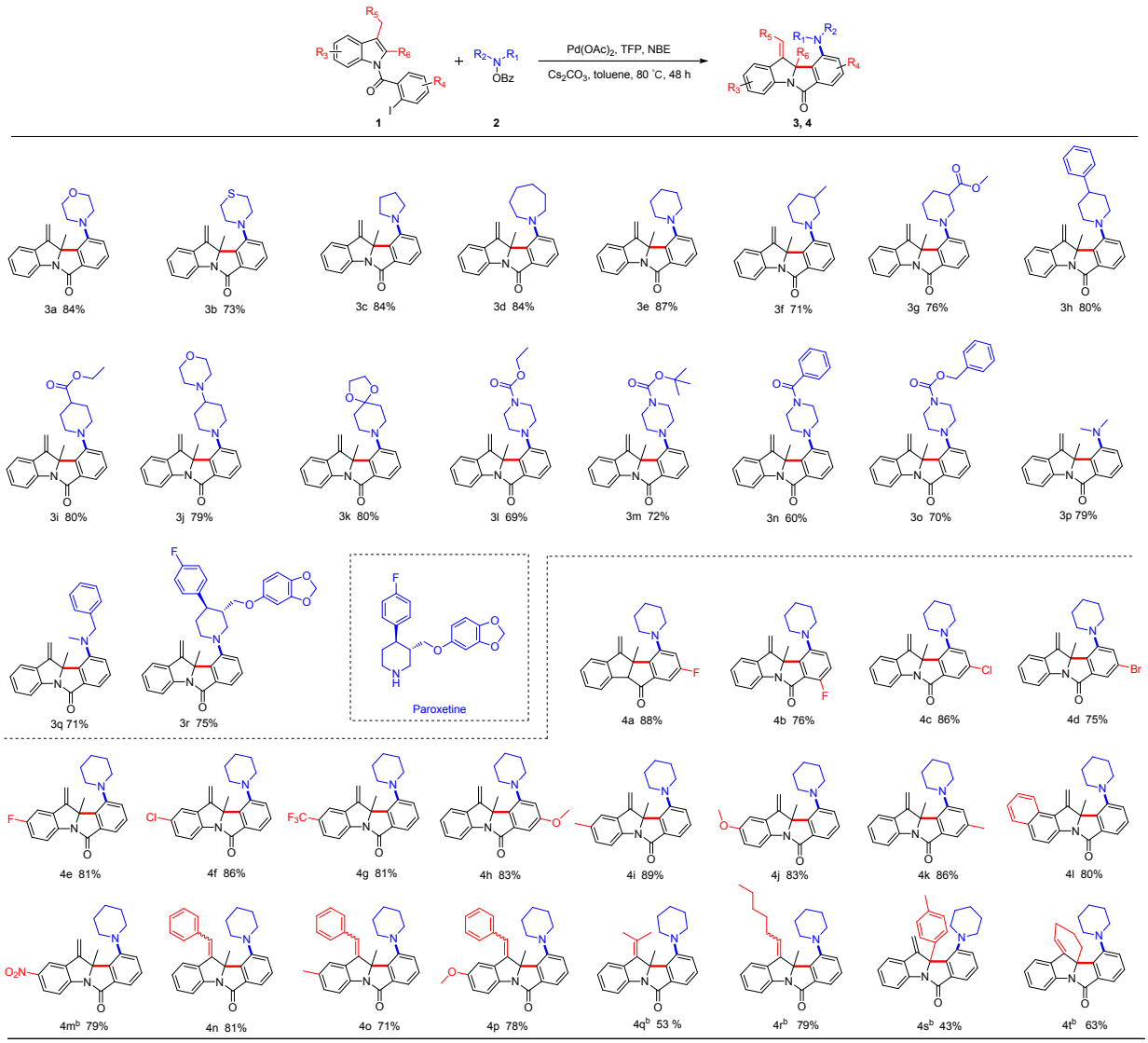
Amination reagents derived from cyclic amines, such as morpholine, thiomorpholine, pyrrolidine, hexamethyleneimine, piperidine and piperazine, provided the required products (**3a-3o**, **3r**) with good yields. Among them, morpholine (**3a**), ketal-protected (**3k**) and piperazinyl products (**3l-3o**) can be found in a large number of natural products or drug molecules.[13e, 20] Noncyclic amination reagents also afforded the target products in good yields (**3p**, **3q**). The structures of representative products **3a**, **3b** and **3c** were confirmed by single-crystal X-ray diffraction technique.[25] In particular, the corresponding product (**3r**) of the antidepressant drug paroxetine was also derived by this method. (Table 2)

We next used piperidin-1-yl benzoate as an amination reagent to expand the substrate scope. The results showed that the target product (**4a-4m**) can be obtained in good yields when including halogenated substrates (-F, -Cl, -Br or $-CF_3$), electron-rich groups ($-CH_3$, $-OCH_3$) or the strong electron-withdrawing group $-NO_2$.[25] It is noteworthy that higher temperature (100 °C) was required to make the reaction proceed smoothly (**4m**, **4q-4t**). When the C3 position of indole was substituted with the benzyl group or there were electron donor groups in the C5 position, the reaction could proceed smoothly (**4n-4p**). The C3-hexyl/isopropyl substituted indoles were also suitable for this reaction system (**4q-4r**). In addition, the reaction still proceeded smoothly when there was a large steric hindrance group at the C2 position of indole (**4s-4t**). (Table 2)

For the tandem reaction conditions of dearomatization and amination of benzofuran derivatives, we found that both $Pd(OAc)_2$/X-Phos/DCE/120 °C and $Pd(OAc)_2$/TFP/toluene/80 °C are suitable for this reaction. On the basis of the optimum conditions, the scope of the amination reagents was investigated again:[25] the ketal-protected skeleton (**6c**) and piperazinyl skeleton products (**6d-6f**) were successfully obtained, but piperidine was not ideal. We then investigated the scope of substrate **5** and found that the desired products (**6g-6l**) could be obtained successfully with either an electron-withdrawing group or electron-donating group. (Table 3)

To study the feasibility of an asymmetric version of this domino reaction, we utilized **1a** and **2b** as the reactants, and preliminary studies with chiral phosphine ligand demonstrated that product **7** could be formed in 32% yield and with 66: 34 er by chiral phosphine ligand **L3**. We realized the asymmetric conversion of the amination/dearomatization reaction; unfortunately, we did not obtain better results after screening various ligands. (Scheme 2)

Table 2. Investigation of Substrate Scope [a]



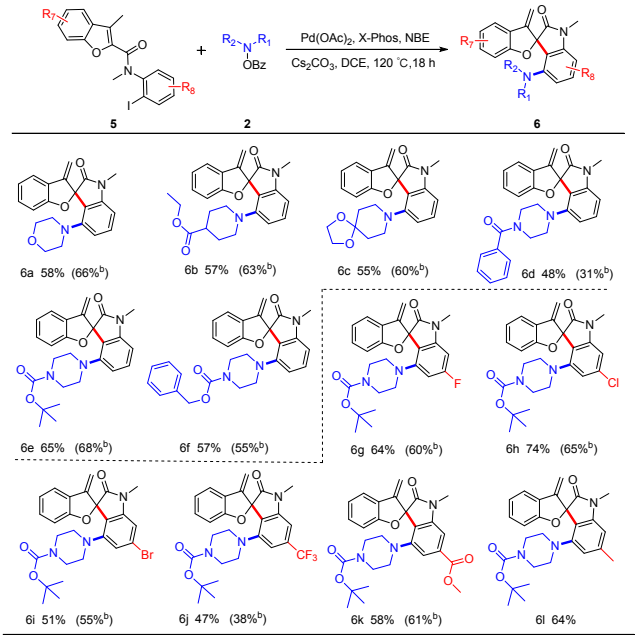
[a] Reaction conditions: substrate **1a** (0.2 mmol), **2** (0.4 mmol, 2.0 equiv.), $Pd(OAc)_2$ (0.02 mmol, 10 mol %), TFP (0.04 mmol, 20 mol %), norbornene (0.8 mmol, 4.0 equiv.), Cs_2CO_3 (0.8 mmol, 4.0 equiv.), toluene (3.0 mL), 80 °C, 48 h. [b] at 100 °C.

To further expand the application of electrophilic reagents, we used n-butane bromide as an electrophilic reagent to explore the tandem reaction of dearomatization and alkylation. After selecting the reaction conditions, it was found that the target product **8** could be obtained in 23% yield after 24 h reaction at 60 ℃ with DMF instead of toluene as the solvent. Unfortunately, this method cannot produce the products of the dearomatization/arylation reaction. (Scheme 3)

To demonstrate the scalability of this method, we expanded the scale of **1a** to 2.7 mmol (1.01 g) and finally obtained the target product **3e** with 79% yield (0.71g). (Scheme 4) To explore the versatility of product skeletons and the potential application of this new method, we also conducted some derivative experiments. Considering that many bioactive compounds and natural products often contain unprotected N-H bonds,[13e] we previously attempted to use TFA and SiO_2, respectively, to remove the Boc-protecting group of **3m**, and we could obtain the target product **9** with yields of 63% and 73%, respectively. Product **9** can be further modified according to specific needs. (Scheme 5) In addition, the hydrogenation reaction could be carried out for **3d** by using Pd/C as catalyst and ethyl acetate as solvent under 1 atm H_2, and product **10** could be obtained in 66% yield.[7c] (Scheme 6)

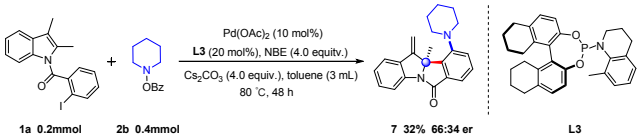
In particular, we attempted to use substrate **11** with H in the C2 position of indole and found that norbornene could not be removed. Therefore, we speculate that the 2-substituent groups of indole are very important for the dearomatization reaction and ortho-amination. (Scheme 7)

Table 3. Reaction Scopea [a]

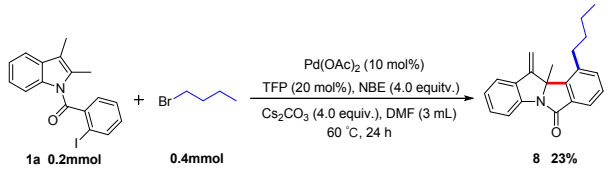


[a] Reaction conditions: substrate **5** (0.2 mmol), **2** (0.4 mmol, 2.0 equiv.), $Pd(OAc)_2$ (0.02 mmol, 10 mol %), X-Phos (0.04 mmol, 20 mol %), norbornene (0.8 mmol, 4.0 equiv.), Cs_2CO_3 (0.8 mmol, 4.0 equiv.), DCE (3.0 mL), 120 °C, 18 h. [b] TFP (0.04 mmol, 20 mol %), toluene (3.0 mL), 80 °C, 48 h.

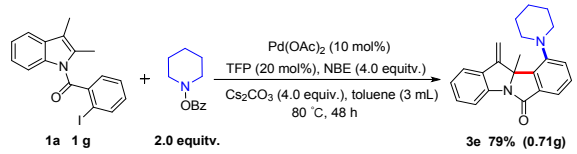
Scheme 2. Asymmetric Tandem Reaction of 1a



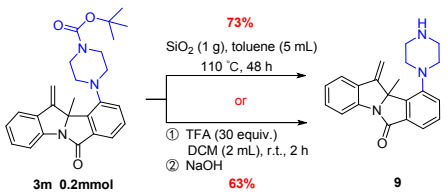
Scheme 3. Alkylation/Dearomatization Reaction of 1a



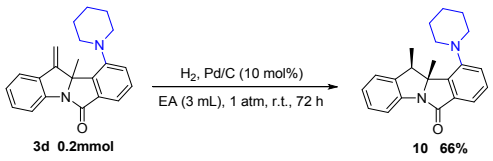
Scheme 4. Gram-scale Synthesis



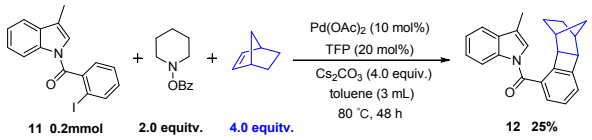
Scheme 5. Deprotection of Production 3m



Scheme 6. Hydrogenation Reaction of 3d



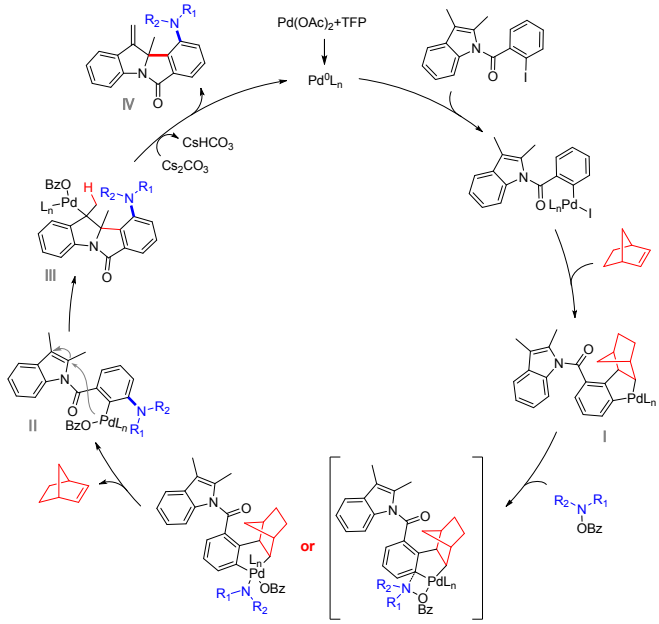
Scheme 7. Amination/Dearomatization Reaction of Substrate 11



Based on the mechanism proposed by Catellani, Lautens, Dong and others, we propose the following reaction mechanism:

First, Pd(0) is bound to iodobenzene by oxidative addition reaction, and then, under the action of norbornene and palladium, intermediate **I** is formed through carbopalladation of norbornene and subsequent ortho-C-H activation. Then, N-(benzoyloxy)amine is added to intermediate **I** by oxidative addition, and aminated aromatic **II** is obtained by reductive elimination. Alternatively, N-(benzoyloxy)amine can undergo electrophilic amination directly with intermediate **I** to produce aminated aromatic **II**. Next, after intramolecular coordination of the indole to Pd and carbopalladation, the beta-hydride elimination reaction of intermediate **III** takes place under the action of cesium carbonate, and the desired target product **Ⅳ** is finally obtained. Pd then participates in the reaction cycle again. (Scheme 8)

Scheme 8. Possible Catalytic Cycle



3. CONCLUSIONS

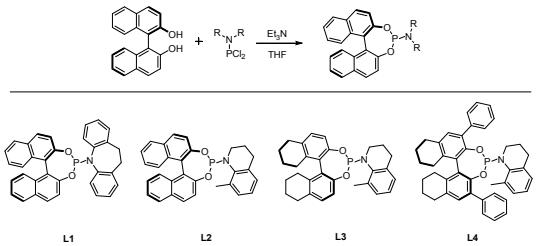
In summary, we have demonstrated a new method for the direct construction of bicyclic compounds of indoles or spiro compounds of benzofurans with C2-quaternary center, C3-exo double bond and amino group by Pd/NBE cooperative catalysis. The synthesis method is efficient and convenient, and it exhibits

good functional group tolerance. It may be useful in industrial production, complex natural product synthesis and asymmetric synthesis. The extension to additional aromatic hydrocarbon substrates and enhancement of enantioselectivity of synthesis are currently being studied in the laboratory.

