JOC The Journal of Organic Chemistry

Anatolian University Libraries Consortium a·n·k·o·s

Subscriber access provided by ORTA DOGU TEKNIK UNIVERSITESI KUTUPHANESI

Article

Ruthenium(II)-catalyzed redox-neutral [3+2] annulation of indoles with internal alkynes via C-H bond activation: Accessing to a pyrroloindolone scaffold

Yanan Xie, Xiaowei Wu, Chunpu Li, Jiang Wang, Jian Li, and Hong Liu

J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 19 Apr 2017

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Ruthenium(II)-catalyzed redox-neutral [3+2] annulation of indoles with internal alkynes via C−H bond activation: Accessing to a pyrroloindolone scaffold

Yanan Xie,[†,&] Xiaowei Wu,[‡,§,&] Chunpu Li,[‡] Jiang Wang,[‡] Jian Li,[*,†] and Hong Liu[*,‡]

[†]Shanghai Key Laboratory of New Drug Design School of Pharmacy, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China.

[‡]State Key Laboratory of Drug Research, Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Shanghai, 201203, China.

[§]University of Chinese Academy of Sciences, No.19A Yuquan Road, Beijing 100049, China.

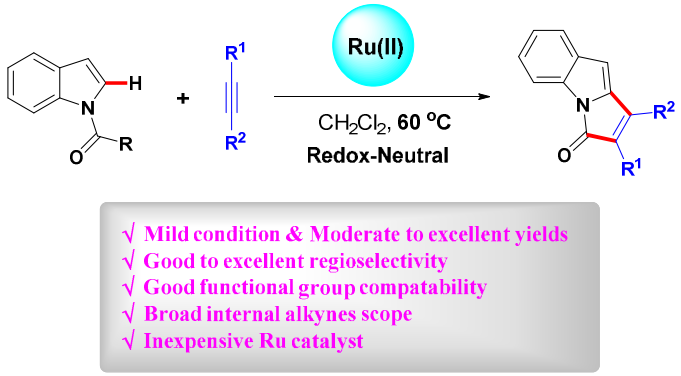
* Corresponding author

Jian Li, Ph. D., Professor and Hong Liu, Ph. D., Professor

Author Contributions

[&]Y. Xie and X. Wu contributed equally to this work.

Graphic Abstract



Abstract

Ru(II)-catalyzed redox-neutral [3+2] annulation reactions of *N*-ethoxycarbamoyl indoles and internal alkynes via C-H bond activation are reported. This method features broad internal alkyne scope including various aryl/alkyl-, alkyl/alkyl-, and diaryl-substituted alkynes, good to excellent regioselectivity, diverse functional group tolerance, and mild reaction conditions. The *N*-ethoxycarbamoyl directing group, temperature, CsOAc, and the ruthenium catalyst proved to be crucial for conversion and high regioselectivity. Additionally, preliminary mechanistic experiments were conducted and a possible mechanism was proposed.

Introduction

The indole ring is an important structural motif that is present in many biologically active natural products and pharmaceuticals.[1] Considering their varied activities, tremendous effort has been devoted to develop synthetic methods to prepare and modify indoles over the past decades.[2] Arguably, transition metal-catalyzed C−H activation reactions represent a powerful approach for the synthesis and direct

transformation of indoles.[2-4] Among these processes, transition metal-catalyzed annulation reactions of indole with diverse coupling partners have received much attention in recent years.[5] These reactions allow the atom-economical and rapid synthesis of more functionalized indole-fused scaffolds from simple starting materials.

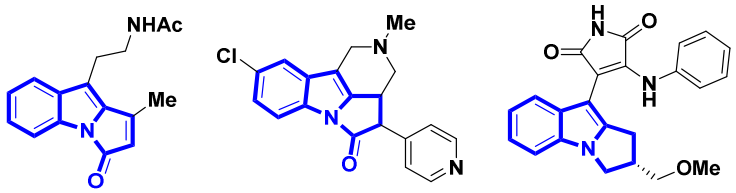
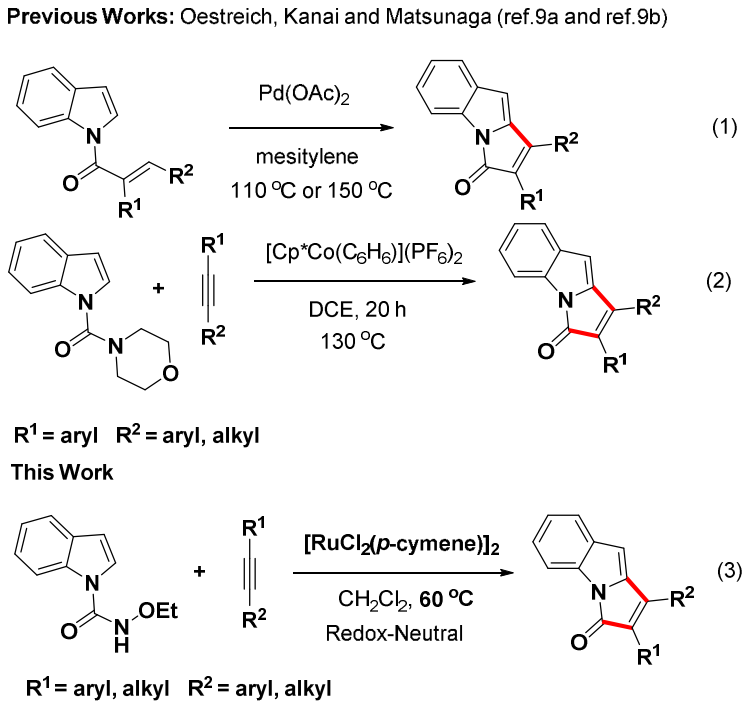


Figure 1. Selected examples of biologically active compounds bearing a pyrrolo[1,2-*a*]indole core.

Among *N*-fused indole cores, the pyrrolo[1,2-*a*]indole core is an integral part of many biologically active natural molecules and pharmaceuticals (Figure 1).[6-8] However, current methods to prepare pyrrolo[1,2-*a*]indole scaffolds usually require harsh reaction conditions or highly functionalized substrates.[9] In 2012, Oestreich and coworkers[9h] reported an example of aerobic palladium(II)-catalyzed intramolecular cyclization to provide 3*H*- pyrrolo[1,2-*a*]indole-3-ones(Scheme 1, eq 1), in which a high reaction temperature (110 ^{o}C or 150 ^{o}C) was required. Recently, Kanai and Matsunaga's group[9b] pioneered the development of Cp*Co(III)-catalyzed redox-neutral C2-selective C−H alkenylation/annulation cascade of *N*-carbamoyl indoles with internal alkynes to produce pyrroloindolones (eq 2). In view of the rigorous reaction conditions in the reported methods, the development of new approaches that allow rapid construction of these scaffolds from readily available starting materials under mild conditions remains an important challenge. To the best

of our knowledge, Ru(II)-catalyzed C2-selective C−H alkenylation and subsequent cyclization with indoles remains underexplored. Herein, based on our interest in developing direct C−H functionalization reactions,[10] we report the first example of Ru(II)-catalyzed redox-neutral [3+2] annulation of *N*-ethoxycarbamoyl indoles which is more reactive than Co(III)-catalyzed *N*-carbamoyl indoles and internal alkynes via C−H bond activation with good regioselectivity under mild conditions (eq 3).

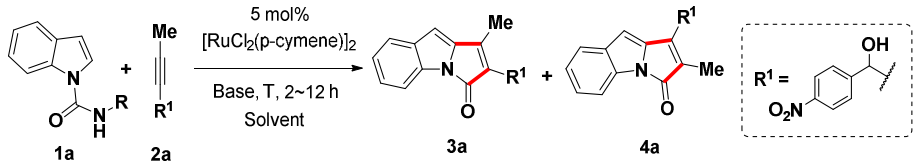
Scheme 1. Transition metal-catalyzed annulations of *N*-protected indoles for pyrroloindolone synthesis.



Results and discussion

We initiated the coupling reaction of *N*-methoxycarbamoyl indole **1a** and the propargyl alcohol **2a** catalyzed by Ru(II) in 1,2-dichloroethane at 60 °C. First, the reaction did not proceed without any base (Table 1, Entry 1). Then, diverse solvents

Table 1. Optimization of reaction conditions.[a]



NO.	R	Solvent	Base	Time(h)	T.(°C)	**3a** Yield (%)[b]	**3a/4a** ratio[c]
1	MeO-	DCE	none	12	60	0	-
2	MeO-	DMSO	CsOAc	12	60	0	-
3	MeO-	DMF	CsOAc	12	60	0	-
4	MeO-	MeCN	CsOAc	12	60	0	-
5	MeO-	DCE	CsOAc	12	60	33	63:37
6	MeO-	THF	CsOAc	12	60	Trace	-
7	MeO-	TFE	CsOAc	12	60	0	-
8	MeO-	PhMe	CsOAc	12	60	34	79:21
9	MeO-	CH_2Cl_2	CsOAc	12	60	52	77:23
10[d]	BuO-	CH_2Cl_2	CsOAc	12	60	24	85:15
11[e]	EtO-	CH_2Cl_2	CsOAc	12	60	59	95:5
12	EtO-	CH_2Cl_2	CsOAc	2	60	72(67)	95:5
13	EtO-	CH_2Cl_2	NaOAc	2	60	0	-
14	EtO-	CH_2Cl_2	KOAc	2	60	0	-
15	EtO-	CH_2Cl_2	$Cu(OAc)_2$	2	60	0	-
16	EtO-	CH_2Cl_2	CsOPiv	2	60	67	93:7
17	EtO-	CH_2Cl_2	$NaHCO_3$	2	60	0	-
18	EtO-	CH_2Cl_2	$CsCO_3$	2	60	0	-
19	EtO-	CH_2Cl_2	CsOAc	2	50	78(71)	91:9
20	EtO-	CH_2Cl_2	CsOAc	2	40	29	63:37
21[f]	EtO-	CH_2Cl_2	CsOAc	2	60	21	93:7
22[g]	EtO-	CH_2Cl_2	CsOAc	2	60	0	-
23[h]	EtO-	CH_2Cl_2	CsOAc	2	60	0	-

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.26 mmol), Catalyst (5 mol %), Base (1 equiv.) in 4 mL Solvent at 60 °C, Ar atmosphere. [b]NMR yields using CH_2Br_2 as an internal standard, isolated yields in parentheses. [c]Determined by ^{1}H-NMR analysis of the crude reaction mixtures. [d]*t*-butyl group instead of methyl group. [e]ethyl group instead of methyl group. [f]2.5 mol% $[RuCl_2(p\text{-cymene})]_2$ was employed. [g]using 5 mol% $RuCl_3$ instead of $[RuCl_2(p\text{-cymene})]_2$. [h]using 5 mol% $[Cp^*RhCl_2]_2$ instead of $[RuCl_2(p\text{-cymene})]_2$.