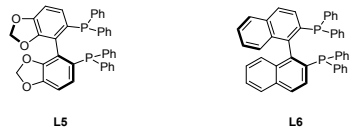
4. EXPERIMENTAL SECTION

General Procedures. Unless otherwise noted, reactions were performed under an argon atmosphere. Plastic syringes were used to transfer air-and moisture-sensitive reagents. Solvent was freshly distilled/degassed prior to use unless otherwise noted. Analytical TLC was performed with silica gel GF254 plates. For column chromatography, a 200-300 mesh silica gel was employed. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Room temperature (r.t.) is 23-25 °C. Commercial reagents were used as received without further purification unless otherwise noticed. Other commercially available reagents and solvents were used without further purification. Ligands **L1-L6** were purchased or prepared according to the literature procedures and used directly as received. Deuterated solvents were purchased from Cambridge Isotope Laboratories. ^{1}H NMR spectra were recorded on Bruker AVANCE III 400 with 400 MHz frequencies, and ^{13}C NMR spectra were recorded on Bruker AVANCE III 400 with 101 MHz frequencies. ^{19}F NMR spectra were recorded on a Bruker AVANCE III 400 spectrometer with a ^{19}F operating frequency of 376 MHz. Chemical shifts (δ) were reported in ppm relative to the residual solvent signal ($CDCl_3$ δ = 7.26 for ^{1}H NMR and δ = 77.00 for ^{13}C NMR). Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets) or td (triplet of doublets). HRMS was obtained using a Q-TOF instrument equipped with an ESI source. Data collection for crystal structure was performed at room temperature using Mo Kα radiation on a Bruker APEXII diffractometer. HPLC analyses were performed using Agilent 1260 chromatography. Chiralpak AD-H columns were purchased from Daicel Corporation.

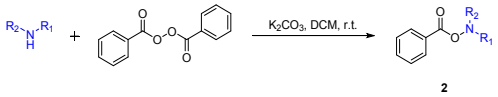
General Methods of Product Preparation and Product Derivatization.



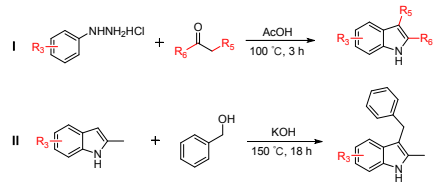
Synthesis of chiral phosphoramidite ligands: The ligands **L1-L4** were prepared according to the literature method with some modification.[7c, 21] To a solution of 10,11-dihydro-5H-dibenzo[b,f]azepine (2.6 mmol) in dry THF (5 mL) at 0 ℃ was added n-BuLi (2.4 M in hexanes, 3.9 mmol) dropwise over 3 min under argon atmosphere. After stirring at 0 ℃ for 30 min, PCl_3 (7.8 mmol) was added to the reaction mixture in one portion. The resulting mixture was warmed to room temperature, stirred for 1 h, and then concentrated at room temperature. The remaining PCl_3 was removed under vacuum. Dry THF (5 mL) was then added to the resulting residue. After stirring for 10 min, the mixture was cooled to 0 ℃, followed by addition of a solution of (R)-[1,1'-binaphthalene]-2,2'-diol (1.3 mmol) and Et_3N (7.8 mmol) in dry THF (5 mL) over 2 min. The mixture was warmed to room temperature and stirred 24 h. It was then filtered and the solid was washed with THF. After evaporation, the residue was purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether to afford the ligands.



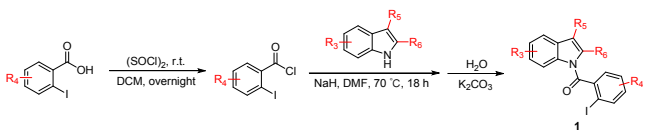
Ligands **L5-L6** are purchased from reagent manufacturers and used without further purification.



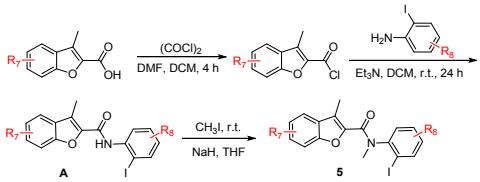
*Typical procedure for the synthesis of O-benzoyl hydroxylamine **2**:* O-Benzoyl hydroxylamines was synthesized using a modified procedure.[11e, 12] To a 100 mL flask equipped with stir bar and benzoyl peroxide (3.46 g, 70% purity 10 mmol, 1 equiv.), K_2CO_3 (2.76g, 20 mmol, 2 equiv.), and CH_2Cl_2 (50 mL) was added sequentially. Then a solution of amine (15 mmol, 1.5 equiv.) was added dropwise at 0 ℃. Upon completion, the reaction was further stirred at room temperature overnight. After monitored by TLC to see the full conversion of benzoyl peroxide, water (100 mL) was added, and the products were extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extract was dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel to give O-benzoyl hydroxylamine **2**.



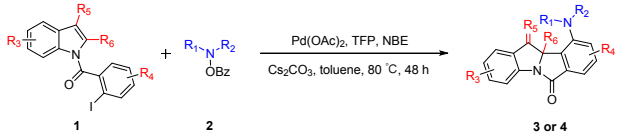
*Typical procedure for the synthesis of **1**:* Methods Ⅰ: Phenylhydrazine hydrochloride (12 mmol), AcOH (5 mL) and ketone (10.0 mmol) were added into a 20 mL tube, the mixture was stirred at 100 ℃ for 3 h. After the reaction was completed, water (10 mL) was added, and the mixture was extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated in vacuo to give crude product, which was purified by flash chromatography on silica gel to afford the fused indole products.[7d] Methods Ⅱ: 2-methyl-1*H*-indole (6 mmol), KOH (7.8 mmol) and phenylmethanol (18 mmol) were added into a 20 mL tube, the mixture was stirred at 150 ℃ for 18 h. After the reaction was completed, water (10 mL) was added, and the mixture was extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated in vacuo to give crude product which was purified by flash chromatography on silica gel to afford the fused indole products.[22]



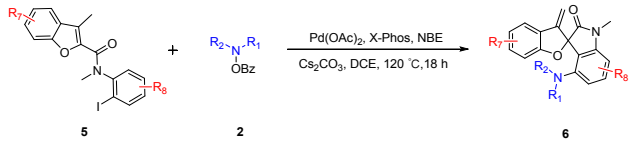
Substrates **1** were prepared according to the known procedure by the condensation of 2-iodobenzoic acid with indole accordingly. The corresponding indoles was synthesis by known methods Ⅰ (Fisher indole synthesis) or methods Ⅱ. Unless otherwise indicated, all other reagents and solvents were obtained from commercial suppliers and used as received. To a solution of substituted indole (6 mmol) in 25 mL DMF was added NaH (60%, 9 mmol) in portion at 0 ℃, after which the mixture was stirred at room temperature for 1 h. A solution of substituted 2-iodobenzoyl chloride (12 mmol) in 5 mL DMF was then introduced to the above mixture and the resulting mixture was reacted at 70 ℃ for 18 h. After quenched by water, the mixture was extracted with ethyl acetate and washed by saturated potassium carbonate solution. The collected organic phase was then dried over Na_2SO_4 followed by filtration and concentration under vacuum to afford the crude product, which was then purified by flash chromatography on slica gel, eluting with petroleum ether/ethyl acetate 100:1 (v/v) to afford the substrates **1**.[7d, 8d]



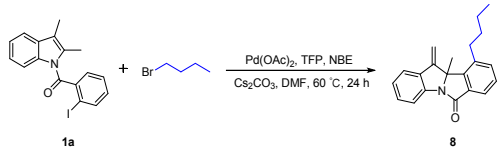
*Typical procedure for the synthesis of **5**:* To a stirred solution of substituted 2-iodobenzoic acid (10 mmol) in CH_2Cl_2 (15 mL) were added a catalytic amount of DMF (18 μL) and $(COCl)_2$ (20 mmol, 0.7 mL), and the mixture was stirred for 4 h at room temperature. The mixture was then concentrated under reduced pressure. To a stirred solution of this residue in DCM (5.0 mL) was added a mixture of Substituted 2-iodoaniline (12 mmol) and Et_3N (3 mL) in DCM (25 mL). The mixture was stirred at room temperature for 24 h. After the reaction was completed, water (10 mL) was added, and the mixture was extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4. After filtration, the solvent was concentrated under vacuum and the residue was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 100:1 (v/v) to afford the substrates **A**. A 60% dispersion of NaH in mineral oil (20 mmol) was added to a stirred solution of the substrates **A** in THF at 0 ℃, after which the mixture was stirred at room temperature for 15 min, CH_3I (20 mmol) was then introduced to the above mixture and the resulting mixture was reacted at room temperature. At this time the extent of completion of the reaction was determined by TLC analysis. After the reaction was completed, water (10 mL) was added, and the mixture was extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated in vacuo to give crude product, which was purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 100:1-20:1 (v/v) to afford the substrates **5**.[7c]



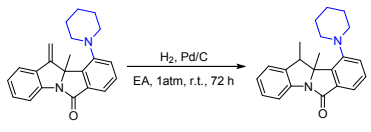
Product Preparation: In a 20 mL tube, **1** (0.2 mmol), **2** (0.4 mmol, 2.0 equiv.), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), TFP (0.04 mmol, 20 mol%), Cs_2CO_3 (0.8 mmol, 4.0 equiv.) were added and charged with argon more than five times (The tube was sealed with tipping plug). Toluene (3 mL) and norbornadiene (0.6 mmol, 3.0 equiv.) was injected into the tube via plastic syringes. Then the white medical adhesive tape was used to reinforce the tipping plug. The resulting light yellow suspension was stirred vigorously at room temperature for 10 minutes before being placed in a preheated oil bath at 80 °C stirring at 700~900 rpm for 48 h. After the reaction was completed, the residue was purified with chromatography column on silica gel, eluting with petroleum ethyl/acetate ether to afford the product **3** or **4**.



In a 20 mL tube, **5** (0.2 mmol), **2** (0.4 mmol, 2.0 equiv.), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), X-Phos (0.04 mmol, 20 mol%), Cs_2CO_3 (0.8 mmol, 4.0 equiv.) were added and charged with argon more than five times (The tube was sealed with tipping plug). DCE (3 mL) and norbornadiene (0.6 mmol, 3.0 equiv.) was injected into the tube via plastic syringes. Then the white medical adhesive tape was used to reinforce the tipping plug. The resulting light yellow suspension was stirred vigorously at room temperature for 10 minutes before being placed in a preheated oil bath at 120 °C stirring at 700~900 rpm for 18 h. After the reaction was completed, the residue was purified with chromatography column on silica gel, eluting with petroleum ethyl/acetate ether to afford the product **6**.

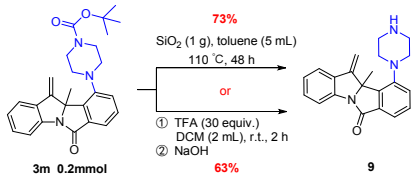


Product Derivatization: In a 20 mL tube, **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), TFP (0.04 mmol, 20 mol%), Cs_2CO_3 (0.8 mmol, 4.0 equiv.) were added and charged with argon more than five times (The tube was sealed with tipping plug). DMF (3 mL), norbornadiene (0.6 mmol, 3.0 equiv.) and 1-bromobutane (0.4 mmol, 2.0 equiv.) was injected into the tube via plastic syringes. Then the white medical adhesive tape was used to reinforce the tipping plug. The resulting light yellow suspension was stirred vigorously at room temperature for 10 minutes before being placed in a preheated oil bath at 60 °C stirring at 700~900 rpm for 24 h. After the reaction was completed, water (10 mL) was added, and the products were extracted with acetate ether (3 × 5 mL). The combined organic extract was dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel to afford the product **8**.

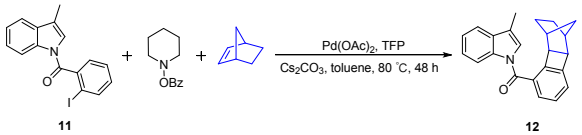


Pd/C (47.3 mg, palladium on activated carbon, 5% Pd basis, 0.1 equiv.) was added to a solution of **3d** (33.1 mg, 0.1 mmol) in EtOAc (3.0 mL). The reaction mixture was stirred under H_2 atmosphere (1 atm) at r.t. for 72 h. After the reaction was complete (monitored by TLC), the crude reaction mixture was filtered with celite and washed with EtOAc. The solvent was removed under reduced pressure. Then the residue was purified

by silica gel column chromatography (PE/EA = 14:1) to afford the desired product **10**.[23]

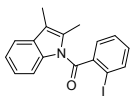


Methods 1: In a 20 mL tube, **3m** (86.4 mg, 0.2 mmol) and silica gel (1.0 g) and toluene (5 mL) were added. The mixture was stirred at 110 ℃ reflux for 24 h. After the reaction was complete (monitored by TLC), the residue was purified with chromatography column on silica gel (CH_2Cl_2/MeOH = 15:1) to afford the desired product **9**.[13d] Methods 2: Product **3m** (86.4 mg, 0.2 mmol) was dissolved in CH_2Cl_2 (2 mL) and then TFA (0.46 mL, 30 equiv.) was added. The reaction was stirred for 2 h at room temperature. Then the reaction was quenched with 6 M NaOH and rapidly stirred for 30 min at room temperature. The crude was extracted with dichloromethane (3 x 5 mL), then dried over Na_2SO_4 and filtered. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH = 15:1) to afford the desired product **9**.[24]

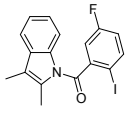


In a 20 mL tube, **11** (0.2 mmol), piperidin-1-yl benzoate (0.4 mmol, 2.0 equiv.), $Pd(OAc)_2$ (0.02 mmol, 10 mol%), TFP (0.04 mmol, 20 mol%), Cs_2CO_3 (0.8 mmol, 4.0 equiv.) were added and charged with argon more than five times (The tube was sealed with tipping plug). Toluene (3 mL) and norbornadiene (0.6 mmol, 3.0 equiv.) was injected into the tube via plastic syringes. Then the white medical adhesive tape was used to reinforce the tipping plug. The resulting light yellow suspension was stirred vigorously at room temperature for 10 minutes before being placed in a preheated oil bath at 80 °C stirring at 700~900 rpm for 48 h. After the reaction was completed, the residue was purified with chromatography column on silica gel, eluting with petroleum ethyl/acetate ether, eluting with petroleum ethyl/acetate ether 100:1 (v/v) to afford the product **12**.

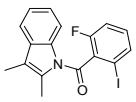
Characterization Data of Substrate.