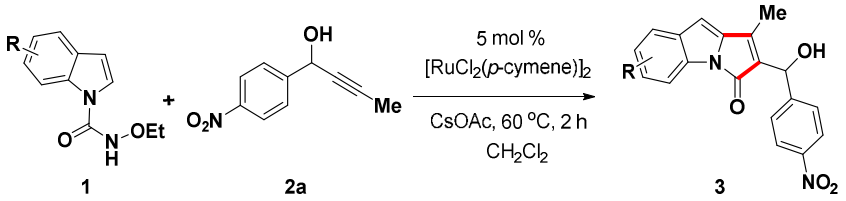
including DMSO, DMF, MeCN, THF, TFE, DCE, PhMe and dichloromethane were

screened, and dichloromethane provided 52% yield of product **3a**, whose structure was confirmed by X-ray analysis (see Supporting Information for more details and entry 2-9 in table 1).[11] Subsequently, the influence of different substituted hydroxamic acid-type substrates was investigated, and an ethyl group in the R moiety gave the product in a moderate yield with good regioselectivity (Table 1, Entries 10-11). When the reaction time was reduced, the ^{1}H NMR yield was improved to 72% and the ratio of **3a**/**4a** (95:5) was maintained. Further screening of a variety of bases such as CsOAc, KOAc, NaOAc, $NaHCO_3$, $Cu(OAc)_2$, CsOPiv, $NaHCO_3$ and $CsCO_3$ demonstrated that CsOAc was the optimal base (Table 1, Entries 12-18). Performing the reaction 50 ^oC produced compound **3a** in 78% yield, but the regioselectivity was reduced (Table 1, Entry 19). Decreasing the reaction temperature or the amount of the catalyst led to a significantly lower coupling efficiency (Table 1, Entries 20-21). Additionally, the reaction did not proceed in the absence of the catalyst $[RuCl_2(p\text{-cymene})]_2$ (Table 1, Entries 22-23). Briefly, the optimum results could be obtained when *N*-ethoxycarbamoyl indole **1a** (0.2 mmol) and **2a** (0.26 mmol, 1.3 equiv) in CH_2Cl_2 were treated with 5 mol % Ru(II) catalyst and CsOAc (0.2 mmol, 1 equiv) at 60 ^oC for 2 h.

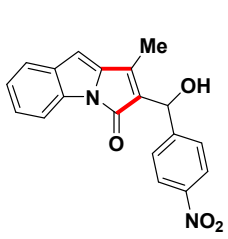
With the optimized reaction conditions in hand, we first examined the scope of differentially substituted *N*-ethoxycarbamoyl indoles in cyclization with propargyl alcohol **2a** (Table 2). In general, the introduction of various electron-donating or electron-withdrawing groups at the C-3, 4, 5, or 6 positions of the indoles all underwent smooth coupling with propargyl alcohol **2a**, and the desired cyclization

products were obtained in acceptable to good yields, with good regioselectivity.

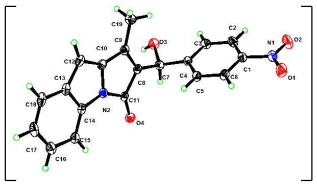
Table 2. Scope of Indoles[a,b,c]



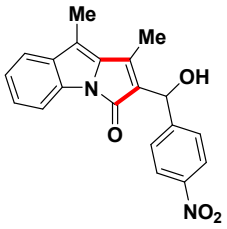
1 2a 3



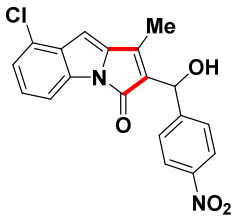
3a, 67%, 95:5



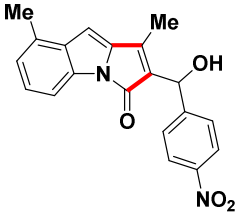
X-Ray of **3a**



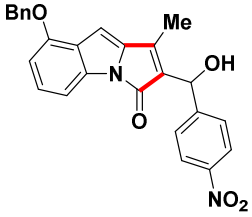
3b, 62%, >99:1[d]



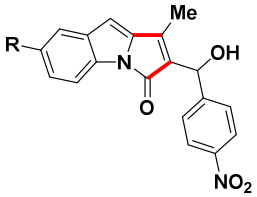
3c, 60%, 95:5[d]



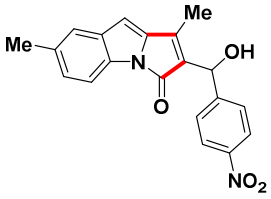
3d, 67%, 92:8



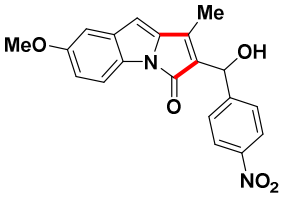
3e, 70%, 97:3



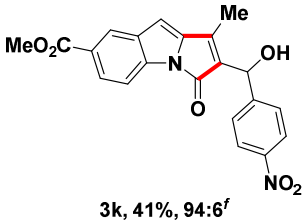
R = F, 3f, 72%, 94:6[d]
R = Cl, 3g, 67%, 93:7
R = Br, 3h, 76%, 90:10



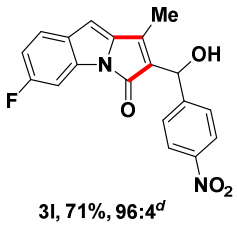
3i, 71%, 90:10[e]



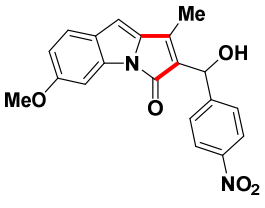
3j, 65%, 93:7[d]



3k, 41%, 94:6[f]



3l, 71%, 96:4[d]



3m, 27%, 50:50

[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.26 mmol), Catalyst (5 mol %), base (1 equiv) in DCM (4 mL) at 60 °C, Ar atmosphere. [b]Isolated yields of product **3** was reported. [c]The ratio of **3**/**4** was determined by 1H-NMR analysis of the crude reaction mixtures. [d]Reaction

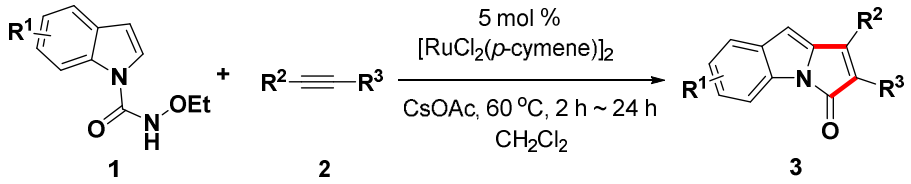
was run for 6 h. [e]Reaction was run for 24 h. [f]Reaction was run for 36 h.

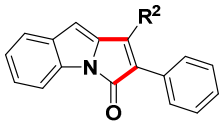
Introduction of a methyl group at the C-3 position of indole gave a single isomer **3b** in 62% yield. Substrates bearing electron-withdrawing or electron-donating substituents, such as chlorine (**3c**), methyl (**3d**), and benzyloxy (**3e**) at the C-4 position of the indoles, also provided the desired products in good yields and with high regioselectivity. In addition, similar results were observed when halogen groups (**3f-3h**), methyl (**3i**), and methoxy (**3j**) were introduced at the C-5 position of the indoles. However, the yield of product **3k** decreased when an ester group was placed at the C-5 position of the indoles. We further investigated the influence of C-6 substituents at the benzene ring of the indoles on the reaction. The results showed that it provided the corresponding product (**3l**) in good yield and regioselectivity when fluorine was introduced at the C-6 position of the indoles. By contrast, the electron-rich substrate bearing a methoxy group provided the desired product (**3m**) in decreased yield. In general, regardless of electron-withdrawing groups, electron-donating groups at the C-4 and C-5 position of indoles; it provided the desired products with good regioselectivity. Besides, it also afforded the corresponding product with good regioselectivity when electron-withdrawing group was introduced at the C-6 position of indoles. However, the electron-rich substrate bearing a methoxy group at the C-6 position gave the desired product with poor regioselectivity.

We also examined the scope of the reaction with respect to the internal alkynes as coupling partners (Table 3). In general, the coupling reaction of the indoles proceeded

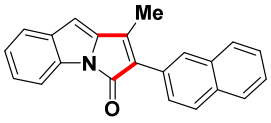
well with various aryl/alkyl-, alkyl/alkyl-, and diaryl-substituted alkynes (**3n-3zj**).