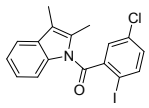
(2,3-dimethyl-1H-indol-1-yl)(2-iodophenyl)methanone ***(1a)*** 1.58 g, yield: 70%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.9 Hz, 1H), 7.49 – 7.36 (m, 3H), 7.32 – 7.16 (m, 3H), 7.15 – 7.06 (m, 1H), 2.25 – 2.15 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 142.5, 139.9, 136.0, 132.4, 131.7, 131.4, 129.0, 128.5, 123.8, 123.3, 118.0, 116.5, 114.8, 93.2, 13.6, 8.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{15}INO$ 376.0193; found 376.0200. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);



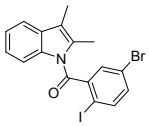
(2,3-dimethyl-1H-indol-1-yl)(5-fluoro-2-iodophenyl)methanone ***(1b)*** 1.25 g, yield: 53%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.7, 5.1 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.07 – 6.98 (m, 2H), 6.84 (td, *J* = 8.4, 3.0 Hz, 1H), 2.08 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.3 (d, *J* = 2.2 Hz), 162.7 (d, *J* = 251.3 Hz), 144.0 (d, *J* = 6.7 Hz), 141.3 (d, *J* = 7.6 Hz), 135.7, 132.0, 131.4, 124.0, 123.5, 119.2 (d, *J* = 21.7 Hz), 118.1, 116.9, 116.5 (d, *J* = 23.7 Hz), 114.6, 86.3 (d, *J* = 3.7 Hz), 13.5, 8.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.96. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}FINO$ 394.0099; found 394.0105. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 90:1 then petroleum ethyl/acetone 3:1 (v/v);



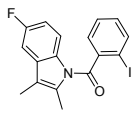
(2,3-dimethyl-1H-indol-1-yl)(2-fluoro-6-iodophenyl)methanone ***(1c)*** 0.90 g, yield: 38%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 – 5.54 (m, 7H), 2.17 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.1, 158.7 (d, *J* = 253.8 Hz), 135.2, 132.6, 132. 6, 131.9, 131.6, 131.6, 124.4, 123.8, 118.1, 117.2, 116.1, 115.9, 93.5, 13.3, 8.8.^{19}F NMR (376 MHz, $CDCl_3$) δ -110.90. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}FINO$ 394.0099; found 394.0105. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 70:1 (v/v);



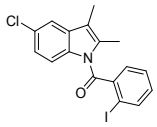
(5-chloro-2-iodophenyl)(2,3-dimethyl-1H-indol-1-yl)methanone ***(1d)*** 1.28 g, yield: 52%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.5 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 2.5 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.20 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 2.20 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.4, 143.9, 141.0, 135.8, 135.1, 132.1, 131.9, 131.5, 129.0, 124.1, 123.6, 118.1, 117.1, 114.7, 90.3, 13.6, 8.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}ClINO$ 409.9803; found 409.9811. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);



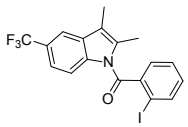
(5-bromo-2-iodophenyl)(2,3-dimethyl-1H-indol-1-yl)methanone ***(1e)*** 1.31 g, yield: 48%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 2.1 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.8 Hz, 1H), 2.20 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.2, 144.2, 141.2, 135.8, 134.8, 132.0, 131.7, 131.5, 124.1, 123.6, 122.8, 118.1, 117.1, 114.7, 91.2, 13.7, 8.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}BrINO$ 453.9298; found 453.9307. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);



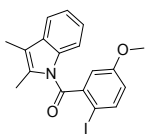
(5-fluoro-2,3-dimethyl-1H-indol-1-yl)(2-iodophenyl)methanone ***(1f)*** 1.23 g, yield: 52%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.85 (m, 1H), 7.47 (td, *J* = 7.5, 0.9 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.32 (dd, *J* = 9.0, 4.5 Hz, 1H), 7.21 (td, *J* = 7.7, 1.9 Hz, 1H), 7.06 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.82 (td, *J* = 9.1, 2.7 Hz, 1H), 2.15 (s, 3H), 2.12 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.6, 159.7 (d, *J* = 240.5 Hz), 142.3, 139.8, 134.0, 132.7 (d, *J* = 9.4 Hz), 132.2, 131.8, 128.9, 128.5, 116.3 (d, *J* = 3.7 Hz), 115.9 (d, *J* = 8.8 Hz), 111.1 (d, *J* = 24.4 Hz), 103.8 (d, *J* = 23.5 Hz), 93.1, 13.6, 8.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.48. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}FINO$ 394.0099; found 394.0104. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 70:1 (v/v);



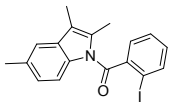
(5-chloro-2,3-dimethyl-1H-indol-1-yl)(2-iodophenyl)methanone ***(1g)*** 1.40 g, yield: 57%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.44 – 7.36 (m, 2H), 7.26 – 7.20 (m, 2H), 7.06 (dd, *J* = 8.8, 2.2 Hz, 1H), 2.16 (s, 3H), 2.15 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.7, 142.1, 139.9, 134.3, 133.9, 132.8, 132.0, 129.0, 129.0, 128.6, 123.8, 117.8, 115.9, 115.8, 93.1, 13.6, 8.7. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}ClINO$ 409.9803; found 409.9802. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);



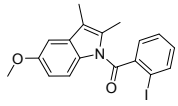
(2,3-dimethyl-5-(trifluoromethyl)-1H-indol-1-yl)(2-iodophenyl)methanone ***(1h)*** 1.22 g, yield: 46%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.69 (s, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.46 – 7.40 (m, 1H), 7.39 – 7.30 (m, 2H), 7.28 – 7.23 (m, 1H), 2.23 (s, 3H), 2.20 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.9, 141.9, 140.0, 137.6, 134.4, 132.2, 131.2, 129.2, 128.6, 125.5 (q, *J* = 32.1 Hz), 124.7 (q, *J* = 271.9 Hz), 120.6 (q, *J* = 3.6 Hz), 116.3, 115.4 (q, *J* = 4.0 Hz), 114.8, 93.06, 13.5, 8.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -61.76. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{14}F_3INO$ 444.0067; found 444.0065. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);



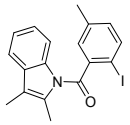
(2,3-dimethyl-1H-indol-1-yl)(2-iodo-5-methoxyphenyl)methanone ***(1i)*** 1.12 g, yield: 46%, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.8 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 3.0 Hz, 1H), 6.74 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.73 (s, 3H), 2.20 (s, 3H), 2.16 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.3, 159.9, 143.1, 140.4, 135.7, 132.2, 131.3, 123.7, 123.2, 118.2, 117.8, 116.4, 114.6, 114.4, 81.4, 55.5, 13.4, 8.7. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{17}INO_2$ 406.0298; found 406.0305. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 21:1 (v/v);



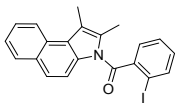
(2-iodophenyl)(2,3,5-trimethyl-1H-indol-1-yl)methanone ***(1j)*** 1.28 g, yield: 55%, yellow soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.87 (m, 1H), 7.48 – 7.42 (m, 1H), 7.41 – 7.36 (m, 1H), 7.22 – 7.16 (m, 2H), 7.13 – 7.05 (m, 1H), 6.93 – 6.88 (m, 1H), 2.43 – 2.38 (m, 3H), 2.21 – 2.15 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.7, 142.6, 139.8, 134.1, 132.9, 132.5, 131.7, 131.6, 128.9, 128.4, 125.0, 118.1, 116.4, 114.5, 93.2, 21.3, 13.6, 8.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{17}INO$ 390.0349; found 390.0343. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);



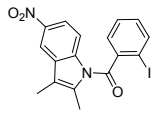
(2-iodophenyl)(5-methoxy-2,3-dimethyl-1H-indol-1-yl)methanone ***(1k)*** 1.29 g, yield: 53%, yellow soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 1H), 7.48 – 7.42 (m, 1H), 7.41 – 7.35 (m, 1H), 7.25 – 7.15 (m, 2H), 6.90 – 6.84 (m, 1H), 6.74 – 6.66 (m, 1H), 3.83 (s, 3H), 2.15 (s, 3H), 2.14 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.4, 156.4, 142.6, 139.7, 133.1, 132.5, 131.6, 130.4, 128.8, 128.4, 116.5, 115.7, 111.4, 101.5, 93.1, 55.6, 13.6, 8.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{17}INO_2$ 406.0298; found 406.0293. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 50:1 (v/v);



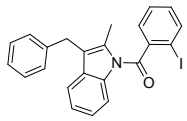
(2,3-dimethyl-1H-indol-1-yl)(2-iodo-5-methylphenyl)methanone ***(1l)*** 1.01 g, yield: 43%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.26 – 7.19 (m, 3H), 7.12 – 7.06 (m, 1H), 7.02 (dd, *J* = 8.1, 2.2 Hz, 1H), 2.33 (s, 3H), 2.21 (s, 3H), 2.19 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.9, 142.3, 139.6, 138.8, 135.9, 132.7, 132.5, 131.4, 129.6, 123.7, 123.2, 117.9, 116.4, 114.7, 89.1, 20.9, 13.5, 8.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{17}INO$ 390.0349; found 390.0356. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 70:1 (v/v);



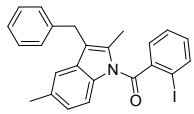
(1,2-dimethyl-3H-benzo[e]indol-3-yl)(2-iodophenyl)methanone ***(1m)*** 1.22 g, yield: 48%, yellow soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.4 Hz, 1H), 7.87 – 7.79 (m, 2H), 7.52 – 7.36 (m, 6H), 7.18 – 7.10 (m, 1H), 2.57 (s, 3H), 2.20 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.3, 142.0, 140.1, 132.9, 132.1, 131.1, 131.0, 129.7, 128.5, 128.4, 128.0, 125.8, 124.6, 124.1, 124.0, 123.6, 117.6, 114.5, 93.4, 13.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{17}INO$ 426.0349; found 426.0342. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);



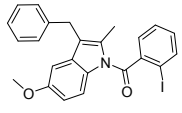
(2,3-dimethyl-5-nitro-1H-indol-1-yl)(2-iodophenyl)methanone ***(1n)*** 1.11 g, yield: 44%, yellow soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 – 8.18 (m, 1H), 7.94 – 7.85 (m, 2H), 7.58 – 7.47 (m, 2H), 7.36 (d, *J* = 9.1 Hz, 1H), 7.27 (t, *J* = 8.2 Hz, 1H), 2.21 (s, 3H), 2.14 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.4, 143.4, 140.9, 139.7, 138.7, 135.4, 132.3, 131.0, 129.2, 128.5, 118.5, 116.2, 114.2, 113.7, 92.7, 13.2, 8.4. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}IN_2O_3$ 421.0044; found 421.0051. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);



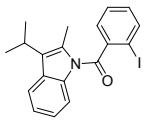
(3-benzyl-2-methyl-1H-indol-1-yl)(2-iodophenyl)methanone ***(1o)*** 1.35 g, yield: 50%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.25 (d, *J* = 8.5 Hz, 1H), 7.22 – 7.09 (m, 7H), 7.07 – 7.03 (m, 1H), 4.01 (s, 2H), 2.23 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.9, 142.2, 139.8, 139.6, 136.1, 133.5, 131.8, 130.6, 129.1, 128.5, 128.4, 128.1, 126.0, 123.8, 123.3, 119.3, 118.5, 114.7, 93.1, 29.8, 13.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{19}INO$ 452.0506; found 452.0516. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);



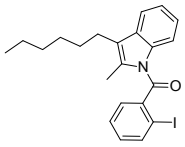
(3-benzyl-2,5-dimethyl-1H-indol-1-yl)(2-iodophenyl)methanone ***(1p)*** 1.12 g, yield: 40%, yellow soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.9 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.24 – 7.08 (m, 8H), 6.88 (d, *J* = 8.4 Hz, 1H), 4.00 (s, 2H), 2.32 (s, 3H), 2.22 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 142.4, 139.8, 139.7, 134.3, 133.7, 132.9, 131.7, 130.9, 129.1, 128.5, 128.4, 128.1, 126.0, 125.1, 119.2, 118.5, 114.4, 93.1, 29.7, 21.3, 13.7. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{21}INO$ 466.0662; found 466.0658. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);



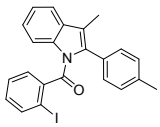
(3-benzyl-5-methoxy-2-methyl-1H-indol-1-yl)(2-iodophenyl)methanone ***(1q)*** 1.21 g, yield: 42%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 4.6 Hz, 2H), 7.26 – 7.17 (m, 5H), 7.15 – 7.06 (m, 2H), 6.78 (d, *J* = 2.5 Hz, 1H), 6.66 (dd, *J* = 8.9, 2.6 Hz, 1H), 3.95 (s, 2H), 3.66 (s, 3H), 2.17 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.4, 156.2, 142.2, 139.6, 139.4, 134.1, 131.7, 131.6, 130.5, 128.8, 128.4, 128.3, 128.0, 126.0, 119.3, 115.5, 111.2, 101.9, 93.0, 55.3, 29.7, 13.7. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{21}INO_2$ $[M+H]^+$ 482.0611; found 482.0609. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);



(2-iodophenyl)(3-isopropyl-2-methyl-1H-indol-1-yl)methanone ***(1r)*** 1.33 g, yield: 55%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.30 (d, *J* = 8.3 Hz, 1H), 7.22 – 7.14 (m, 2H), 7.06 (t, *J* = 7.8 Hz, 1H), 3.24 – 3.10 (m, 1H), 2.18 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.0, 142.3, 140.0, 136.4, 131.8, 130.9, 129.3, 129.2, 128.4, 126.2, 123.3, 122.8, 119.6, 114.8, 93.3, 25.7, 22.0, 13.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{19}INO$ 404.0504; found 404.0506. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);

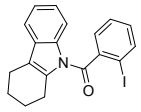


(3-hexyl-2-methyl-1H-indol-1-yl)(2-iodophenyl)methanone ***(1s)*** 1.15 g, yield: 43%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.49 – 7.40 (m, 3H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.08 (t, *J* = 7.7 Hz, 1H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.18 (s, 3H), 1.64 – 1.53 (m, 2H), 1.39 – 1.26 (m, 6H), 0.92 – 0.82 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.9, 142.4, 139.9, 136.1, 132.3, 131.7, 130.8, 129.1, 128.4, 123.6, 123.2, 121.4, 118.1, 114.8, 93.2, 31.7, 29.8, 29.2, 23.9, 22.6, 14.1, 13.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{25}INO$ 446.0975; found 446.0969. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);

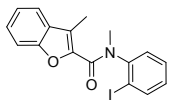


(2-iodophenyl)(3-methyl-2-(p-tolyl)-1H-indol-1-yl)methanone ***(1t)*** 1.57 g, yield: 58%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.06 (m, 1H), 7.57 – 7.53 (m, 2H), 7.38 – 7.32 (m, 2H), 7.09 – 7.02 (m, 4H), 6.96 – 6.91 (m, 2H), 6.86 – 6.79 (m, 1H), 2.23 (s, 3H), 2.15 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.3, 141.4, 139.3, 137.2, 136.9, 135.5, 130.9, 130.3, 130.0, 129.2, 128.3, 127.3, 125.1, 123.7, 118.7, 118.3, 115.4, 94.3, 21.1, 9.3. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{19}INO$ 452.0506; found 452.0500. Purified by chromatography on

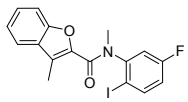
silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);



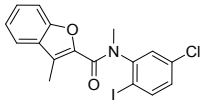
(3,4-dihydro-1H-carbazol-9(2H)-yl)(2-iodophenyl)methanone ***(1u)*** 0.91 g, yield: 38%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.36 – 7.28 (m, 3H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.13 – 7.04 (m, 2H), 2.58 (s, 2H), 2.33 (d, *J* = 20.9 Hz, 2H), 1.77 – 1.61 (m, 4H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.1, 142.2, 139.3, 135.9, 134.7, 131.3, 130.2, 128.4, 128.1, 123.8, 123.3, 119.0, 117.4, 115.1, 92.9, 25.3, 23.3, 21.6, 20.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{17}INO$ 402.0349; found 402.0354. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 70:1 (v/v);



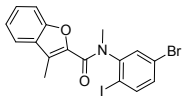
N-(2-iodophenyl)-N,3-dimethylbenzofuran-2-carboxamide ***(5a)*** 2.82 g, yield: 72%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.24 – 7.13 (m, 2H), 7.03 – 6.96 (m, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 3.37 (s, 3H), 2.58 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.2, 153.2, 146.5, 143.7, 139.5, 129.1, 129.0, 128.8, 126.4, 123.5, 122.6, 120.5, 111.2, 98.9, 37.3, 9.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{15}INO_2$ 392.0142; found 392.0140. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1-20:1 (v/v);



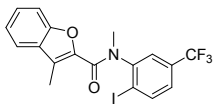
N-(5-fluoro-2-iodophenyl)-N,3-dimethylbenzofuran-2-carboxamide ***(5b)*** 2.01 g, yield: 49%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.72 (m, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.29 – 7.17 (m, 2H), 7.11 (dd, *J* = 8.9, 2.9 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 1H), 6.82 (td, *J* = 8.3, 2.9 Hz, 1H), 3.36 (s, 3H), 2.59 (s, 3H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.2, 161.8, 160.9, 153.2, 148.0, 147.9, 143.4, 140.1, 140.1, 128.7, 126.6, 124.2, 122.8, 120.6, 116.8, 116.8, 116.6, 116.5, 111.3, 92.3, 37.2, 9.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.37. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}FINO_2$ 410.0048; found 410.0045. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1-20:1 (v/v);



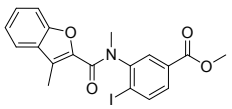
N-(5-chloro-2-iodophenyl)-N,3-dimethylbenzofuran-2-carboxamide ***(5c)*** 2.72 g, yield: 64%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.68 (m, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 2.3 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.23 – 7.17 (m, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 3.36 (s, 3H), 2.60 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.8, 153.2, 147.7, 143.3, 140.1, 134.7, 129.4, 129.3, 128.7, 126.7, 124.3, 122.8, 120.6, 111.3, 96.4, 37.2, 9.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}ClINO_2$ 425.9752; found 425.9748. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1-20:1 (v/v);



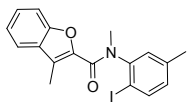
N-(5-bromo-2-iodophenyl)-N,3-dimethylbenzofuran-2-carboxamide ***(5d)*** 1.79 g, yield: 38%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.4 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.30 – 7.23 (m, 1H), 7.23 – 7.11 (m, 2H), 6.98 (d, *J* = 7.8 Hz, 1H), 3.35 (s, 3H), 2.59 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.8, 153.2, 147.8, 143.3, 140.3, 132.2, 132.2, 128.7, 126.6, 124.3, 122.7, 122.2, 120.6, 111.3, 97.3, 37.2, 9.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{14}BrINO_2$ 469.9247; found 469.9243. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1-20:1 (v/v);



N-(2-iodo-5-(trifluoromethyl)phenyl)-N,3-dimethylbenzofuran-2-carboxamide ***(5e)*** 1.88 g, yield: 41%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.3 Hz, 1H), 7.67 (s, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.28 – 7.15 (m, 3H), 6.88 (d, *J* = 8.1 Hz, 1H), 3.39 (s, 3H), 2.59 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.8, 153.1, 147.3, 143.2, 140.2, 132.3, 131.9, 131.6, 131.3, 128.6, 127.4, 126.7, 126.3, 126.2, 125.5, 125.5, 125.4, 125.4, 124.7, 124.4, 122.8, 122.0, 120.6, 119.3, 111.1, 103.5, 37.1, 9.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.81. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{14}F_3INO_2$ 460.0016; found 460.0012. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1-20:1 (v/v);

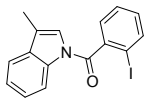


methyl 3-(N,3-dimethylbenzofuran-2-carboxamido)-4-iodobenzoate ***(5f)*** 2.02 g, yield: 45%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.88 (m, 2H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.25 – 7.13 (m, 2H), 6.89 (d, *J* = 7.9 Hz, 1H), 3.90 (s, 3H), 3.38 (s, 3H), 2.60 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.7, 160.8, 153.1, 147.0, 143.3, 139.7, 131.4, 129.6, 129.6, 128.7, 126.6, 124.3, 122.7, 120.5, 111.2, 105.6, 52.4, 37.2, 9.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{17}INO_4$ 450.0197; found 450.0190. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 8:1 (v/v);



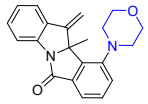
*N-(2-iodo-5-methylphenyl)-N,3-dimethylbenzofuran-2-carboxamide****(5g)*** 2.03 g, yield: 50%, white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.1 Hz, 1H), 7.51 (d, *J* = 7.4 Hz, 1H), 7.26 – 7.12 (m, 3H), 6.95 (d, *J* = 8.1 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 3.36 (s, 3H), 2.58 (s, 3H), 2.28 (s, 3H). ^{13}C{^{1}H}

NMR (101 MHz, $CDCl_3$) δ 161.1, 153.2, 146.2, 143.8, 139.3, 139.0, 130.0, 129.7, 128.8, 126.3, 123.4, 122.5, 120.4, 111.2, 94.6, 37.3, 20.7, 9.4. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{17}INO_2$ 406.0298; found 406.0294. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1-20:1 (v/v);

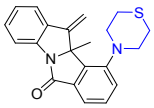


(2-iodophenyl)(3-methyl-1H-indol-1-yl)methanone ***(11)*** 1.19 g, yield: 55%, white soild. ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.41 (m, 2H), 7.41 – 7.27 (m, 3H), 7.22 – 7.14 (m, 1H), 6.68 (s, 1H), 2.20 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 167.5, 141.3, 139.4, 135.6, 132.1, 131.3, 128.1, 125.2, 124.1, 123.3, 119.0, 119.0, 118.9, 116.5, 92.4, 9.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}INO$ 362.0036; found 362.0032. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);

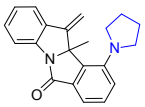
Characterization Data of Product.



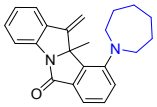
10b-methyl-11-methylene-10-morpholino-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3a)*** 56.0 mg, yield: 84%, white soild, mp 146℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.72 (m, 2H), 7.68 – 7.64 (m, 1H), 7.53 – 7.46 (m, 2H), 7.37 (td, *J* = 7.7, 1.0 Hz, 1H), 7.14 (td, *J* = 7.6, 0.8 Hz, 1H), 6.15 (s, 1H), 5.67 (s, 1H), 3.94 (t, *J* = 4.6 Hz, 4H), 3.16 – 3.07 (m, 2H), 2.99 – 2.89 (m, 2H), 1.88 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.6, 149.4, 147.9, 146.5, 140.8, 134.2, 133.2, 130.2, 129.9, 129.7, 124.7, 123.2, 121.3, 117.5, 106.0, 75.6, 67.1, 54.5, 30.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{21}N_2O_2$ 333.1598; found 333.1601. IR (cm^{-1}): 2962.66, 2853.84, 1712.00, 1483.97, 1369.28, 1300.26, 1114.70, 761.86, 735.27. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 6:1 (v/v);



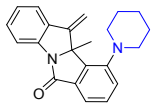
10b-methyl-11-methylene-10-thiomorpholino-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3b)*** 51.0 mg, yield: 73%, white soild, mp 186℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.7 Hz, 2H), 7.65 – 7.61 (m, 1H), 7.52 – 7.46 (m, 2H), 7.40 – 7.34 (m, 1H), 7.17 – 7.12 (m, 1H), 6.09 (s, 1H), 5.66 (s, 1H), 3.36 – 3.29 (m, 2H), 3.20 – 3.12 (m, 2H), 2.90 (s, 4H), 1.86 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.6, 150.4, 147.9, 145.8, 140.7, 134.3, 133.2, 130.2, 130.0, 129.8, 124.7, 123.2, 121.3, 117.5, 106.0, 75.6, 56.1, 29.7, 28.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{21}N_2OS$ 349.1369; found 349.1365. IR (cm^{-1}): 2923.74, 2828.49, 1708.06, 1481.85, 1352.78, 1301.82, 946.83, 762.13, 734.96. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 10:1 (v/v);



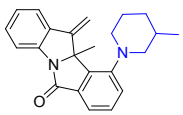
10b-methyl-11-methylene-10-(pyrrolidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3c)*** 53.3 mg, yield: 84%, white soild, mp 150℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.3 Hz, 1H), 7.63 (d, J = 7.9 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.02 (s, 1H), 5.66 (s, 1H), 3.25 – 3.15 (m, 2H), 3.07 – 2.98 (m, 2H), 2.06 – 1.97 (m, 4H), 1.86 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.9, 148.2, 147.7, 147.6, 140.8, 133.9, 133.4, 130.1, 130.0, 129.7, 124.5, 122.3, 121.2, 117.3, 106.1, 106.1, 75.6, 56.1, 30.2, 24.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{21}N_2O$ 317.1648; found 317.1646. IR (cm^{-1}): 2969.37, 2823.15, 1710.26, 1465.73, 1348.47, 1299.67, 900.47, 760.36. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 15:1 (v/v);



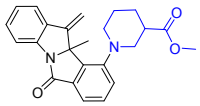
10-(azepan-1-yl)-10b-methyl-11-methylene-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3d)*** 58.0 mg, yield: 84%, white soild, mp 134℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 1H), 7.67 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.49 – 7.40 (m, 2H), 7.35 (td, *J* = 7.8, 1.0 Hz, 1H), 7.12 (td, *J* = 7.6, 1.0 Hz, 1H), 6.28 (s, 1H), 5.68 (s, 1H), 3.18 – 3.02 (m, 4H), 1.91 – 1.78 (m, 11H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.8, 153.6, 147.7, 145.0, 140.8, 133.9, 133.4, 130.6, 130.1, 129.7, 124.6, 122.2, 121.2, 117.4, 106.6, 75.7, 59.8, 29.9, 28.5, 26.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{25}N_2O$ 345.1961; found 345.1965. IR (cm^{-1}): 2929.21, 2857.88, 1710.52, 1465.54, 1349.19, 1301.70, 1134.84, 899.27, 759.85. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 15:1 (v/v);



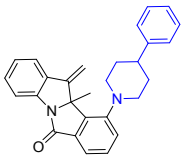
10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3e)*** 57.7 mg, yield: 87%, yellow soild, mp 130℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 1H), 7.69 (dd, *J* = 7.3, 0.8 Hz, 1H), 7.62 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.35 (td, *J* = 7.8, 1.0 Hz, 1H), 7.12 (td, *J* = 7.7, 1.0 Hz, 1H), 6.21 (s, 1H), 5.66 (s, 1H), 3.06 – 2.98 (m, 2H), 2.91 – 2.76 (m, 2H), 1.88 (s, 3H), 1.82 – 1.74 (m, 4H), 1.65 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.9, 151.2, 147.8, 146.3, 140.8, 134.0, 133.5, 129.9, 129.8, 129.6, 124.6, 122.6, 121.2, 117.5, 106.3, 75.7, 55.6, 29.6, 26.1, 24.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{23}N_2O$ 331.1805; found 331.1807. IR (cm^{-1}): 2935.97, 2853.94, 1710.68, 1465.87, 1349.94, 1301.96, 898.95, 761.19. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 20:1 (v/v);



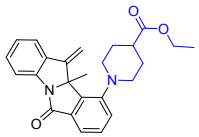
10b-methyl-11-methylene-10-(3-methylpiperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3f)*** 49.1 mg, yield: 71%, yellow soild, mp 108℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.48 – 7.42 (m, 2H), 7.35 (td, *J* = 7.7, 1.2 Hz, 1H), 7.12 (td, *J* = 7.6, 1.1 Hz, 1H), 6.18 (d, *J* = 5.5 Hz, 1H), 5.65 (d, *J* = 2.6 Hz, 1H), 3.09 – 2.93 (m, 2H), 2.91 – 2.25 (m, 2H), 1.99 – 1.73 (m, 7H), 1.17 – 1.02 (m, 1H), 0.94 (dd, *J* = 27.7, 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.9, 168.9, 151.0, 151.0, 147.9, 147.9, 146.3, 140.9, 140.9, 134.0, 133.4, 129.9, 129.8, 129.6, 129.5, 124.6, 122.6, 121.2, 117.5, 106.2, 75.7, 64.5, 61.5, 56.6, 53.6, 32.8, 32.7, 31.8, 31.2, 29.6, 29.6, 25.9, 25.7, 19.7, 19.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{25}N_2O$ 345.1961; found 345.1966. IR (cm^{-1}): 2928.17, 2851.58, 1711.67, 1464.79, 1350.40, 1301.72, 1133.32, 760.71, 735.92. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);



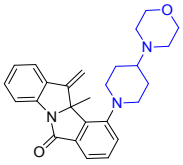
methyl 1-(10b-methyl-11-methylene-6-oxo-10b,11-dihydro-6H-isoindolo[2,1-a]indol-10-yl)piperidine-3-carboxylate ***(3g)*** 59.2 mg, yield: 76%, yellow soild, mp 102℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 2H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.06 (s, 1H), 5.68 – 5.63 (m, 1H), 3.72 – 3.67 (m, 3H), 3.35 – 3.22 (m, 1H), 3.18 – 2.90 (m, 2H), 2.88 – 2.65 (m, 2H), 2.25 – 2.07 (m, 1H), 1.97 – 1.90 (m, 1H), 1.88 – 1.84 (m, 3H), 1.82 – 1.56 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 174.1, 173.9, 168.7, 150.1, 150.1, 147.9, 147.8, 146.1, 146.1, 140.8, 134.2, 133.3, 133.3, 130.1, 130.0, 129.9, 129.9, 129.5, 129.5, 124.7, 123.1, 123.0, 121.3, 117.5, 117.4, 106.0, 106.0, 75.6, 75.6, 57.7, 56.4, 55.3, 53.6, 51.8, 51.7, 42.4, 41.7, 29.7, 29.6, 26.8, 26.5, 24.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{25}N_2O_3$ 389.1860; found 389.1865. IR (cm^{-1}): 2949.83, 2854.11, 1713.27, 1465.14, 1352.06, 1302.82, 761.93. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 8:1 (v/v);