Table 3. The Scope of Internal Alkynes[a,b,c,d,e]

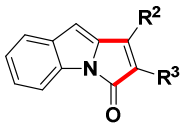




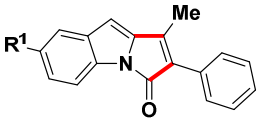
R^2 = Me, 3n, 91%, >99:1
R^2 = Et, 3o, 71%, >99:1
R^2 = H, 3p, 0%



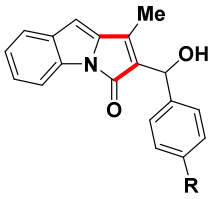
3q, 76%, >99:1



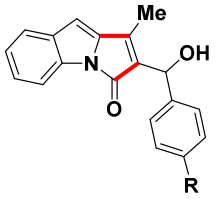
R^2 = R^3= Ph, 3r, 72%
R^2 = R^3= Et, 3s, 35%
R^2 = R^3 = 4-OMe-Ph, 3t, 79%
R^2 = R^3 = 4-Br-Ph, 3u, 40%



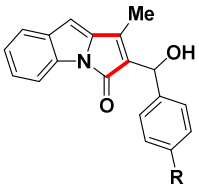
R^1 = Me, 3v, 29%, >99:1
R^1 = OMe, 3w, 45%, >99:1
R^1 = COOMe, 3x, 87%, >99:1



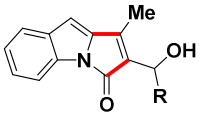
R = H, 3y, 75%, 80:20
R = Me, 3z, trace[e,f]



R = F, 3za, 68%, 77:23
R = Cl, 3zb, 74%, 83:17
R = Br, 3zc, 54%, 86:14
R = I, 3zd, 62%, 83:17



R = 4-CF_3, 3ze, 83%, 87:13
R = 4-COOMe, 3zf, 77%, 84:16
R = 4-OMe, 3zg, trace



R = 2-Thienyl, 3zh, 34%, 70:30
R = 2-Benzofuran, 3zi, 74%, 88:12[e,f]
R = 2-Naphyl, 3zj, 64%, 80:20[e,f]

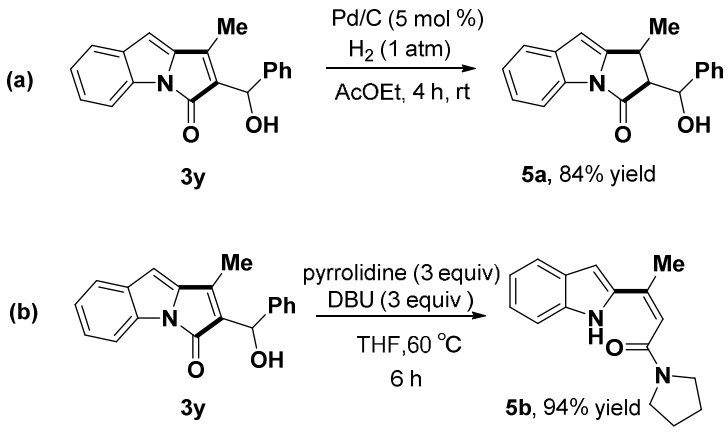
[a]Reaction conditions: **1** (0.2 mmol), **2** (0.26 mmol), Catalyst (5 mol %), CsOAc (1 equiv) in CH_2Cl_2 (4 mL) at 60 °C, Ar atmosphere. [b]Isolated yields of **3** was reported. [c]The ratio of **3**/**4** was determined by ^{1}H-NMR analysis of the crude reaction mixtures. [d]Reaction of **3n-3x** was run for 2h. [e]Reaction of **3y-3zj** was run for 24 h. fusing **2a** (0.4 mmol) and Catalyst (10 mol %).

With unsymmetrical aryl/alkyl-alkynes, each cyclization product was obtained as a single isomer in moderate to good yield (**3n**, **3o**, **3q**, **3v**, **3w**, and **3x**). However, it did not provide the desired product when using a terminal alkyne as the coupling partner (**3p**). In addition, annulation adducts were obtained from diaryl-substituted alkynes in good yields, regardless of the use of electron-rich or electron-poor alkynes (**3r**, **3t**, and **3u**). Notably, diethyl-substituted alkynes was compatible in this method (**3s**); in contrast, it did not work in the Cp*Co(III)-catalyzed annulation reaction. Furthermore, we investigated the scope of propargyl alcohols. Generally, the coupling of *N*-ethoxycarbamoyl indole **1a** and various substituted propargyl alcohols **2** provided the annulation adducts in moderate to good yields (**3y**-**3zk**). Substrates bearing electron-withdrawing groups, such as halides, trifluoromethyl, and an eater, at the benzene ring of propargyl alcohols were well tolerated under the reaction conditions (**3za-3zf**). However, some electron-rich substrates did not provide the desired products (**3z** and **3zg**). In addition, diverse heteroaryl groups were compatible in this method (**3zh**-**3zj**).

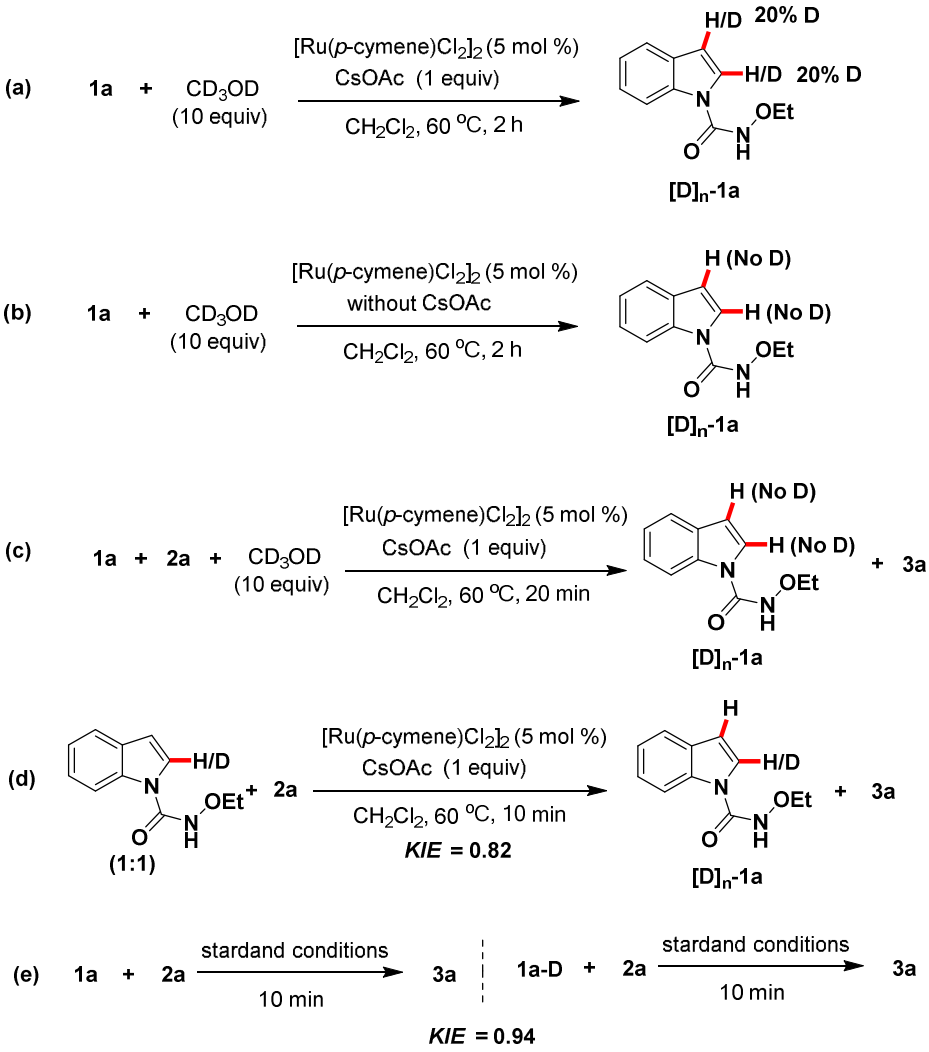
To evaluate the efficiency and potential for the synthetic utility of the method, we carried out some transformations of pyrroloindolones (Scheme 2). Reduction of **3y** with Pd/C under H_2 atmosphere gave pyrroloindolone **5a** in 84% yield. Interestingly, ring-opening by cleavage of the amide linkage would provide a C-2 alkenylated indole **5b** in 94% yield, which is hardly accessible through direct C-H coupling with trisubstituted α,β-unsaturated acceptors.

To shed more light on the reaction mechanism, H/D exchange and deuterium-labeling experiments were conducted. We performed the reaction in the presence of methanol-d_4 to determine the reversibility of C−H activation by removing

Scheme 2. Transformation of Pyrroloindolones



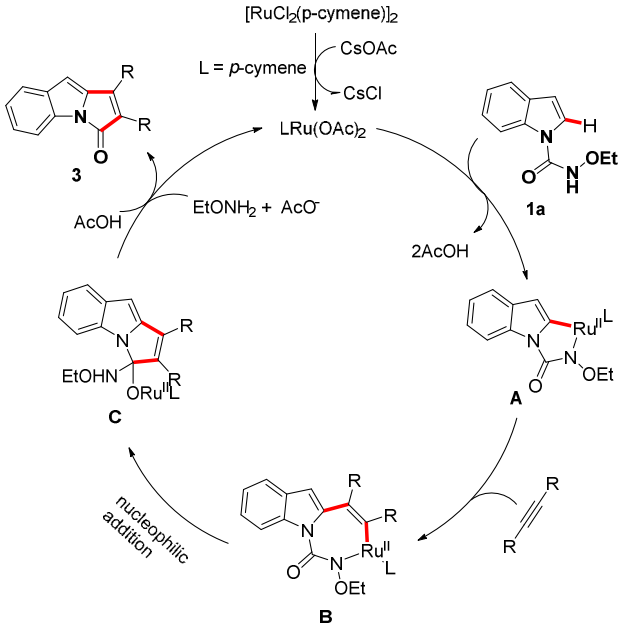
Scheme 3. Deuteration Experiments



the other coupling partner (Scheme 3a). ^{1}H NMR analysis showed that about 20% deuteration was observed both at the C-2 and C-3 positions of indoles. In contrast, no deuteration was observed when removing the base CsOAc (Scheme 3b). Carrying out the same reaction in the presence of **2a** also led to no deuterium incorporated into indole **1a** (Scheme 3c). These results suggest that the C2-selective C−H activation might be reversible and that cycloruthenation occurs under Ru catalysis with the aid of acetate.[12] To explore the C−H activation process further, kinetic isotope effect (KIE) experiments were performed. An intermolecular competitive coupling reaction of an

equimolar mixture of **1a** and **1a-D** with propargyl alcohol **2a** was carried out, and a k_H/k_D value of 0.82 was obtained based on recovered substrates **1a** and **1a-D** (Scheme 3d). Besides, two independent reactions using **1a** and **1a-D** gave a KIE value of 0.94. The results suggested that C−H bond cleavage is unlikely involved in the rate-limiting step[9a].

Scheme 4. Proposed catalytic cycle.



Based on these experiments and previous literatures,[5e,9b] a possible mechanism is proposed (Scheme 4). As the initial step, an active catalyst is generated through ligand exchange to cesium acetate. Coordination of *N*-carboxamides of indoles **1a** to the Ru(II) catalyst and subsequent C-2 selective C-H bond activation with the aid of CsOAc forms a five-membered ruthenacycle **A**. Then, the regioselective coordination and migratory insertion of internal alkynes into the Ru-C bond of ruthenacycle **A** produces intermediate **B**. Intramolecular nucleophilic addition of intermediate **II**

would give the intermediate **C**, which was followed by release of ethoxyamine to give product **3**, with the regeneration of the Ru(II) catalyst.

Conclusions

In summary, we have developed novel Ru(II)-catalyzed redox-neutral [3+2] annulation reactions of *N*-ethoxycarbamoyl indoles and internal alkynes. Moderate to excellent yields of pyrroloindolone derivatives were obtained, with broad internal alkynes scope, good to excellent regioselectivities, and mild reaction conditions. Preliminary mechanistic experiments were conducted, and a plausible mechanism was proposed. Additionally, the easy transformations of the products might further underscore its synthetic utility and versatile applicability.

Experimental Section

General Information. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15-0.2 mm thickness). Preparative thin layer chromatography (PTLC) was HSGF 254 (0.4-0.5 mm thickness). All products were characterized by their NMR and MS spectra. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz, 500 MHz or 600 MHz instrument. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd) and broad (br). High-resolution mass spectra (HRMS) were measured on Micromass Ultra Q-TOF spectrometer. All *N*-carbamoylindoles were prepared by following the same procedure as described in the literature[12]. Alkynes (**2e**,[13] **2j**,[14] **2k**,[15] **2m**,[15] **2n**,[16] **2o**,[14]

2p,[17] **2r**,[15]) were prepared by following the same procedure as described in the literature. **2a**, **2l**, **2q**, **2s**, **2t**, **2u** were prepared using modified literature procedures.[14] Other reagents (chemicals) were purchased and used without further purification.

Typical Synthesis Procedure of 1a-1m and [D]-1a.

In a 250 mL three-necked flask a solution of n-BuLi (19.2 mL, 2.5 M in hexane) was added dropwise to a solution of indole I (4.7g, 40.0 mmol) in THF (120 mL) over 30 min at 0 ^{o}C under Ar atmosphere. The reaction mixture was stirred for another 30 min at 0 ^{o}C. CO_2 was bubbled to the solution for 1 h at 0 ^{o}C, then H_2O (20 mL) was dropped to quench the reaction. The solution was concentrated to about 30 mL under vacuum. Aqueous HCl (6 M) was added dropwise to adjust the pH value of the solution to 3. After the solution was extracted with ethyl acetate (60 mL × 3), the combined organic layer was dried over anhydrous Na_2SO_4, evaporated to afford crude *N*- carboxyl indole II. $(COCl)_2$ (1.72 mL, 20.0 mmol) was dropped to a solution of crude product II (10.0 mmol) in anhydrous DCM (20 mL) and DMF (0.1 mL) over 30 min at 0 ^{o}C. The solution was kept at room temperature for 2 h. Then the solution was concentrated to afford crude acyl chloride III for next step without further purification.

The crude acyl chloride III in EA (5ml) was dropped to a solution of ethoxylamine hydrhloride (1.67 g, 20.0 mmol) and $NaHCO_3$ (3.36 g, 40.0 mmol) in EA (50 mL) and H_2O (10 mL) over 30 min at 0 ^{o}C. The solution was kept at room temperature for 3 h. Then the solution was filtered and the filtrate was concentrated to give a residue. The residue was subject to flash column chromatography [silica gel, ethyl

acetate/petroleum ether (v/v, 1/5) as eluent] to afford *N*-carbamoyl indoles **1a**.

2-Deuterium indole was prepared according to the literature and NMR spectral data matched the data[18]. According to the general procedures **[D]-1a** was synthesized with 94% D-incorporation.

Typical Synthesis Procedure of 2a, **2l**, **2q**, **2s**, **2t**, **2u**

In a dry 100ml three-necked flask was dissolved the corresponding aldehyde (10 m mol) in dry THF under nitrogen atmosphere and then cooled to 0 ^{o}C. The Grignard reagent (12 mmol, 0.5 M in THF) was added to the mixture and then was kept at 0 ^{o}C for one hour and then 1 hour at room temperature. The completion of the reactions was confirmed by TLC, and then the saturated solution of ammonium chloride was added. The organic mixture was extracted by EA, dried with Na_2SO_4 and the solvent removed under vacuum. The crude product was purified by column chromatography using silica gel [silica gel, ethyl acetate/petroleum ether (v/v, 1/8) as eluent].

Typical Synthesis Procedure and Characterization of 3a-3o, 3q-3y, 3za-3zf and 3zh-3zj.

To a reaction tube was added *N*-ethoxy-1*H*-indole-1-carboxamide **1a** (41 mg, 0.2 mmol), alkyne **2a** (50mg, 0.26mmol), CsOAc (39 mg, 0.2 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (6mg, 5% mmol) and dichloromethane (4.0 mL), then was evacuated and purged with Ar three times. The solution was kept at 60 ^{o}C for 2 h – 24 h. After the solution was cooled to room temperature, it was diluted with $CHCl_3$ and then transferred to a round bottom flask. The crude mixture was purified by silica gel

column chromatography [ethyl acetate/petroleum ether (v/v, 1:6) as eluent] to give a corresponding product **3a**.

Transformation of Pyrroloindolones

(a) Hydrogenation of **3y**

To a solution of **3y** (29 mg, 0.1 mmol) in AcOEt (2 mL) was added Pd/C (5 wt%, 11mg, 5%mmol) .The solution was stirred under H2 atmosphere for 4h at room temperature. Then the solution was Filtrated and evaporated, The residue was subject to flash column chromatography [silica gel, ethyl acetate/petroleum ether (v/v, 1/6) as eluent] to afford colorless oil **5a** (24.5 mg, 84% yield).

(b) Transformation of pyrroloindolone **3y** to α,β-unsaturated amide **5b**

To a solution of **3y** (29 mg, 0.1 mmol) in THF (2 mL) were added DBU (45 μL, 0.3 mmol), and pyrrolidine (25 μL, 0.3 mmol) at room temperature. After the mixture was stirred at 60 ^{o}C for 6 h, saturated *aq.* NH_4Cl was added. Then the mixture was extracted with AcOEt (x 3), and dried over Na_2SO_4. The residue was subject to flash column chromatography [silica gel, ethyl acetate/petroleum ether (v/v, 1/6) as eluent] to afford colorless oil **5b** (24.0 mg, 94% yield).

Analytical Characterization Data of Substrates and Products.

***N*-ethoxy-1*H*-indole-1-carboxamide 1a.** Yellow solid (5.9 g, 72% yield). m.p. 73–74 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.14 – 8.09 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.61 – 7.56 (d, *J* = 7.8 Hz, 1H), 7.44 – 7.40 (d, *J* = 3.7 Hz, 1H), 7.37 – 7.30 (m, 1H), 7.26 – 7.22 (m, 1H), 6.65 – 6.61 (dd, *J* = 3.7, 0.6 Hz, 1H), 4.13 – 4.06 (q, *J* = 7.0 Hz, 1H), 1.37 – 1.32 (t, *J* = 7.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.4, 135.2,

130.2, 124.8, 123.7, 123.0, 121.4, 114.7, 108.3, 72.8, 13.6. HRMS (ESI) m/z: calculated for $C_{11}H_{11}N_2O_2^-$ [M - H]$^-$: 203.0826, found: 203.0820.

***N*-ethoxy-3-methyl-1*H*-indole-1-carboxamide 1b.** Yellow solid (4.4 g, 50% yield). m.p. 72–73 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (br, 1H), 8.15 – 8.10 (m, 1H), 7.52 – 7.47 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.28 (m, 1H), 7.26 – 7.21 (m, 1H), 7.17 (s, 1H), 4.10 – 4.02 (m, 2H), 2.24 (m, 3H), 1.34 – 1.28 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 135.6, 131.0, 124.9, 122.7, 120.4, 119.3, 117.8, 114.8, 72.8, 13.7, 13.7, 9.8, 9.8. HRMS (ESI) m/z: calculated for $C_{12}H_{13}N_2O_2^-$ [M - H]$^-$: 217.0983, found: 217.0978.