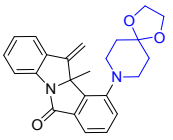
10b-methyl-11-methylene-10-(4-phenylpiperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3h)*** 65.2 mg, yield: 80%, yellow soild, mp 216℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.70 (m, 2H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.38 – 7.30 (m, 5H), 7.27 – 7.21 (m, 1H), 7.16 – 7.10 (m, 1H), 6.24 (s, 1H), 5.69 (s, 1H), 3.27 – 3.18 (m, 1H), 3.18 – 3.10 (m, 2H), 2.92 – 2.81 (m, 1H), 2.81 – 2.69 (m, 1H), 2.09 – 1.96 (m, 4H), 1.91 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.0, 150.9, 148.1, 146.5, 146.0, 141.0, 134.3, 133.6, 130.2, 130.0, 129.6, 128.7, 126.9, 126.5, 124.8, 123.0, 121.5, 117.7, 106.4, 75.8, 57.1, 54.1, 42.2, 33.9, 33.7, 29.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{28}H_{27}N_2O$ 407.2118; found 407.2122. IR (cm^{-1}): 2934.53, 2811.47, 1709.52, 1466.00, 1348.95, 1301.09, 759.66, 700.63. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 14:1 (v/v);



ethyl 1-(10b-methyl-11-methylene-6-oxo-10b,11-dihydro-6H-isoindolo[2,1-a]indol-10-yl)piperidine-4-carboxylate ***(3i)*** 64.6 mg, yield: 80%, white soild, mp 160℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.67 (m, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.11 (s, 1H), 5.66 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.20 – 3.12 (m, 1H), 3.12 – 3.05 (m, 1H), 3.00 (td, *J* = 11.2, 2.9 Hz, 1H), 2.74 (td, *J* = 11.4, 2.8 Hz, 1H), 2.57 – 2.47 (m, 1H), 2.15 – 1.95 (m, 4H), 1.87 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 174.8, 168.7, 150.3, 147.7, 146.2, 140.7, 134.1, 133.3, 130.0, 129.8, 129.3, 124.6, 122.9, 121.3, 117 .4, 106.2, 75.6, 60.5, 55.3, 52.9, 40.6, 29.5, 28.6, 28.3, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{27}N_2O_3$ 403.2016; found 403.2020. IR (cm^{-1}): 2952.80, 2814.09, 1716.22, 1466.17, 1348.62, 1302.06, 1135.37, 1045.08, 762.21. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 8:1 (v/v);

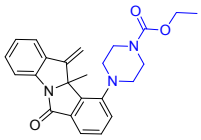


10b-methyl-11-methylene-10-(4-morpholinopiperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3j)*** 65.8 mg, yield: 79%, white soild, mp 218℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.69 (m, 2H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.39 – 7.33 (m, 1H), 7.17 – 7.10 (m, 1H), 6.12 (s, 1H), 5.64 (s, 1H), 3.87 – 3.71 (m, 4H), 3.21 – 3.08 (m, 2H), 3.07 – 2.98 (m, 1H), 2.78 – 2.70 (m, 1H), 2.68 – 2.58 (m, 4H), 2.43 – 2.33 (m, 1H), 2.11 – 1.98 (m, 2H), 1.87 (s, 3H), 1.83 – 1.68 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 150.2, 147.7, 146.2, 140.8, 134.1, 133.4, 129.9, 129.8, 129.2, 124.6, 122.9, 121.2, 117.5, 106.2, 75.6, 67.2, 61.7, 55.6, 52.7, 50.1, 29.5, 29.1, 28.7. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{30}N_3O_2$ 416.2333; found 416.2333. IR (cm^{-1}): 2952.12, 2853.18, 1710.06, 1465.81, 1348.83, 1301.90, 1119.64, 898.58, 762.10. Purified by chromatography on silica gel, eluting with dichloromethane/methanol 25:1 (v/v);

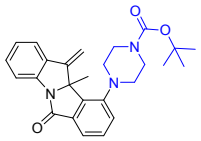


10b-methyl-11-methylene-10-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3k)*** 62.3 mg, yield: 80%, yellow soild, mp 150℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.66 (m, 3H), 7.49 – 7.42 (m, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.15 (s, 1H), 5.65 (s, 1H), 4.04 (s, 4H), 3.23 – 3.12 (m, 2H), 3.05 – 2.95 (m, 2H), 2.00 – 1.92 (m, 4H), 1.88 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.7, 150.1, 147.8, 146.1, 140.8, 134.0, 133.3, 130.0, 129.8, 129.5, 124.6, 122.9, 121.3, 117.4, 106.5, 106.0, 75.6, 64.3, 52.6, 35.3, 29.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{25}N_2O_3$ 389.1860; found 389.1864. IR

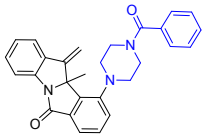
(cm^{-1}): 2959.45, 2835.30, 1710.22, 1482.87, 1366.15, 1306.27, 1140.81, 1112.64, 1042.59, 762.46, 735.29. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 5:1 (v/v);



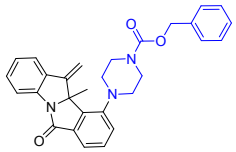
ethyl 4-(10b-methyl-11-methylene-6-oxo-10b,11-dihydro-6H-isoindolo[2,1-a]indol-10-yl)piperazine-1-carboxylate ***(3l)*** 64.7 mg, yield: 69%, yellow soild, mp 130℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 7.9 Hz, 1H), 7.48 (t, J = 7.4 Hz, 2H), 7.37 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 6.12 (s, 1H), 5.66 (s, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.73 (s, 4H), 3.14 – 3.03 (m, 2H), 2.97 – 2.86 (m, 2H), 1.88 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.5, 155.5, 149.3, 147.8, 146.1, 140.7, 134.2, 133.1, 130.1, 129.9, 129.3, 124.7, 123.2, 121.3, 117.4, 105.9, 75.5, 61.5, 53.9, 45.7, 43.8, 29.9, 14.6, 8.5. HRMS (ESI) *m/z*: [M+H]$^+$ Calcd for $C_{24}H_{26}N_3O_3$ 404.1969; found 404.1974. IR (cm^{-1}): 2981.38, 2859.74, 1704.42, 1466.21, 1353.31, 1304.12, 1245.73, 1130.82, 989.21, 762.65. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 4:1 (v/v);



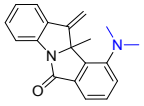
tert-butyl 4-(10b-methyl-11-methylene-6-oxo-10b,11-dihydro-6H-isoindolo[2,1-a]indol-10-yl)piperazine-1-carboxylate ***(3m)*** 62.3 mg, yield: 72%, yellow soild, mp 120℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.4 Hz, 2H), 7.60 (d, J = 7.8 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 7.36 (t, J = 7.7 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 6.13 (s, 1H), 5.65 (s, 1H), 3.67 (s, 4H), 3.12 – 3.02 (m, 2H), 2.94 – 2.86 (m, 2H), 1.88 (s, 3H), 1.52 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.5, 154.8, 149.5, 147.9, 146.2, 140.7, 134.2, 133.2, 130.2, 129.9, 129.4, 124.7, 123.3, 121.3, 117.5, 105.9, 80.0, 75.5, 54.1, 29.9, 28.4. HRMS (ESI) *m/z*: [M+H]$^+$ Calcd for $C_{26}H_{30}N_3O_3$ 432.2282; found 432.2285. IR (cm^{-1}): 2977.73, 2861.06, 1696.21, 1484.78, 1368.24, 1248.15, 1168.54, 762.22, 735.90. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 7:1 (v/v);



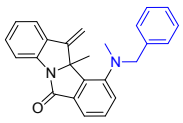
10-(4-benzoylpiperazin-1-yl)-10b-methyl-11-methylene-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3n)*** 52.4 mg, yield: 60%, yellow soild, mp 90℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, J = 7.5, 3.1 Hz, 2H), 7.62 (d, J = 7.4 Hz, 1H), 7.52 – 7.46 (m, 4H), 7.46 – 7.43 (m, 3H), 7.37 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 6.10 (s, 1H), 5.66 (s, 1H), 4.25 – 3.51 (m, 4H), 3.25 – 2.79 (m, 4H), 1.88 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.8, 168.6, 149.0, 148.1, 146.3, 140.9, 135.6, 134.5, 133.2, 130.4, 130.2, 130.1, 129.5, 128.7, 127.2, 124.9, 123.6, 121.5, 117.6, 105.9, 75.6, 54.5, 48.1, 42.4, 30.1. HRMS (ESI) *m/z*: [M+H]$^+$ Calcd for $C_{28}H_{26}N_3O_2$ 436.2020; found 436.2025. IR (cm^{-1}): 3058.18, 2923.08, 2826.84, 1712.41, 1633.50, 1485.57, 1369.77, 1014.79, 762.44, 733.80, 709.23. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 2:1 (v/v);



benzyl 4-(10b-methyl-11-methylene-6-oxo-10b,11-dihydro-6H-isoindolo[2,1-a]indol-10-yl)piperazine-1-carboxylate ***(3o)*** 65.3 mg, yield: 70%, yellow soild, mp 76℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.68 (m, 2H), 7.59 – 7.54 (m, 1H), 7.49 – 7.44 (m, 2H), 7.40 – 7.32 (m, 6H), 7.12 (t, J = 7.5 Hz, 1H), 6.09 (s, 1H), 5.64 (s, 1H), 5.20 (s, 2H), 3.74 (s, 4H), 3.06 (s, 2H), 2.91 (s, 2H), 1.86 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.4, 155.2, 149.2, 147.9, 146.1, 140.7, 136.5, 134.2, 133.1, 130.1, 129.9, 129.3, 128.4, 128.0, 127.9, 124.7, 123.3, 121.2, 117.4, 105.8, 75.5, 67.3, 55.6, 53.9, 44.0, 42.1, 29.9. HRMS (ESI) *m/z*: [M+H]$^+$ Calcd for $C_{29}H_{28}N_3O_3$ 466.2125; found 466.2132. IR (cm^{-1}): 3061.03, 2949.06, 2859.71, 1704.51, 1464.70, 1431.11, 1359.05, 1244.27, 976.08, 761.73, 735.19, 700.58. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 4:1 (v/v);

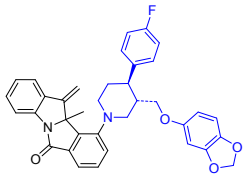


10-(dimethylamino)-10b-methyl-11-methylene-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3p)*** 46.1 mg, yield: 79%, white soild, mp 136℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.9 Hz, 1H), 7.70 (dd, J = 7.4, 1.1 Hz, 1H), 7.65 (dd, J = 8.0, 1.1 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.35 (td, J = 7.7, 1.2 Hz, 1H), 7.12 (td, J = 7.5, 1.1 Hz, 1H), 6.14 (s, 1H), 5.69 (s, 1H), 2.75 (s, 6H), 1.88 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 151.5, 147.4, 146.4, 140.8, 133.9, 133.3, 130.0, 129.7, 129.1, 124.5, 122.6, 121.2, 117.3, 106.3, 75.5, 47.1, 30.1. HRMS (ESI) *m/z*: [M+H]$^+$ Calcd for $C_{19}H_{19}N_2O$ 291.1492; found 291.1495. IR (cm^{-1}): 3051.46, 2975.75, 2938.96, 2861.56, 2827.31, 2786.70, 1711.52, 1465.85, 1350.13, 1300.34, 761.14. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 15:1 (v/v);

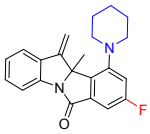


10-(benzyl(methyl)amino)-10b-methyl-11-methylene-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3q)*** 52.0 mg, yield: 71%, light yellow soild, mp 124℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.73 (m, 2H), 7.71 (d, J = 7.9 Hz, 1H), 7.54 – 7.46 (m, 4H), 7.42 – 7.30 (m, 4H), 7.17 – 7.11 (m, 1H), 6.20 (s, 1H), 5.71 (s, 1H), 4.26 (d, J = 13.5 Hz, 1H), 3.99 (d, J = 13.5 Hz, 1H), 2.63 (s, 3H), 1.94 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.6, 151.0, 147.6, 146.0, 140.7, 137.7, 134.4, 133.4, 130.0, 130.0, 129.9, 128.8, 128.6, 127.5, 124.6, 123.0, 121.3, 117.3, 106.7, 75.8, 63.6, 43.6, 29.7. HRMS (ESI) *m/z*: [M+H]$^+$ Calcd for $C_{25}H_{23}N_2O$ 366.1805; found 366.1810. IR (cm^{-1}): 3030.32,

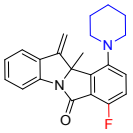
2924.20, 2847.46, 2797.33, 1709.90, 1464.77, 1353.30, 1300.08, 760.28. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 20:1 (v/v);



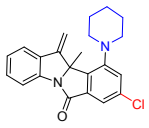
10-((3S,4R)-3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)piperidin-1-yl)-10b-methyl-11-methylene-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(3r)*** 86.3 mg, yield: 75%, yellow soild, mp 94℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.66 (m, 3H), 7.51 – 7.45 (m, 2H), 7.37 (td, *J* = 7.7, 1.2 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.17 – 7.11 (m, 1H), 7.03 (t, *J* = 8.6 Hz, 2H), 6.60 (dd, *J* = 15.0, 8.5 Hz, 1H), 6.31 (dd, *J* = 20.5, 2.5 Hz, 1H), 6.22 (d, *J* = 16.0 Hz, 1H), 6.16 – 6.06 (m, 1H), 5.86 (s, 1H), 5.84 (s, 1H), 5.69 (d, *J* = 12.3 Hz, 1H), 3.70 – 3.40 (m, 3H), 3.26 – 3.05 (m, 2H), 2.91 – 2.66 (m, 2H), 2.50 – 2.38 (m, 1H), 2.12 – 1.96 (m, 2H), 1.95 – 1.90 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.7 (d, *J* = 2.4 Hz), 161.6 (d, *J* = 244.8 Hz), 154.0 (d, *J* = 4.4 Hz), 150.3 (d, *J* = 3.4 Hz), 148.1, 148.1 (d, *J* = 9.1 Hz), 146.1 (d, *J* = 2.7 Hz), 141.6 (d, *J* = 2.7 Hz), 140.8, 139.2 (d, *J* = 3.0 Hz), 134.2 (d, *J* = 5.5 Hz), 133.4 (d, *J* = 1.5 Hz), 130.0, 129.9, 129.3 (d, *J* = 21.1 Hz), 128.8 (d, *J* = 7.9 Hz), 124.7 (d, *J* = 1.6 Hz), 123.0 (d, *J* = 6.2 Hz), 121.3, 117.5, 115.6, 115.4, 107.8 (d, *J* = 3.3 Hz), 106.0 (d, *J* = 11.7 Hz), 105.6 (d, *J* = 7.5 Hz), 101.0 (d, *J* = 2.3 Hz), 97.9 (d, *J* = 10.1 Hz), 75.7 (d, *J* = 2.3 Hz), 69.2 (d, *J* = 13.0 Hz), 60.2, 57.0 (d, *J* = 40.2 Hz), 53.6, 43.8 (d, *J* = 2.3 Hz), 42.5 (d, *J* = 38.2 Hz), 34.7 (d, *J* = 30.0 Hz), 29.6 (d, *J* = 2.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.92. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{36}H_{32}FN_2O_4$ 575.2341; found 575.2344. IR (cm^{-1}): 2918.58, 1709.99, 1507.17, 1486.09, 1350.49, 1222.63, 1185.99, 1037.08, 761.61. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 7:1 (v/v);