4-chloro-*N*-ethoxy-1*H*-indole-1-carboxamide 1c. Yellow solid (6.4 g, 67% yield). m.p. 103–104 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.07 – 8.00 (m, 1H), 7.46 – 7.42 (d, *J* = 3.7 Hz, 1H), 7.25 (d, *J* = 2.1 Hz, 1H), 7.24 (s, 1H), 6.77 – 6.74 (dd, *J* = 3.7, 0.7 Hz, 1H), 4.14 – 4.06 (q, *J* = 7.0 Hz, 2H), 1.37 – 1.31 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.1, 136.0, 128.9, 126.5, 125.5, 124.1, 122.8, 113.3, 106.6, 72.9, 13.7, 13.6. HRMS (ESI) m/z: calculated for $C_{11}H_{10}ClN_2O_2^-$ [M - H]$^-$: 2370436, found: 237.0430.

***N*-ethoxy-4-methyl-1*H*-indole-1-carboxamide 1d.** Yellow solid (4.8 g, 55% yield). m.p. 69–70 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (br, 1H), 7.93 – 7.89 (dd, *J* = 8.4, 0.5 Hz, 1H), 7.44 – 7.41 (d, *J* = 3.7 Hz, 1H), 7.26 – 7.20 (t, *J* = 7.8 Hz, 1H), 7.07 – 7.02 (m, 1H), 6.68 – 6.63 (m, 1H), 4.14 – 4.06 (m, 2H), 2.52 (s, 3H), 1.38 – 1.33 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 134.9, 130.9, 129.9, 124.8, 123.4, 123.2, 112.0, 106.7, 72.8, 18.7, 18.66, 13.7, 13.6. HRMS (ESI) m/z: calculated for

$C_{12}H_{13}N_2O_2^-$ [M - H]$^-$: 217.0983, found: 217.0978.

4-(benzyloxy)-*N*-ethoxy-1*H*-indole-1-carboxamide 1e. Yellow solid (5.2 g, 42% yield). m.p. 107–108 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (br, 1H), 7.72 – 7.67 (d, *J* = 8.4 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.43 – 7.47 (m, 2H), 7.37 – 7.31 (m, 2H), 7.26 – 7.20 (m, 1H), 6.83 – 6.80 (m, 1H), 6.76 – 6.71 (d, *J* = 8.0 Hz, 1H), 5.21 (s, 2H), 4.14 – 4.07 (m, 2H), 1.39 – 1.32 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.4, 152.5, 137.2, 136.5, 128.7, 128.1, 127.5, 125.7, 122.2, 120.9, 107.8, 105.6, 104.7, 72.9, 70.2, 13.7, 13.6. HRMS (ESI) m/z: calculated for $C_{18}H_{19}N_2O_3^+$ [M + H]$^+$: 311.1390, found: 311.1392.

***N*-ethoxy-5-fluoro-1*H*-indole-1-carboxamide 1f.** Yellow solid (6.9 g, 78% yield). m.p. 105–106 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.12 – 8.07 (m, 1H), 7.45 – 7.41 (d, *J* = 3.7 Hz, 1H), 7.25 – 7.19 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.09 – 7.01 (td, *J* = 9.1, 2.6 Hz, 1H), 6.60 – 6.56 (dd, *J* = 3.7, 0.7 Hz, 1H), 4.12 – 4.04 (q, *J* = 7.0 Hz, 2H), 1.36 – 1.30 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.39 (d, *J* = 239.3 Hz) 153.2, 131.9, 130.9 (d, *J* = 10.1 Hz), 124.9, 115.8 (d, *J* = 9.2 Hz), 112.7 (d, *J* = 25.3 Hz), 108.1 (d, *J* = 4.0 Hz), 106.6 (d, *J* = 23.8 Hz), 72.9, 13.6. ^{19}F NMR (471 MHz, CDCl3) δ -120.9 ppm. HRMS (ESI) m/z: calculated for $C_{11}H_{10}FN_2O_2^-$ [M - H]$^-$: 221.0732, found: 221.0725.

5-chloro-*N*-ethoxy-1*H*-indole-1-carboxamide 1g. Yellow solid (6.4 g, 67% yield). m.p. 124–125 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.08 – 8.04 (d, *J* = 8.9 Hz, 1H), 7.54 – 7.51 (d, *J* = 2.1 Hz, 1H), 7.44 – 7.40 (d, *J* = 3.7 Hz, 1H), 7.28 – 7.24 (dd, *J* = 8.8, 2.1 Hz, 1H), 6.56 – 6.53 (d, *J* = 3.7 Hz, 1H), 4.11 – 4.03 (q, *J* = 7.0 Hz,

2H), 1.35 – 1.29 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.1, 133.8, 131.2, 128.7, 124.9, 124.7, 120.8, 115.9, 107.7, 72.9, 13.6. HRMS (ESI) m/z: calculated for $C_{11}H_{10}ClN_2O_2^-$ [M - H]$^-$: 237.0436, found: 237.0430.

5-bromo-*N*-ethoxy-1*H*-indole-1-carboxamide 1h. Yellow solid (9.9 g, 88% yield). m.p. 120–121 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (br, 1H), 8.04 – 7.99 (d, *J* = 8.8 Hz, 1H), 7.70 (d, *J* = 1.7 Hz, 1H), 7.43 – 7.37 (m, 2.8 Hz, 1H), 6.57 – 6.53 (d, *J* = 3.5 Hz, 1H), 4.12 – 4.03 (q, *J* = 7.0 Hz, 2H), 1.29 – 1.36 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.1, 134.2, 131.7, 127.6, 124.6, 123.9, 116.3, 116.3, 107.6, 72.9, 13.6. HRMS (ESI) m/z: calculated for $C_{11}H_{10}BrN_2O_2^-$ [M - H]$^-$: 280.9931, found: 280.9930.

***N*-ethoxy-5-methyl-1*H*-indole-1-carboxamide 1i.** Yellow solid (5.8 g, 66% yield). m.p. 74–76 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (br, 1H), 7.99 – 7.94 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 3.7 Hz, 1H), 7.37 (d, *J* = 0.7 Hz, 1H), 7.17 – 7.12 (d, *J* = 8.5 Hz, 1H), 6.57 – 6.53 (m, 1H), 4.13 – 4.05 (m, 2H), 2.44 (m, 3H), 1.37 – 1.31 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 133.4, 132.5, 130.4, 126.1, 123.7, 121.2, 114.2, 108.0, 72.8, 21.4, 21.4, 13.7, 13.6. HRMS (ESI) m/z: calculated for $C_{12}H_{13}N_2O_2^-$ [M - H]$^-$: 217.0983, found: 217.0978.

***N*-ethoxy-5-methoxy-1*H*-indole-1-carboxamide 1j.** Yellow solid (4.1 g, 44% yield). m.p. 76–78 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (br, 1H), 8.02 – 7.97 (d, *J* = 9.0 Hz, 1H), 7.41 – 7.37 (d, *J* = 3.6 Hz, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.97 – 6.91 (m, 1H), 6.55 (m, 1H), 4.14 – 4.04 (m, 2H), 3.84 (s, 3H), 1.38 – 1.30 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.1, 153.4, 131.0, 130.0, 124.2, 115.5, 113.7, 108.2, 103.7, 72.8,

55.8, 13.6. HRMS (ESI) m/z: calculated for $C_{12}H_{14}N_2NaO_3^-$ $[M + Na]^+$: 257.0897, found: 257.0902.

methyl 1-(ethoxycarbamoyl)-1*H*-indole-5-carboxylate 1k. Yellow solid (7.6 g, 72% yield). m.p. 104–105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.28 – 8.25 (m, 1H), 8.18 – 8.13 (m, 1H), 8.00 – 7.95 (dd, *J* = 8.8, 1.7 Hz, 1H), 7.59 – 7.45 (d, *J* = 3.7 Hz, 1H), 6.67 – 6.64 (dd, *J* = 3.7, 0.6 Hz, 1H), 4.13 – 4.06 (q, *J* = 7.0 Hz, 2H), 3.93 (s, 3H), 1.36 – 1.30 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 153.0, 138.0, 129.8, 125.9, 124.9, 124.9, 123.6, 114.5, 108.7, 72.9, 52.3, 13.6. HRMS (ESI) m/z: calculated for $C_{13}H_{13}N_2O_4^-$ $[M - H]^-$: 261.0881, found: 261.0874.

***N*-ethoxy-6-fluoro-1*H*-indole-1-carboxamide 1l.** Yellow solid (6.2 g, 70% yield). m.p. 74–76 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (br, 1H), 7.87 – 7.94 (dd, *J* = 10.2, 1.7 Hz, 1H), 7.53 – 7.44 (m, 1H), 7.37 – 7.31 (d, *J* = 3.6 Hz, 1H), 7.04 – 6.96 (m, 1H), 6.62 – 6.59 (m, 1H), 4.14 – 4.04 (q, *J* = 7.0 Hz, 2H), 1.39 – 1.29 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.17 (d, *J* = 240.9 Hz), 153.2, 135.7 (d, *J* = 12.9 Hz), 126.2, 123.6 (d, *J* = 3.9 Hz), 121.9 (d, *J* = 10.0 Hz), 111.5 (d, *J* = 24.4 Hz), 108.3, 102.3 (d, *J* = 28.6 Hz), 72.9, 13.6. ^{19}F NMR (471 MHz, $CDCl_3$) δ -116.7 ppm. HRMS (ESI) m/z: calculated for $C_{11}H_{10}FN_2O_2^-$ $[M - H]^-$: 221.0732, found: 221.0725.

***N*-ethoxy-6-methoxy-1*H*-indole-1-carboxamide 1m.** Yellow solid. (3.0 g, 32% yield). m.p. 75–76 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (br, 1H), 7.78 (d, *J* = 2.3 Hz, 1H), 7.45 – 7.41 (d, *J* = 8.6 Hz, 1H), 7.23 – 7.20 (d, *J* = 3.7 Hz, 1H), 6.91 – 6.85 (m, 1H), 6.57 – 6.54 (m, 1H), 4.13– 4.06 (m, 2H), 3.87 (d, *J* = 0.8 Hz, 3H), 1.38 – 1.32 (m, 3H) ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2, 153.6, 136.6, 123.6, 121.7, 121.6,

112.6, 108.5, 98.9, 72.8, 55.8, 13.7. HRMS (ESI) m/z: calculated for $C_{12}H_{14}N_2NaO_3^-$ $[M + Na]^+$: 257.0897, found: 257.0902.

N-ethoxy-1*H*-indole-2-*d*-1-carboxamide. Brown solid. (5.5 g, 67% yield). m.p. 69–70 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.12 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.58 (m, 1H), 7.43 (d, *J* = 3.7 Hz, 0.06H), 7.33 (m, 1H), 7.26 – 7.22 (m, 1H), 6.62 (d, *J* = 0.5 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.34 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 135.2, 130.2, 124.7, 123.0, 121.3, 114.7, 108.1, 72.8, 13.6. HRMS (ESI) m/z: calculated for $C_{11}H_{10}DN_2O_2^+$ $[M – H]^-$: 204.0889, found: 204.0884.

1-(4-nitrophenyl)but-2-yn-1-ol 2a. pale yellow solid. (1.6 g, 85% yield). m.p. 171–173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.19(m, 2H), 7.70 (d, *J* = 8.4 Hz, 2H), 5.52 (d, *J* = 2.1 Hz, 1H), 2.21 (br, 1H), 1.91 (d, *J* = 2.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.1, 147.8, 127.4, 123.9, 84.6, 78.2, 63.9, 3.8. HRMS (ESI) m/z: calculated for $C_{10}H_8NO_3^-$ $[M–H]^-$: 190.0510, found: 190.0512.

1-(4-fluorophenyl)but-2-yn-1-ol 2l. colorless oil. (1.3 g, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.65 (m, 2H), 7.07 – 7.02 (m, 2H), 5.40 (d, *J* = 2.2 Hz, 1H), 2.25 (br, 1H), 1.91 (d, *J* = 2.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7 (d, *J* = 246.5 Hz), 137.2 (d, *J* = 3.0 Hz), 128.5 (d, *J* = 8.3 Hz), 115.5 (d, *J* = 21.6 Hz), 83.5, 79.1, 64.2, 3.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -114.1 ppm. HRMS (EI) m/z: calculated for $C_{10}H_9FO$ $[M]^+$: 164.0637, found: 164.0636.

methyl 4-(1-hydroxybut-2-yn-1-yl)benzoate 2q. colorless oil. (1.7 g, 83% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 - 8.02 (d, *J* = 8.4 Hz, 2H), 7.61 - 7.58 (d, *J* = 8.1 Hz, 2H), 5.49 - 5.46 (d, *J* = 2.1 Hz, 1H), 3.91 (s, 3H), 2.24 (s, 1H), 1.91 (d, *J* = 2.2 Hz,

3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.0, 146.1, 130.0, 126.6, 83.9, 78.8, 64.4, 52.3, 3.9. HRMS (EI) m/z: calculated for $C_{12}H_{12}O_3$ $[M]^+$: 204.0788, found: 204.0786.

1-(thiophen-3-yl)but-2-yn-1-ol 2s. colorless oil. (1.0 g, 63% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 - 7.35 (m, 1H), 7.33 - 7.28 (m, 1H), 7.22 - 7.17 (m, 1H), 5.46 (s, 1H), 2.19 (br, 1H), 1.91 (d, *J* = 1.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.9, 126.5, 126.5, 122.5, 82.4, 79.1, 60.9, 3.8. HRMS (EI) m/z: calculated for C_8H_8OS $[M]^+$: 152.0296, found: 152.0298.

1-(benzofuran-2-yl)but-2-yn-1-ol 2t. colorless oil. (1.0 g, 55% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 - 7.54 (m, 1H), 7.50 - 7.48 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.31 – 7.28(m, 1H), 7.25 - 7.21 (td, *J* = 7.7, 0.9 Hz, 1H), 6.81 (s, 1H), 5.56 - 5.58 (m, 1H), 2.43 (s, 1H), 1.94 (d, *J* = 2.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.9, 155.3, 127.9, 124.8, 123.1, 121.5, 111.6, 104.2, 83.4, 76.3, 59.0, 3.9. HRMS (EI) m/z: calculated for $C_{12}H_{10}O_2$ $[M]^+$: 186.0682, found:186.0681.

1-(naphthalen-2-yl)but-2-yn-1-ol 2u. colorless oil. (1.3 g, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.89 - 7.80 (m, 3H), 7.65 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.56 – 7.44 (m, 2H), 5.59 (d, *J* = 2.2 Hz, 1H), 2.36 (br, 1H), 1.94 (d, *J* = 2.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.7, 133.3, 133.3, 128.6, 128.3, 127.8, 126.3, 126.3, 125.3, 124.7, 83.5, 79.3, 65.0, 3.9. HRMS (EI) m/z: calculated for $C_{14}H_{12}O$ $[M]^+$: 196.0888, found: 196.0891.

2-(hydroxy(4-nitrophenyl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3a. Yellow solid (44.8 mg, 67% yield). m.p. 179–181 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, *J* = 8.8 Hz, 2H), 7.73 – 7.69 (d, *J* = 8.9 Hz, 2H), 7.51 – 7.45 (m, 2H),

7.29 – 7.22 (m, 1H), 7.11 – 7.05 (m, 1H), 6.80 – 6.76 (d, *J* = 2.7 Hz, 1H), 6.25 – 6.21 (m, 1H), 5.76 – 5.72 (d, *J* = 4.0 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.7, 150.6, 146.5, 143.2, 142.3, 134.8, 133.7, 133.5, 127.3, 127.1, 123.4, 123.2, 111.4, 107.1, 65.5, 11.2. HRMS (ESI) m/z: calculated for $C_{19}H_{13}N_2O_4^-$ [M - H]$^-$: 333.0881, found: 333.0878.

1-(hydroxy(4-nitrophenyl)methyl)-2-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 4a. Yellow solid. (2.4 mg, 3.5% yield) m.p. 199–201 ^{o}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.25 – 8.22 (d, *J* = 8.9 Hz, 2H), 7.82 – 7.78 (d, *J* = 8.6 Hz, 2H), 7.50 – 7.47 (dd, *J* = 7.9, 0.6 Hz, 1H), 7.45 – 7.42 (d, *J* = 7.7 Hz, 1H), 7.24 – 7.20 (td, *J* = 7.9, 1.0 Hz, 1H), 7.08 – 7.04 (td, *J* = 7.6, 0.9 Hz, 1H), 6.54 – 6.51 (d, *J* = 3.8 Hz, 1H), 6.50 (s, 1H), 6.00 – 5.98 (d, *J* = 3.7 Hz, 1H), 1.99 (s, 3H).. ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.8, 149.7, 146.9, 145.2, 139.5, 133.8, 133.5, 130.9, 127.3, 126.8, 123.6, 123.2, 123.0, 111.3, 107.5, 66.8, 9.1. HRMS (ESI) m/z: calculated for $C_{19}H_{13}N_2O_4^-$ [M - H]$^-$: 333.0881, found: 333.0878.

2-(hydroxy(4-nitrophenyl)methyl)-1,9-dimethyl-3*H*-pyrrolo[1,2-a]indol-3-one

3b. Yellow solid (43.2 mg, 62% yield). m.p. 205–207 ^{o}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, *J* = 8.9 Hz, 2H), 7.67 – 7.69 (d, *J* = 8.4 Hz, 2H), 7.45 – 7.43 (t, *J* = 7.8 Hz, 2H), 7.24 – 7.26 (td, *J* = 7.8, 1.0 Hz, 1H), 7.13 – 7.09 (td, *J* = 7.6, 1.0 Hz, 1H), 6.19 – 6.15 (d, *J* = 4.2 Hz, 1H), 5.76 – 5.72 (d, *J* = 4.1 Hz, 1H), 2.30 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.2, 151.0, 146.4, 143.7, 137.1, 134.7, 134.2, 133.1, 127.7, 126.9, 123.4, 122.9, 121.2, 119.1, 111.1, 65.2, 11.9, 8.9. HRMS (ESI) m/z: calculated for $C_{20}H_{15}N_2O_4^-$ [M - H]$^-$: 347.1037, found:

347.1041.

8-chloro-2-(hydroxy(4-nitrophenyl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3c.

Yellow solid (44.3 mg, 60% yield). m.p. 223–225 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, J = 8.7 Hz, 2H), 7.74 – 7.70 (d, J = 8.6 Hz, 2H), 7.47 – 7.43 (d, J = 7.9 Hz, 1H), 7.30 – 7.26 (t, J = 8.0 Hz, 1H), 7.19 – 7.15 (d, J = 7.9 Hz, 1H), 6.87 (s, 1H), 6.25 (d, J = 4.1 Hz, 1H), 5.75 (d, J = 4.0 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6, 150.3, 146.5, 143.5, 142.9, 135.1, 134.2, 131.7, 128.5, 127.1, 126.6, 123.4, 122.9, 110.3, 104.2, 65.4, 11.2. HRMS (ESI) m/z: calculated for $C_{19}H_{12}ClN_2O_4^-$ [M - H]$^-$: 367.0491, found: 367.0490

2-(hydroxy(4-nitrophenyl)methyl)-1,8-dimethyl-3*H*-pyrrolo[1,2-a]indol-3-one 3d.