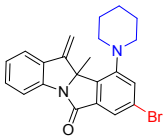
8-fluoro-10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4a)*** 61.5 mg, yield: 88%, white soild, mp 129℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.8 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.39 – 7.29 (m, 3H), 7.13 (td, *J* = 7.6, 1.1 Hz, 1H), 6.16 (s, 1H), 5.65 (s, 1H), 3.03 – 2.92 (m, 2H), 2.89 – 2.70 (m, 2H), 1.86 (s, 3H), 1.82 – 1.75 (m, 4H), 1.64 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.7 (d, *J* = 3.8 Hz), 163.6 (d, *J* = 251.1 Hz), 152.9 (d, *J* = 6.7 Hz), 147.6, 142.1 (d, *J* = 2.8 Hz), 140.5, 135.6 (d, *J* = 9.2 Hz), 133.4, 129.8, 124.8, 121.3, 117.5, 116.8 (d, *J* = 21.2 Hz), 109.3 (d, *J* = 23.6 Hz), 106.3, 75.4, 55.7, 29.5, 26.0, 23.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.51. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{22}FN_2O$ 349.1711; found 349.1715. IR (cm^{-1}): 3052.35, 2937.33, 2855.19, 2810.55, 1714.24, 1606.55, 1472.35, 1345.51, 1307.40, 1119.41, 868.56, 745.28. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 45:1 (v/v);



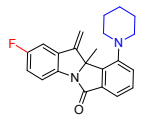
7-fluoro-10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4b)*** 53.1 mg, yield: 76%, yellow soild, mp 109℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.9 Hz, 1H), 7.62 – 7.53 (m, 1H), 7.47 (d, *J* = 7.4 Hz, 1H), 7.35 (td, *J* = 7.8, 1.0 Hz, 1H), 7.13 (td, *J* = 7.6, 0.8 Hz, 1H), 7.08 (t, *J* = 8.6 Hz, 1H), 6.19 (s, 1H), 5.67 (s, 1H), 3.00 – 2.92 (m, 2H), 2.80 (s, 2H), 1.86 (s, 3H), 1.80 – 1.73 (m, 4H), 1.64 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.7, 157.2 (d, *J* = 260.9 Hz), 148.2, 147.5, 147.0 (d, *J* = 4.2 Hz), 140.7, 133.2, 131.4 (d, *J* = 7.9 Hz), 129.8, 124.8, 121.2, 120.3 (d, *J* = 12.9 Hz), 117.6, 117.1 (d, *J* = 20.2 Hz), 106.5, 75.3, 55.8, 29.5, 26.0, 23.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.41. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{22}FN_2O$ 349.1711; found 349.1716. IR (cm^{-1}): 2936.37, 2854.16, 2810.54, 1715.76, 1495.07, 1465.22, 1342.94, 1300.11, 1261.42, 752.76. Purified by chromatography on silica gel, eluting with dichloromethane/petroleum ethyl 3:2 (v/v);



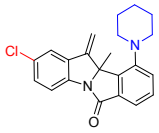
8-chloro-10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4c)*** 62.9 mg, yield: 86%, white soild, mp 129℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.9 Hz, 1H), 7.68 – 7.62 (m, 1H), 7.55 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.16 (s, 1H), 5.65 (s, 1H), 3.04 – 2.94 (m, 2H), 2.87 – 2.75 (m, 2H), 1.85 (s, 3H), 1.82 – 1.75 (m, 4H), 1.65 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.4, 152.3, 147.5, 144.7, 140.5, 135.6, 135.5, 133.3, 130.0, 129.8, 124.9, 122.7, 121.3, 117.5, 106.4, 75.5, 55.7, 29.5, 26.0, 23.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{22}ClN_2O$ 365.1415; found 365.1422. IR (cm^{-1}): 3075.04, 2919.16, 2850.56, 1707.99, 1461.05, 1263.16, 740.26. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 50:1 (v/v);



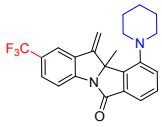
8-bromo-10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4d)*** 61.4 mg, yield: 75%, yellow soild, mp 200℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.79 (m, 1H), 7.73 – 7.68 (m, 2H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.15 (s, 1H), 5.65 (s, 1H), 3.03 – 2.96 (m, 2H), 2.87 – 2.77 (m, 2H), 1.85 (s, 3H), 1.81 – 1.74 (m, 4H), 1.65 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.3, 152.4, 147.4, 145.2, 140.5, 135.8, 133.4, 132.9, 129.9, 125.7, 124.9, 123.3, 121.3, 117.5, 106.4, 75.5, 55.7, 29.5, 26.0, 23.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{22}BrN_2O$ 409.0910; found 409.0919. IR (cm^{-1}): 3072.02, 2936.63, 2853.79, 1713.11, 1464.39, 1348.04, 1302.77, 760.25, 737.17. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 50:1 (v/v);



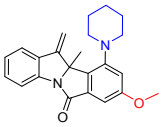
2-fluoro-10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4e)*** 56.6 mg, yield: 81%, yellow soild, mp 128℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.65 (m, 2H), 7.65 – 7.60 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.5 Hz, 1H), 7.04 (td, *J* = 8.8, 2.6 Hz, 1H), 6.26 (s, 1H), 5.64 (s, 1H), 3.05 – 2.97 (m, 2H), 2.89 – 2.73 (m, 2H), 1.87 (s, 3H), 1.82 – 1.74 (m, 4H), 1.65 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.0, 160.4 (d, *J* = 242.6 Hz), 151.2, 147.4 (d, *J* = 2.9 Hz), 146.1, 137.0, 135.1 (d, *J* = 8.6 Hz), 133.7, 130.0, 129.7, 122.6, 118.4 (d, *J* = 8.6 Hz), 116.4 (d, *J* = 24.0 Hz), 108.2 (d, *J* = 24.2 Hz), 107.7, 76.1, 55.6, 29.5, 26.1, 23.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.04. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{22}FN_2O$ 349.1711; found 349.1715. IR (cm^{-1}): 2936.79, 2854.58, 2807.84, 1712.10, 1479.26, 1349.03, 1270.38, 904.50, 817.44, 737.91. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 20:1 (v/v);



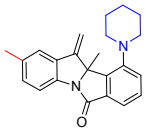
2-chloro-10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4f)*** 62.8 mg, yield: 86%, white soild, mp 129℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.58 (m, 3H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 1.7 Hz, 1H), 7.30 (dd, *J* = 8.3, 1.8 Hz, 1H), 6.26 (s, 1H), 5.65 (s, 1H), 3.06 – 2.96 (m, 2H), 2.90 – 2.71 (m, 2H), 1.86 (s, 3H), 1.81 – 1.74 (m, 4H), 1.65 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 151.2, 146.9, 146.0, 139.4, 135.1, 133.6, 130.1, 130.1, 129.8, 129.6, 122.7, 121.4, 118.4, 107.7, 76.0, 55.6, 29.6, 26.1, 23.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{22}ClN_2O$ 365.1415; found 365.1412. IR (cm^{-1}): 2932.90, 1714.08, 1468.47, 1342.55, 1265.91, 880.28, 817.63, 757.05. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 24:1 (v/v);



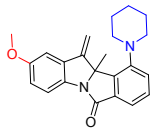
10b-methyl-11-methylene-10-(piperidin-1-yl)-2-(trifluoromethyl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4g)*** 64.7 mg, yield: 81%, yellow soild, mp 180℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 1H), 7.73 – 7.63 (m, 2H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 6.34 (s, 1H), 5.76 (s, 1H), 3.06 – 2.98 (m, 2H), 2.90 – 2.76 (m, 2H), 1.88 (s, 3H), 1.83 – 1.76 (m, 4H), 1.67 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 151.3, 146.7, 146.2, 143.4, 133.9, 133.4, 130.2, 130.1, 127.0 (q, *J* = 3.8 Hz), 126.9 (q, *J* = 32.5 Hz), 125.6, 122.9, 118.4 (q, *J* = 3.8 Hz), 117.4, 108.3, 76.0, 55.7, 29.7, 26.1, 23.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.80. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{22}F_3N_2O$ 399.1679; found 399.1676. IR (cm^{-1}): 2937.60, 1719.37, 1346.40, 1324.95, 1270.91, 1161.99, 1122.18, 888.96, 832.05, 759.49. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);



8-methoxy-10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4h)*** 60.0 mg, yield: 83%,, yellow soild, mp 238℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.20 – 7.16 (m, 2H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.16 (s, 1H), 5.63 (s, 1H), 3.85 (s, 3H), 3.05 – 2.94 (m, 2H), 2.88 – 2.74 (m, 2H), 1.85 (s, 3H), 1.82 – 1.73 (m, 4H), 1.64 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.0, 161.2, 152.2, 148.0, 140.8, 139.2, 134.9, 133.6, 129.7, 124.6, 121.3, 117.7, 117.5, 106.0, 105.1, 75.4, 55.8, 29.6, 26.2, 24.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{25}N_2O_2$ 361.1911; found 361.1917. IR (cm^{-1}): 2935.15, 2852.45, 1710.38, 1611.34, 1464.95, 1347.50, 1131.75, 745.14. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 15:1 (v/v);

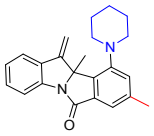


2,10b-dimethyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4i)*** 61.5 mg, yield: 89%, yellow soild, mp 122℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.3 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.27 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 6.17 (s, 1H), 5.62 (s, 1H), 3.05 – 2.95 (m, 2H), 2.89 – 2.74 (m, 2H), 2.35 (s, 3H), 1.86 (s, 3H), 1.81 – 1.73 (m, 4H), 1.64 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 151.2, 147.9, 146.2, 138.6, 134.2, 134.1, 133.5, 130.5, 129.8, 129.4, 122.5, 121.6, 117.1, 105.9, 75.9, 55.6, 29.5, 26.1, 24.0, 21.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{25}N_2O$ 345.1961; found 345.1960. IR (cm^{-1}): 2935.56, 2854.66, 2806.91, 1709.75, 1482.67, 1344.29, 1286.06, 1234.64, 967.12, 899.64, 815.21, 737.02. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 15:1 (v/v);

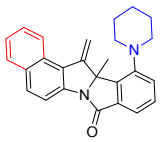


2-methoxy-10b-methyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4j)*** 60.0 mg, yield: 83%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.59 (m, 3H), 7.45 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 2.5 Hz, 1H), 6.92 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.20 (s, 1H), 5.63 (s, 1H), 3.82 (s, 3H), 3.07 – 2.95 (m, 2H), 2.91 – 2.71 (m, 2H), 1.87 (s, 3H), 1.81 – 1.74 (m, 4H), 1.65 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.9, 157.3, 151.1, 148.0, 146.1, 134.7, 134.6, 134.0, 129.9, 129.4, 122.5, 118.1, 115.6, 106.4, 76.1, 55.7, 29.4, 26.1, 24.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{25}N_2O_2$ 361.1911; found 361.1907. IR (cm^{-1}): 2935.94, 1707.00, 1592.13, 1483.07, 1351.48, 1279.28, 1230.82, 1067.34, 1032.37, 900.41, 759.66, 659.79. Purified by chromatography

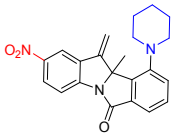
on silica gel, eluting with petroleum ethyl/acetate ether 14:1 (v/v);



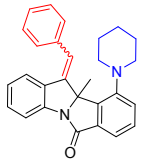
8,10b-dimethyl-11-methylene-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4k)*** 59.4 mg, yield: 86%, white soild, mp 136°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.9 Hz, 1H), 7.49 (s, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.41 (s, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.18 (s, 1H), 5.63 (s, 1H), 3.04 – 2.95 (m, 2H), 2.88 – 2.74 (m, 2H), 2.39 (s, 3H), 1.85 (s, 3H), 1.80 – 1.73 (m, 4H), 1.63 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.0, 150.9, 148.0, 143.5, 140.9, 140.1, 133.9, 133.4, 130.3, 129.6, 124.5, 122.8, 121.2, 117.4, 106.0, 75.4, 55.6, 29.5, 26.1, 24.0, 21.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{25}N_2O$ 345.1961; found 345.1965. IR (cm^{-1}): 3049.64, 2935.26, 2853.91, 2807.87, 1711.01, 1602.61, 1465.16, 1341.33, 1302.79, 896.32, 744.28. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 (v/v);



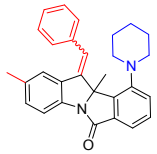
12b-methyl-13-methylene-12-(piperidin-1-yl)-12b,13-dihydro-8H-benzo[e]isoindolo[2,1-a]indol-8-one ***(4l)*** 61.0 mg, yield: 80%, yellow soild, mp 198°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 6.46 (s, 1H), 6.09 (s, 1H), 3.07 – 2.99 (m, 2H), 2.84 (s, 2H), 1.96 (s, 3H), 1.83 – 1.76 (m, 4H), 1.65 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.4, 151.2, 149.0, 146.3, 140.3, 134.4, 131.8, 131.1, 130.0, 130.0, 129.7, 129.5, 127.5, 125.4, 124.5, 122.8, 122.7, 117.3, 110.1, 76.8, 55.7, 29.2, 26.1, 24.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{25}N_2O$ 381.1961; found 381.1959. IR (cm^{-1}): 3055.01, 2935.56, 2853.57, 2806.94, 1708.84, 1588.22, 1480.07, 1330.61, 819.32, 739.75. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 16:1 (v/v);



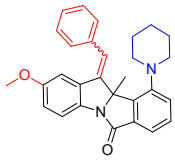
10b-methyl-11-methylene-2-nitro-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4m)*** 59.5 mg, yield: 79%, white soild, mp 192°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 2.2 Hz, 1H), 8.26 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.51 (t, *J* = 7.7 Hz, 1H), 6.44 (s, 1H), 5.86 (s, 1H), 3.06 – 2.99 (m, 2H), 2.91 – 2.77 (m, 2H), 1.89 (s, 3H), 1.84 – 1.77 (m, 4H), 1.68 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.5, 151.3, 146.1, 145.9, 145.7, 144.9, 134.4, 132.9, 130.5, 130.4, 125.8, 123.0, 117.0, 116.9, 109.6, 76.3, 55.7, 30.0, 26.1, 23.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{22}N_3O_3$ 376.1656; found 376.1663. IR (cm^{-1}): 2935.29, 1720.93, 1592.04, 1521.32, 1469.50, 1320.36, 1268.94, 1130.14, 903.97, 740.86. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 20:1 (v/v);



11-benzylidene-10b-methyl-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4n)*** 66.0 mg, yield: 81%, white soild, mp 152°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.94 (m, 1H), 7.78 – 6.50 (m, 12H), 3.61 – 2.33 (m, 4H), 2.04 – 1.90 (m, 3H), 1.80 – 1.33 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.4, 167.9, 153.6, 151.1, 146.4, 142.8, 141.9, 141.5, 140.8, 138.8, 138.6, 137.1, 136.3, 134.3, 132.8, 132.1, 130.3, 129.9, 129.7, 129.5, 129.3, 129.1, 128.9, 128.5, 128.3, 128.1, 127.9, 127.8, 127.2, 126.8, 125.7, 125.0, 124.7, 124.0, 124.0, 122.7, 121.2, 120.6, 118.9, 117.8, 76.6, 75.5, 57.4, 55.6, 29.4, 26.7, 26.2, 26.1, 24.9, 24.2, 23.9, 23.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{28}H_{27}N_2O$ 407.2118; found 407.2124. IR (cm^{-1}): 3054.44, 2935.50, 2854.17, 2805.67, 1709.33, 1599.96, 1464.40, 1333.12, 759.33, 735.57, 702.36. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 15:1 (v/v);

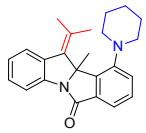


11-benzylidene-2,10b-dimethyl-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4o)*** 59.8 mg, yield: 71%, white soild, mp 160°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.91 (m, 1H), 7.79 – 7.67 (m, 1H), 7.66 – 7.50 (m, 2H), 7.49 – 7.41 (m, 1H), 7.41 – 7.15 (m, 5H), 7.11 – 6.94 (m, 2H), 3.10 – 2.44 (m, 4H), 2.41 – 2.12 (m, 3H), 2.03 – 1.92 (m, 3H), 1.89 – 1.54 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.3, 151.1, 146.4, 140.9, 139.3, 137.2, 134.4, 133.5, 132.2, 130.2, 129.9, 129.5, 128.4, 128.2, 127.2, 125.4, 125.2, 122.6, 117.5, 76.8, 55.7, 29.3, 26.2, 24.0, 21.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{29}N_2O$ 421.2274; found 421.2273. IR (cm^{-1}): 3054.45, 3027.32, 2934.97, 2854.61, 2806.63, 1709.05, 1602.03, 1480.01, 1444.77, 1339.27, 814.71, 737.26, 702.66. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 16:1 (v/v);

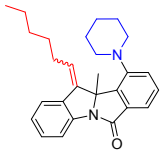


11-benzylidene-2-methoxy-10b-methyl-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4p)*** 68.2 mg, yield: 78%, white soild, mp 144°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.41 – 7.33 (m, 4H), 7.31 – 7.26 (m, 1H), 6.84 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.80 – 6.69 (m, 1H), 3.53 (s, 3H), 3.12 – 2.98 (m, 2H), 2.84 (s, 2H), 1.96 (s, 3H), 1.86 – 1.73 (m, 4H), 1.65 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ

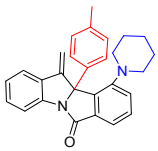
168.5, 156.3, 151.0, 146.3, 141.0, 137.0, 135.3, 134.4, 133.2, 129.9, 129.5, 128.4, 128.3, 127.4, 125.9, 122.6, 118.3, 115.7, 109.8, 55.5, 55.2, 29.3, 26.2, 23.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{29}N_2O_2$ 437.2224; found 437.2218. IR (cm^{-1}): 3054.80, 3025.98, 2935.93, 2852.97, 2832.65, 2807.00, 1706.84, 1590.18, 1481.11, 1442.00, 1359.19, 1329.81, 1272.70, 1226.29, 1032.66, 736.94. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 10:1 (v/v);



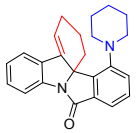
10b-methyl-10-(piperidin-1-yl)-11-(propan-2-ylidene)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4q)*** 38.1 mg, yield: 53%, yellow soild, mp 192℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.72 (m, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.60 – 7.56 (m, 1H), 7.53 – 7.45 (m, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.9 Hz, 1H), 3.11 – 2.99 (m, 2H), 2.79 – 2.61 (m, 2H), 2.19 (s, 3H), 1.99 (s, 3H), 1.89 (s, 3H), 1.81 – 1.66 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.1, 153.3, 142.4, 139.3, 137.1, 136.3, 135.5, 130.8, 130.3, 128.2, 126.1, 124.4, 121.9, 119.0, 78.2, 26.2, 25.6, 24.1, 23.1, 21.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{27}N_2O$ 359.2118; found 359.2118. IR (cm^{-1}): 2934.26, 1707.23, 1476.64, 1361.56, 1321.18, 965.99, 758.00. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 14:1 (v/v);



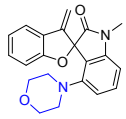
11-hexylidene-10b-methyl-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4r)*** 63.4 mg, yield: 79%, yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 – 7.37 (m, 5H), 7.36 – 7.27 (m, 1H), 7.18 – 7.08 (m, 1H), 6.78 – 5.89 (m, 1H), 4.27 – 2.98 (m, 2H), 2.94 – 2.29 (m, 4H), 1.94 – 1.83 (m, 3H), 1.82 – 1.60 (m, 6H), 1.59 – 1.39 (m, 2H), 1.39 – 1.28 (m, 4H), 0.91 – 0.77 (m, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.0, 168.4, 153.0, 151.1, 146.6, 141.6, 140.9, 140.0, 138.9, 138.7, 137.2, 135.0, 134.3, 133.7, 130.8, 130.3, 129.7, 129.4, 128.7, 128.5, 128.2, 128.0, 128.0, 125.3, 124.9, 124.4, 122.5, 121.9, 120.3, 118.7, 117.7, 76.4, 76.2, 55.6, 31.8, 30.8, 29.4, 29.3, 29.2, 28.6, 26.2, 26.1, 24.0, 24.0, 22.7, 22.5, 14.0, 14.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{33}N_2O$ 401.2587; found 401.2582. IR (cm^{-1}): 3055.28, 2930.71, 2857.03, 2808.85, 1710.87, 1602.92, 1479.75, 1463.18, 1347.60, 759.93, 736.92. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 20:1 (v/v);



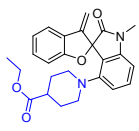
11-methylene-10-(piperidin-1-yl)-10b-(p-tolyl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(4s)*** 35.1 mg, yield: 43%, yellow soild, mp 170℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 6.1, 2.5 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.47 – 7.42 (m, 4H), 7.29 – 7.24 (m, 1H), 7.10 – 7.02 (m, 3H), 6.44 (s, 1H), 6.00 (s, 1H), 2.55 – 2.35 (m, 2H), 2.27 – 2.13 (m, 5H), 1.56 – 1.37 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.8, 150.6, 146.5, 144.1, 140.3, 137.4, 137.0, 134.8, 134.1, 130.3, 129.8, 129.2, 128.6, 127.1, 124.8, 122.1, 121.1, 117.5, 110.5, 80.3, 54.5, 26.1, 23.9, 20.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{28}H_{27}N_2O$ 407.2118; found 407.2116. IR (cm^{-1}): 2935.40, 2853.57, 2805.70, 1709.31, 1465.63, 1350.18, 1304.49, 758.94. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 20:1 (v/v);



5-(piperidin-1-yl)-3,4-dihydroisoindolo[1,2-k]carbazol-9(2H)-one ***(4t)*** 45.1 mg, yield: 63%, white soild, mp 196℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.0 Hz, 1H), 7.62 (dd, *J* = 6.1, 2.4 Hz, 1H), 7.40 – 7.35 (m, 3H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.21 – 6.17 (m, 1H), 3.26 – 2.77 (m, 4H), 2.56 – 2.42 (m, 1H), 2.32 – 2.18 (m, 1H), 2.09 – 1.98 (m, 1H), 1.88 – 1.37 (m, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 175.6, 151.8, 150.9, 143.6, 136.0, 133.6, 131.1, 129.7, 128.4, 126.0, 123.6, 123.3, 121.7, 119.6, 114.0, 74.1, 40.0, 26.1, 25.7, 23.8, 16.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{25}N_2O$ 357.1961; found 357.1969. IR (cm^{-1}): 2930.18, 2856.74, 2812.14, 1716.86, 1598.70, 1461.34, 1358.50, 1324.75, 1294.50, 1133.29, 1099.34, 765.31. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 50:1 (v/v);

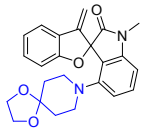


1'-methyl-3-methylene-4'-morpholino-3H-spiro[benzofuran-2,3'-indolin]-2'-one ***(6a)*** 40.6 mg, yield: 58%, white soild, mp 234℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 7.7 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.1 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.67 (d, *J* = 7.7 Hz, 1H), 5.41 (s, 1H), 4.56 (s, 1H), 3.26 – 3.20 (m, 5H), 3.11 – 3.03 (m, 2H), 3.03 – 2.97 (m, 2H), 2.71 – 2.64 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.3, 161.9, 151.4, 145.6, 131.7, 130.9, 126.4, 122.9, 121.6, 121.0, 116.3, 110.6, 104.6, 101.3, 88.7, 66.8, 52.8, 26.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{21}N_2O_3$ 349.1547; found 349.1543. IR (cm^{-1}): 2858.46, 1725.21, 1601.35, 1464.93, 1340.34, 1354.95, 1229.99, 1108.70, 854.33, 739.70. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 5:1 (v/v);

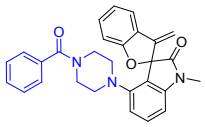


ethyl 1-(1'-methyl-3-methylene-2'-oxo-3H-spiro[benzofuran-2,3'-indolin]-4'-yl)piperidine-4-carboxylate ***(6b)*** 47.8 mg, yield: 57%, yellow soild, mp 118℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.26

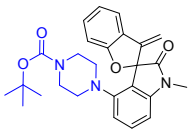
(t, J = 7.6 Hz, 1H), 7.02 – 6.91 (m, 2H), 6.82 (d, J = 8.3 Hz, 1H), 6.64 (d, J = 7.7 Hz, 1H), 5.40 (s, 1H), 4.55 (s, 1H), 4.05 (q, J = 7.1 Hz, 2H), 3.29 – 3.15 (m, 4H), 2.97 – 2.86 (m, 1H), 2.76 – 2.64 (m, 1H), 2.54 – 2.42 (m, 1H), 2.17 – 2.07 (m, 1H), 1.58 (d, J = 12.4 Hz, 1H), 1.46 (d, J = 12.7 Hz, 1H), 1.30 – 1.18 (m, 4H), 0.89 – 0.77 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 174.7, 173.4, 162.1, 152.2, 145.6, 145.5, 131.5, 130.7, 126.3, 122.6, 121.4, 121.0, 116.5, 110.7, 104.2, 101.1, 88.7, 60.0, 53.4, 51.0, 40.5, 28.1, 28.0, 26.6, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{27}N_2O_4$ 419.1965; found 419.1963. IR (cm^{-1}): 2950.99, 2806.97, 1732.73, 1603.82, 1463.13, 1340.73, 1303.70, 1253.82, 1169.87, 1046.00, 1013.19, 865.07, 749.08. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 7:1 (v/v);



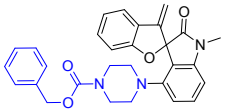
1'-methyl-3-methylene-4'-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3H-spiro[benzofuran-2,3'-indolin]-2'-one ***(6c)*** 44.6 mg, yield: 55%, yellow soild, mp 202℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.5 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 7.01 (t, J = 7.5 Hz, 1H), 6.93 (d, J = 8.1 Hz, 1H), 6.87 (d, J = 8.2 Hz, 1H), 6.64 (d, J = 7.7 Hz, 1H), 5.41 (s, 1H), 4.56 (s, 1H), 3.86 – 3.82 (m, 4H), 3.21 (s, 3H), 3.11 – 3.03 (m, 2H), 2.83 – 2.75 (m, 2H), 1.32 – 1.25 (m, 2H), 1.18 – 1.10 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.3, 162.1, 151.9, 145.6, 145.3, 131.5, 130.8, 126.3, 122.2, 121.4, 120.9, 116.6, 110.5, 106.6, 104.2, 101.2, 88.7, 64.0, 50.7, 34.7, 26.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{25}N_2O_4$ 405.1809; found 405.1806. IR (cm^{-1}): 2957.43, 1731.77, 1604.59, 1462.47, 1340.27, 1254.55, 1110.09, 749.17. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 5:1 (v/v);



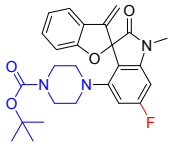
4'-(4-benzoylpiperazin-1-yl)-1'-methyl-3-methylene-3H-spiro[benzofuran-2,3'-indolin]-2'-one ***(6d)*** 43.5 mg, yield: 48%, yellow soild, mp 187℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.5 Hz, 1H), 7.46 – 7.33 (m, 5H), 7.31 – 7.28 (m, 2H), 7.03 (t, J = 7.5 Hz, 1H), 6.93 (d, J = 8.1 Hz, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.70 (d, J = 7.7 Hz, 1H), 5.42 (s, 1H), 4.58 (s, 1H), 3.29 – 3.22 (m, 4H), 3.10 – 2.88 (m, 3H), 2.82 – 2.57 (m, 3H), 1.74 – 1.57 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.3, 170.0, 162.0, 151.0, 145.8, 145.7, 135.7, 131.9, 131.1, 129.6, 128.4, 127.0, 126.4, 123.4, 121.7, 121.0, 116.6, 110.7, 105.2, 101.5, 88.7, 26.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{28}H_{26}N_3O_3$ 452.1969; found 452.1966. IR (cm^{-1}): 1731.80, 1633.81, 1605.33, 1461.92, 1256.61, 1011.51, 750.08, 710.09. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 2:1 (v/v);



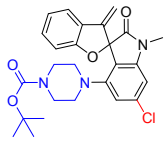
tert-butyl 4-(1'-methyl-3-methylene-2'-oxo-3H-spiro[benzofuran-2,3'-indolin]-4'-yl)piperazine-1-carboxylate ***(6e)*** 58.3 mg, yield: 65%, light yellow soild, mp 240℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.02 – 6.97 (m, 1H), 6.94 (d, J = 8.1 Hz, 1H), 6.81 (d, J = 7.9 Hz, 1H), 6.68 (d, J = 7.5 Hz, 1H), 5.40 (d, J = 1.2 Hz, 1H), 4.56 (d, J = 1.2 Hz, 1H), 3.22 (s, 3H), 3.00 – 2.88 (m, 4H), 2.88 – 2.74 (m, 2H), 2.65 – 2.57 (m, 2H), 1.41 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.3, 162.0, 154.4, 151.5, 145.7, 145.6, 131.7, 131.0, 126.3, 123.0, 121.6, 120.9, 116.5, 110.6, 104.8, 101.3, 88.7, 79.5, 52.4, 44.0, 43.0, 28.3, 26.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{30}N_3O_4$ 448.2231; found 448.2227. IR (cm^{-1}): 2975.79, 2818.02, 1733.77, 1691.66, 1605.01, 1462.59, 1422.60, 1365.35, 1252.62, 1170.48, 1126.78, 1014.36, 738.04. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 5:1 (v/v);