Yellow solid (46.7 mg, 67% yield). m.p. 198–201 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.22 – 8.18 (d, J = 8.8 Hz, 2H), 7.72 – 7.68 (d, J = 8.7 Hz, 2H), 7.27 – 7.21 (d, J = 7.9 Hz, 1H), 7.12 – 7.09 (t, J = 7.7 Hz, 1H), 6.91 – 6.87 (m, 2H), 6.18 (d, J = 4.1 Hz, 1H), 5.72 (d, J = 4.1 Hz, 1H), 2.38 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.8, 150.7, 146.5, 143.1, 141.7, 134.5, 133.5, 133.0, 132.6, 127.4, 127.0, 123.8, 123.4, 108.9, 105.9, 65.4, 18.0, 11.2. HRMS (ESI) m/z: calculated for $C_{20}H_{15}N_2O_4^-$ [M - H]$^-$: 347.1037, found: 347.1041.

8-(benzyloxy)-2-(hydroxy(4-nitrophenyl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3e. Yellow solid (61.7 mg, 70% yield). m.p. 164–165 °C.^{1}H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, J = 8.8 Hz, 2H), 7.73 – 7.69 (d, J = 8.5 Hz, 2H), 7.51 – 7.47 (d, J = 7.3 Hz, 2H), 7.42 – 7.38 (m, 2H), 7.36 – 7.32 (m, 2H), 7.24 – 7.20 (t, J =

8.1 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 6.87 (s, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.18 (d, *J* = 4.1 Hz, 1H), 5.73 (d, *J* = 4.1 Hz, 1H), 5.22 (s, 1H), 2.18 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.9, 152.9, 150.7, 146.4, 143.4, 140.8, 136.8, 134.7, 134.2, 128.9, 128.5, 127.9, 127.6, 127.0, 123.4, 122.8, 106.4, 104.8, 104.4, 69.4, 65.4, 11.13. HRMS (ESI) m/z: calculated for $C_{26}H_{19}N_2O_5^-$ [M - H]$^-$: 439.1299, found: 439.1295.

7-fluoro-2-(hydroxy(4-nitrophenyl)methyl)-1-methyl-3H-pyrrolo[1,2-*a*]indol-3-one 3f. Yellow solid (50.7 mg, 72% yield). m.p. 113–115 ^{o}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, *J* = 8.8 Hz, 2H), 7.74 – 7.70 (d, *J* = 8.8 Hz, 2H), 7.46 – 7.42 (dd, *J* = 8.7, 4.5 Hz, 1H), 7.38 – 7.34 (dd, *J* = 9.2, 2.5 Hz, 1H), 7.13 – 7.09 (td, *J* = 9.2, 2.5 Hz, 1H), 6.78 (s, 1H), 6.22 (d, *J* = 4.1 Hz, 1H), 5.74 (d, *J* = 4.1 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.4, 158.5 (d, *J* = 236.9 Hz), 150.5, 146.5, 143.9, 143.2, 135.0, 134.6 (d, *J* = 10.2 Hz), 130.1, 127.1, 123.4, 114.3 (d, *J* = 25.3 Hz), 112.1 (d, *J* = 9.5 Hz), 109.3 (d, *J* = 24.7 Hz), 106.5 (d, *J* = 3.8 Hz), 65.4, 11.2. ^{19}F NMR (471 MHz, DMSO-d_6) δ -119.9 ppm. HRMS (ESI) m/z: calculated for $C_{19}H_{12}FN_2O_4^-$ [M - H]$^-$: 351.0787, found: 351.0787.

7-chloro-2-(hydroxy(4-nitrophenyl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3g. Yellow solid (49.4 mg, 67% yield). m.p. 150–152 ^{o}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.22 – 8.18 (d, *J* = 8.9 Hz, 2H), 7.73 – 7.69 (d, *J* = 8.5 Hz, 2H), 7.59 – 7.56 (d, *J* = 2.0 Hz, 1H), 7.47 – 7.43 (d, *J* = 8.5 Hz, 1H), 7.30 – 7.26 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.76 (s, 1H), 6.23 (d, *J* = 4.1 Hz, 1H), 5.73 (d, *J* = 4.0 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.4, 150.4, 146.5, 143.6, 143.3, 135.2, 135.0, 132.0, 127.3, 127.1, 126.9, 123.4, 122.7, 112.5, 106.1, 65.4, 11.2. HRMS (ESI) m/z:

calculated for $C_{19}H_{12}ClN_2O_4^-$ [M - H]$^-$: 367.0491, found: 367.0489.

7-bromo-2-(hydroxy(4-nitrophenyl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3h. Yellow solid (62.8 mg, 76% yield). m.p. 182–184 ^oC. ^1H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, J = 8.9 Hz, 2H), 7.74 – 7.69 (m, 3H), 7.43 – 7.41(m, 2H), 6.77 (s, 1H), 6.23 (d, J = 3.5 Hz, 1H), 5.74 (d, 1H), 2.20 (s,3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.5, 150.4, 146.5, 143.4, 143.3, 135.5, 135.2, 132.3, 129.6, 127.1, 125.6, 123.4, 115.2, 113.0, 106.0, 65.4, 11.3. HRMS (ESI) m/z: calculated for $C_{19}H_{12}BrN_2O_4^-$ [M - H]$^-$: 410.9986, found: 410.9977.

2-(hydroxy(4-nitrophenyl)methyl)-1,7-dimethyl-3*H*-pyrrolo[1,2-a]indol-3-one 3i Yellow solid (49.5 mg, 71% yield). m.p. 165–166 ^oC. ^1H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, J = 8.6 Hz, 2H), 7.73 – 7.69 (d, J = 8.8 Hz, 2H), 7.38 – 7.34 (d, J = 8.1 Hz, 1H), 7.29 (s, 1H), 7.10 – 7.06 (d, J = 8.3 Hz, 1H), 6.72 (s, 1H), 6.18 (d, J = 4.1 Hz, 1H), 5.73 (d, J = 4.1 Hz, 1H), 2.30 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6, 150.7, 146.4, 142.9, 142.5, 134.7, 133.7, 132.2, 131.8, 128.2, 127.0, 123.4, 123.2, 111.0, 106.9, 65.4, 20.8, 11.2. HRMS (ESI) m/z: calculated for $C_{20}H_{15}N_2O_4^-$ [M - H]$^-$: 347.1037, found: 347.1041.

2-(hydroxy(4-nitrophenyl)methyl)-7-methoxy-1-methyl-3H-pyrrolo[1,2-a]indol-3-one 3j. Yellow solid (47.4 mg, 65% yield). m.p. 166–167 ^oC. ^1H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, J = 8.6 Hz, 2H), 7.73 – 7.69 (d, J = 8.7 Hz, 2H), 7.38-7.34 (d, J = 8.7 Hz, 1H), 7.09 – 7.05 (d, J = 2.3 Hz, 1H), 6.86 – 6.84 (dd, J = 8.7, 2.3 Hz, 1H), 6.71 (s, 1H), 6.18 (d, J = 4.1 Hz, 1H), 5.72 (d, J = 4.0 Hz, 1H), 3.74 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.4, 155.7, 150.7, 146.5 143.1,

142.9 134.7 134.5, 128.3 127.1 126.9, 123.4, 114.6, 111.8, 107.1, 107.0, 65.5, 55.5, 11.2. HRMS (ESI) m/z: calculated for $C_{20}H_{15}N_2O_5^-$ [M - H]$^-$: 363.0986, found: 363.0981.

methyl 2-(hydroxy(4-nitrophenyl)methyl)-1-methyl-3-oxo-3*H*-pyrrolo[1,2-a]indole-7-carboxylate 3k. Yellow solid (32.3 mg, 41% yield). m.p. 204–206 ^oC. ^1H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, J = 8.8 Hz, 2H), 8.15 – 8.11 (d, J = 1.7 Hz, 1H), 7.90 – 7.86 (d, J = 8.4 Hz, 1H), 7.75 – 7.71 (d, J = 8.5 Hz, 2H), 7.59 – 7.55 (dd, J = 8.3, 2.1 Hz, 1H), 6.91 (d, J = 3.2 Hz, 1H), 6.25 (d, J = 4.2 Hz, 1H), 5.76 (d, J = 4.1 Hz, 1H), 3.84 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 166.1, 163.5, 150.4, 146.5, 143.8, 143.3, 136.1, 135.3, 133.6, 128.5, 127.1, 124.5, 124.4, 123.4, 111.2, 107.0, 65.4, 52.1, 11.3. HRMS (ESI) m/z: calculated for $C_{21}H_{15}N_2O_6^-$ [M - H]$^-$: 391.0936, found: 391.0932.

6-fluoro-2-(hydroxy(4-nitrophenyl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3l. Yellow solid (50.0 mg, 71% yield). m.p. 178–181 ^oC. ^1H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, J = 8.8 Hz, 2H), 7.74 – 7.70 (d, J = 8.7 Hz, 2H), 7.54 – 7.50 (m, 1H), 7.26 – 7.22 (d, J = 8.8 Hz, 1H), 6.97 – 6.93 (t, J = 9.2 Hz, 1H), 6.80 (s, 1H), 6.21 (d, J = 4.1 Hz, 1H), 5.74 (d, J = 3.7 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.47, 161.90 (d, J = 243.3 Hz), 150.5, 146.5, 143.7, 142.7 (d, J = 4.0 Hz), 134.6, 133.9 (d, J = 13.0 Hz), 130.0, 127.0, 124.4 (d, J = 10.1 Hz), 123.4, 110.6 (d, J = 23.8 Hz), 106.7, 99.0 (d, J = 27.7 Hz), 65.4. ^{19}F NMR (471 MHz, DMSO-d_6) δ -113.3 ppm. HRMS (ESI) m/z: calculated for $C_{19}H_{12}FN_2O_4^-$ [M - H]$^-$: 351.0787, found: 351.0779.