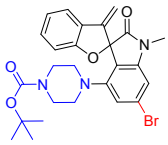
benzyl 4-(1'-methyl-3-methylene-2'-oxo-3H-spiro[benzofuran-2,3'-indolin]-4'-yl)piperazine-1-carboxylate ***(6f)*** 55.0 mg, yield: 57%, yellow soild, mp 196℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.37 – 7.29 (m, 6H), 7.27 – 7.24 (m, 1H), 6.99 (t, J = 7.4 Hz, 1H), 6.93 (d, J = 8.1 Hz, 1H), 6.80 (d, J = 8.2 Hz, 1H), 6.68 (d, J = 7.7 Hz, 1H), 5.40 (s, 1H), 5.11 – 5.02 (m, 2H), 4.56 (s, 1H), 3.22 (s, 3H), 3.10 – 3.00 (m, 2H), 2.98 – 2.83 (m, 4H), 2.64 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.2, 161.9, 154.9, 151.3, 145.7, 145.6, 136.6, 131.8, 131.0, 128.4, 127.9, 127.8, 126.3, 123.1, 121.6, 120.9, 116.5, 110.6, 104.9, 101.3, 88.6, 67.0, 52.3, 43.7, 26.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{28}N_3O_4$ 482.2074; found 482.2071. IR (cm^{-1}): 2936.07, 1732.99, 1700.27, 1604.71, 1463.31, 1430.30, 1246.84, 1123.84, 1013.85, 749.95, 699.21. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 4:1 (v/v);



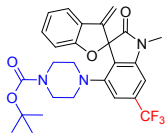
tert-butyl 4-(6'-fluoro-1'-methyl-3-methylene-2'-oxo-3H-spiro[benzofuran-2,3'-indolin]-4'-yl)piperazine-1-carboxylate ***(6g)*** 59.7 mg, yield: 64%, white soild, mp 80℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.32 – 7.25 (m, 1H), 7.00 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 8.1 Hz, 1H), 6.50 – 6.44 (m, 1H), 6.41 (dd, J = 8.1, 2.2 Hz, 1H), 5.41 (s, 1H), 4.56 (s, 1H), 3.20 (s, 3H), 3.02 – 2.90 (m, 4H), 2.88 – 2.79 (m, 2H), 2.68 – 2.59 (m, 2H), 1.41 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.3, 165.3 (d, J = 249.5 Hz), 161.7, 154.3, 153.0 (d, J = 9.5 Hz), 147.2 (d, J = 13.8 Hz), 145.0, 131.1, 126.1, 121.8, 121.0, 117.1 (d, J = 3.2 Hz), 110.7, 102.6 (d, J = 22.5 Hz), 101.6, 93.3 (d, J = 28.0 Hz), 88.3, 79.6, 55.8, 52.2, 28.3, 26.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.27. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{29}FN_3O_4$ 466.2137; found 466.2134. IR (cm^{-1}): 2976.49, 1740.33, 1693.03, 1608.51, 1454.66, 1420.51, 1252.16, 1170.89, 1130.03, 1017.39, 749.89. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 11:2 (v/v);



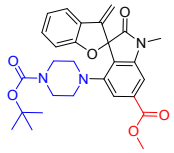
tert-butyl 4-(6'-chloro-1'-methyl-3-methylene-2'-oxo-3H-spiro[benzofuran-2,3'-indolin]-4'-yl)piperazine-1-carboxylate ***(6h)*** 71.4 mg, yield: 74%, yellow soild, mp 74℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.5 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.76 (d, *J* = 1.8 Hz, 1H), 6.67 (d, *J* = 1.8 Hz, 1H), 5.41 (s, 1H), 4.56 (s, 1H), 3.21 (s, 3H), 3.02 – 2.89 (m, 4H), 2.87 – 2.77 (m, 2H), 2.67 – 2.58 (m, 2H), 1.41 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 173.1, 161.7, 154.3, 152.1, 146.7, 145.0, 137.4, 131.2, 126.1, 121.8, 121.0, 120.4, 116.5, 110.7, 105.3, 101.6, 88.2, 79.6, 52.2, 43.1, 28.3, 26.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{29}ClN_3O_4$ 482.1841; found 482.1837. IR (cm^{-1}): 2975.25, 1739.79, 1692.77, 1597.92, 1460.81, 1422.51, 1251.12, 1170.49, 1015.81, 976.03, 748.22. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 6:1 (v/v);



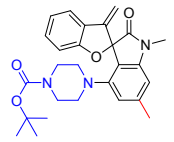
tert-butyl 4-(6'-bromo-1'-methyl-3-methylene-2'-oxo-3H-spiro[benzofuran-2,3'-indolin]-4'-yl)piperazine-1-carboxylate ***(6i)*** 53.7 mg, yield: 51%, yellow soild, mp 94℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.5 Hz, 1H), 7.32 – 7.25 (m, 2H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.96 – 6.90 (m, 2H), 6.84 – 6.81 (m, 1H), 5.41 (s, 1H), 4.56 (s, 1H), 3.21 (s, 3H), 3.00 – 2.89 (m, 4H), 2.87 – 2.76 (m, 2H), 2.67 – 2.57 (m, 2H), 1.41 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 173.0, 161.7, 154.3, 152.3, 146.8, 145.0, 131.2, 126.1, 125.3, 121.8, 121.1, 119.6, 110.7, 108.2, 101.7, 88.3, 79.7, 52.3, 43.7, 28.4, 26.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{29}BrN_3O_4$ 526.1336; found 526.1335. IR (cm^{-1}): 2975.48, 1739.96, 1692.78, 1592, 28, 1460.68, 1422.78, 1250.94, 1170.387, 1014.91, 973.10, 749.50. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 6:1 (v/v);



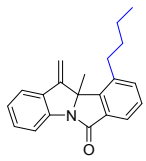
tert-butyl 4-(1'-methyl-3-methylene-2'-oxo-6'-(trifluoromethyl)-3H-spiro[benzofuran-2,3'-indolin]-4'-yl)piperazine-1-carboxylate ***(6j)*** 48.6 mg, yield: 47%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.5 Hz, 1H), 7.33 – 7.28 (m, 1H), 7.06 (s, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.88 (s, 1H), 5.44 – 5.42 (m, 1H), 4.58 – 4.55 (m, 1H), 3.26 (s, 3H), 3.03 – 2.93 (m, 4H), 2.88 – 2.79 (m, 2H), 2.70 – 2.63 (m, 2H), 1.41 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.9, 161.8, 154.2, 151.6, 146.5, 144.9, 134.0 (q, *J* = 32.5 Hz), 131.3, 126.0, 123.5 (q, *J* = 272.8 Hz), 122.0, 121.1, 113.6 (q, *J* = 3.5 Hz), 110.8, 101.7, 101.3 (q, *J* = 3.6 Hz), 88.0, 79.7, 52.2, 43.6, 43.0, 28.3, 26.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.84. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{29}F_3N_3O_4$ 516.2105; found 516.2101. IR (cm^{-1}): 2977.05, 1740.84, 1693.46, 1616.90, 1454.73, 1420.71, 1286.83, 1251.74, 1167.82, 1128.31, 1016.96, 860.20, 749.19. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 6:1 (v/v);



methyl 4'-(4-(tert-butoxycarbonyl)piperazin-1-yl)-1'-methyl-3-methylene-2'-oxo-3H-spiro[benzofuran-2,3'-indoline]-6'-carboxylate ***(6k)*** 58.8 mg, yield: 58%, yellow soild, mp 64℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.52 (m, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 5.41 (s, 1H), 4.54 (s, 1H), 3.95 (s, 3H), 3.28 (s, 3H), 3.02 – 2.92 (m, 4H), 2.88 – 2.79 (m, 2H), 2.69 – 2.60 (m, 2H), 1.41 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 173.0, 166.2, 161.9, 154.3, 151.3, 145.9, 145.2, 133.6, 131.2, 127.5, 126.1, 121.9, 121.1, 118.4, 110.8, 105.4, 101.6, 88.3, 79.6, 52.4, 28.4, 26.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{28}H_{32}N_3O_6$ 506.2286; found 506.2282. IR (cm^{-1}): 2925.50, 1726.41, 1693.27, 1447.02, 1251.86, 1171.47, 1016.60, 750.59. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 4:1 (v/v);

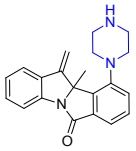


tert-butyl 4-(1',6'-dimethyl-3-methylene-2'-oxo-3H-spiro[benzofuran-2,3'-indolin]-4'-yl)piperazine-1-carboxylate ***(6l)*** 59.2 mg, yield: 64%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.5 Hz, 1H), 7.26 (t, *J* = 7.7 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 8.1 Hz, 1H), 6.60 (s, 1H), 6.50 (s, 1H), 5.39 (s, 1H), 4.56 (s, 1H), 3.20 (s, 3H), 3.00 – 2.88 (m, 4H), 2.87 – 2.76 (m, 2H), 2.65 – 2.56 (m, 2H), 2.37 (s, 3H), 1.41 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 173.5, 161.9, 154.3, 151.2, 145.7, 145.6, 142.3, 130.9, 126.3, 121.5, 120.9, 119.7, 116.8, 110.6, 105.6, 101.2, 88.7, 79.4, 52.3, 43.9, 43.1, 28.3, 26.6, 22.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{32}N_3O_4$ 462.2387; found 462.2382. IR (cm^{-1}): 2975.35, 2816.56, 1734.09, 1692.74, 1614.38, 1460.03, 1365.82, 1252.21, 1170.72, 1127.32, 1016.09, 862.53, 749.81. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 5:1 (v/v);

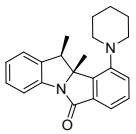


10-butyl-10b-methyl-11-methylene-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(8)*** 14.0 mg, yield: 23%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (t, *J* = 8.0 Hz, 2H), 7.54 – 7.49 (m, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 5.59 (s, 1H), 5.40 (s, 1H), 3.09 – 2.92 (m, 2H), 1.84 (s, 3H), 1.77 – 1.71 (m, 2H), 1.58 – 1.46 (m, 2H), 1.02 (t, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H}

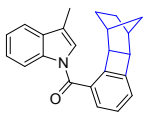
NMR (101 MHz, $CDCl_3$) δ 168.3, 148.4, 146.2, 140.3, 138.2, 134.5, 134.0, 133.1, 130.1, 129.0, 124.7, 122.8, 121.4, 117.8, 105.6, 75.8, 34.3, 33.3, 28.6, 23.0, 14.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{22}NO$ 304.1692; found 304.1696. IR (cm^{-1}): 2958.48, 2928.22, 2869.18, 1712.81, 1603.45, 1465.03, 1310.00, 1139.21, 760.03. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 25:1 then petroleum ethyl/dichloromethane 1:1 (v/v);



10b-methyl-11-methylene-10-(piperazin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(9)*** 48.5 mg, yield: 73%, white soild, mp 232℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.71 (m, 2H), 7.70 – 7.66 (m, 1H), 7.54 – 7.46 (m, 2H), 7.37 (td, *J* = 7.7, 1.2 Hz, 1H), 7.14 (td, *J* = 7.6, 1.1 Hz, 1H), 6.09 (s, 1H), 5.66 (s, 1H), 3.30 – 3.13 (m, 6H), 3.07 – 2.99 (m, 2H), 1.87 (s, 3H), 1.29 – 1.22 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.6, 149.4, 147.9, 146.2, 140.7, 134.2, 133.2, 130.2, 130.0, 129.7, 124.7, 123.3, 121.3, 117.5, 105.9, 75.5, 54.0, 45.4, 29.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{22}N_3O$ 332.1755; found 332.1757. IR (cm^{-1}): 2925.32, 2851.85, 1709.67, 1601.36, 1464.84, 1352.72, 1301.03, 1132.96, 761.83, 734.39. Purified by chromatography on silica gel, eluting with dichloromethane/methanol 15:1 (v/v);



10b,11-dimethyl-10-(piperidin-1-yl)-10b,11-dihydro-6H-isoindolo[2,1-a]indol-6-one ***(10)*** 44.0 mg, yield: 66%, white soild, mp 208℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.3 Hz, 1H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.19 – 7.15 (m, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 3.36 (q, *J* = 7.1 Hz, 1H), 2.96 – 2.87 (m, 2H), 2.87 – 2.78 (m, 2H), 1.87 – 1.73 (m, 7H), 1.71 – 1.59 (m, 2H), 1.57 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 167.1, 151.0, 148.0, 141.7, 138.4, 134.6, 129.7, 128.5, 127.7, 124.6, 123.8, 122.3, 116.8, 76.5, 55.6, 43.8, 26.2, 24.0, 20.6, 12.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{25}N_2O$ 333.1959; found 333.1961. IR (cm^{-1}): 2932.66, 2851.99, 2800.38, 1702.99, 1480.00, 1367.12, 1309.73, 762.32. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 14:1 (v/v);



((1R,4S,4aS,8bR)-1,2,3,4,4a,8b-hexahydro-1,4-methanobiphenylen-5-yl)(3-methyl-1H-indol-1-yl)methanone ***(12)*** 21.9 mg, yield: 25%, white soild, mp 128℃. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.41 – 7.30 (m, 3H), 7.19 (d, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 1.4 Hz, 1H), 3.27 (s, 2H), 2.35 – 2.29 (m, 1H), 2.27 – 2.23 (m, 4H), 1.63 – 1.47 (m, 2H), 1.22 – 1.05 (m, 2H), 1.03 – 0.84 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.9, 147.3, 146.0, 136.1, 131.9, 129.2, 127.7, 127.3, 125.0, 124.9, 124.4, 123.6, 118.8, 117.7, 116.5, 50.9, 50.6, 36.6, 36.5, 32.1, 27.6, 27.6, 9.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{22}NO$ 437.2224; found 437.2218. IR (cm^{-1}): 3053.08, 2955.97, 2870.19, 1682.46, 1605.13, 1451.00, 1349.21, 1263.49, 1188.50, 1065.59, 769.44, 750.33. Purified by chromatography on silica gel, eluting with petroleum ethyl/acetate ether 100:1 (v/v);

ASSOCIATED CONTENT

SUPPORTING INFORMATION

Crystallographic data for compound **3a** (CIF)
Crystallographic data for compound **3b** (CIF)
Crystallographic data for compound **3c** (CIF)
Crystallographic data for compound **4c** (CIF)
Crystallographic data for compound **6a** (CIF)
Experimental procedures, compound characterization, and NMR spectra (PDF)
This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(25) CCDC 1966190, 1966189, 1966188, 1966191 and 1966187 (**3a**, **3b**, **3c**, **4c** and **6a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the cambridge crystallographic data centre.