2-(hydroxy(4-nitrophenyl)methyl)-6-methoxy-1-methyl-3*H*-pyrrolo[1,2-*a*]indol-3-one 3m. Yellow solid (19.7 mg, 27% yield). m.p. 208–210 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.23 – 8.19 (d, J = 8.8 Hz, 2H), 7.73 – 7.69 (d, J = 8.5 Hz, 2H), 7.41 – 7.37 (d, J = 8.6 Hz, 1H), 7.04 – 7.00 (d, J = 2.3 Hz, 1H), 6.72 (s, 1H), 6.71 – 6.68 (dd, J = 8.6, 2.4 Hz, 1H), 6.17 – 6.15 (d, J = 4.1 Hz, 1H), 5.72 (d, J = 4.0 Hz, 1H), 3.78 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.7, 159.8, 150.8, 146.4, 143.5, 140.9, 135.0, 133.7, 127.0, 126.8, 123.9, 123.4, 110.8, 107.5, 96.6, 65.4, 55.49, 11.2. HRMS (ESI) m/z: calculated for $C_{20}H_{15}N_2O_5^-$ [M - H]$^-$: 363.0986, found: 363.0981.

1-(hydroxy(4-nitrophenyl)methyl)-6-methoxy-2-methyl-3*H*-pyrrolo[1,2-*a*]indol-3-one 4m. Yellow solid (19.7 mg, 27% yield). m.p. 201–202 °C.^{1}H NMR (600 MHz, DMSO-d_6) δ 8.25 – 8.22 (d, J = 8.8 Hz, 2H), 7.80 – 7.76 (d, J = 8.8 Hz, 2H), 7.34 – 7.31 (m, 1H), 7.03 (m, 1H), 6.68 – 7.65 (m, 1H), 6.49 (d, J = 3.8 Hz, 1H), 6.42 (s, 1H), 5.96 (d, J = 3.7 Hz, 1H), 3.77 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 164.9, 159.4, 149.8, 146.8, 145.5, 138.1, 134.8, 129.6, 127.3, 127.1, 123.7, 123.6, 110.5, 107.9, 96.8, 66.9, 55.5, 9.1. HRMS (ESI) m/z: calculated for $C_{20}H_{15}N_2O_5^-$ [M - H]$^-$: 363.0986, found: 363.0984.

1-methyl-2-phenyl-3*H*-pyrrolo[1,2-a]indol-3-one 3n. Yellow solid (47.2 mg, 91% yield). m.p. 108–111 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.60 – 7.51 (m, 4H), 7.51 – 7.45 (t, J = 7.6 Hz, 2H), 7.43 – 7.37 (m, 1H), 7.33 – 7.27 (t, J = 7.6 Hz, 1H), 7.15 – 7.09 (t, J = 7.6 Hz, 1H), 6.86 (s, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.0, 142.5, 141.1, 133.8, 132.1, 130.5, 128.9, 128.4, 128.2, 127.3, 123.3, 123.1,

111.5, 106.8, 12.1. HRMS (ESI) m/z: calculated for $C_{18}H_{14}NO^+$ $[M + H]^+$: 260.1070, found: 260.1067. **The structure was determined by NOE analysis.**

1-ethyl-2-phenyl-3*H*-pyrrolo[1,2-a]indol-3-one 3o. Yellow solid (38.3 mg, 71% yield). m.p. 111–113 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.60 – 7.57 (d, J = 7.9 Hz, 1H), 7.56 – 7.52 (d, J = 7.8 Hz, 1H), 7.50 – 7.46 (m, 4H), 7.45 – 7.39 (m, 1H), 7.33 – 7.28 (t, J = 7.7 Hz, 1H), 7.16 – 7.11 (t, J = 7.6 Hz, 1H), 6.91 (s, 1H), 2.71 – 2.64 (q, J = 7.6 Hz, 2H), 1.31 – 1.24 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.0, 146.7, 141.1, 133.9, 133.6, 132.0, 130.3, 129.0, 128.4, 128.3, 127.3, 123.3, 123.1, 111.5, 107.4, 19.6, 13.4. HRMS (ESI) m/z: calculated for $C_{19}H_{16}NO^+$ $[M + H]^+$: 274.1226, found: 274.1234.

1-methyl-2-(naphthalen-2-yl)-3*H*-pyrrolo[1,2-a]indol-3-one 3q. Yellow solid (41.5 mg, 67% yield). m.p. 160–163 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.13 (s, 1H), 8.03 – 7.98 (m, 2H), 7.97 – 7.93 (m, 1H), 7.73 – 7.68 (dd, J = 8.5, 1.5 Hz, 1H), 7.63 – 7.59 (d, J = 7.9 Hz, 1H), 7.59 – 7.53 (m, 3H), 7.35 – 7.29 (m, 1H), 7.17 – 7.11 (t, J = 7.6 Hz, 1H), 6.91 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.1, 142.6, 141.4, 133.9, 132.7, 132.3, 132.1, 128.3, 128.2, 128.1, 127.7, 127.6, 127.4, 126.7, 126.5, 126.5, 123.3, 123.2, 111.6, 107.0, 12.2. HRMS (ESI) m/z: calculated for $C_{22}H_{16}NO^+$ $[M + H]^+$: 310.1226, found: 310.1224.

1,2-diphenyl-3*H*-pyrrolo[1,2-a]indol-3-one 3r. Yellow solid (46.3 mg, 72% yield). m.p. 163–165 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.67 – 7.63 (d, J = 7.9 Hz, 1H), 7.58 – 7.54 (d, J = 7.7 Hz, 1H), 7.51 – 7.42 (m, 5H), 7.41 – 7.33 (m, 6H), 7.19 – 7.14 (m, 1H), 6.89 (s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.7, 141.6, 140.7, 133.8,

133.6, 131.5, 130.6, 130.3, 130.1, 129.4, 129.0, 128.6, 128.38, 128.36, 127.6, 123.6, 123.3, 111.7, 108.9. HRMS (ESI) m/z: calculated for $C_{23}H_{15}NNaO^+$ $[M + Na]^+$: 344.1046, found: 344.1040.

1,2-diethyl-3*H*-pyrrolo[1,2-a]indol-3-one 3s. Yellow oil (39.4 mg, 35% yield). ^1H NMR (500 MHz, DMSO-d_6) δ 7.52 – 7.48 (d, J = 7.9 Hz, 1H), 7.48 – 7.44 (d, J = 7.8 Hz, 1H), 7.26 – 7.20 (t, J = 7.7 Hz, 1H), 7.09 – 7.05 (t, J = 7.6 Hz, 1H), 6.68 (s, 1H), 2.54 – 2.50 (q, J = 7.6 Hz, 1H), 2.29 – 2.22 (q, J = 7.5 Hz, 2H), 1.25 – 1.16 (t, J = 7.6 Hz, 4H), 1.09 – 1.02 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.1, 145.8, 141.6, 135.4, 133.8, 133.6, 126.7, 122.9, 122.8, 111.2, 105.6, 18.7, 16.4, 13.6, 13.5. HRMS (EI) calculated for $C_{15}H_{15}NO$ $[M]^+$ 225.1154, found 225.1159.

1,2-bis(4-methoxyphenyl)-3*H*-pyrrolo[1,2-a]indol-3-one 3t. Red solid (60.3 mg, 79% yield). m.p. 141–143 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 7.64 – 7.60 (d, J = 7.9 Hz, 1H), 7.55 – 7.51 (d, J = 7.7 Hz, 1H), 7.47 – 7.42 (d, J = 8.4 Hz, 2H), 7.35 – 7.29 (m, 3H), 7.17 – 7.11 (t, J = 7.6 Hz, 1H), 7.02 – 6.98 (d, J = 8.5 Hz, 2H), 6.97 – 6.92 (d, J = 8.6 Hz, 2H), 6.82 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.3, 160.5, 159.3, 140.8, 140.0, 133.64, 133.59, 130.7, 129.9, 129.6, 127.2, 123.3, 123.1, 123.0, 122.7, 114.5, 113.9, 111.6, 108.1, 55.3, 55.1. HRMS (ESI) m/z: calculated for $C_{25}H_{20}NO_3^+$ $[M + H]^+$: 382.1438, found: 382.1444.

1,2-bis(4-bromophenyl)-3*H*-pyrrolo[1,2-a]indol-3-one 3u. Red solid (38.3 mg, 40% yield). m.p. 156–158 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 7.69–7.65 (d, J = 8.4 Hz, 2H), 7.64–7.58 (m, 3H), 7.56–7.53 (d, J = 7.8 Hz, 1H), 7.43–7.39 (m, 2H), 7.36–7.32 (m, 1H), 7.32–7.28 (m, 2H), 7.18–7.13 (t, J = 7.6 Hz, 1H), 6.88 (s, 1H). ^{13}C NMR

(151 MHz, DMSO-d_6) δ 163.2, 140.7, 140.1, 133.8, 133.6, 132.2, 131.6, 131.4, 130.7, 130.4, 129.6, 129.2, 127.8, 123.7, 123.7, 123.4, 122.2, 111.8, 109.3. HRMS (EI) calculated for $C_{23}H_{13}NOBr_2$ $[M]^+$476.9364, found 476.9356.

1,7-dimethyl-2-phenyl-3*H*-pyrrolo[1,2-a]indol-3-one 3v. Yellow solid (15.9 mg, 29% yield). m.p. 118–120 °C. ^{1}H NMR (126 MHz, DMSO-d_6) δ 7.57 – 7.53 (m, 2H), 7.51 – 7.45 (m, 3H), 7.42 – 7.37(m, 1H), 7.33 (s, 1H), 7.14 – 7.10 (dd, J = 8.1, 0.8 Hz, 1H), 6.80 (s, 1H), 2.33 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.9, 142.7, 140.8, 134.0, 132.3, 133.0, 130.5, 128.9, 128.3, 128.2, 128.1, 123.2, 111.2, 106.7, 20.9, 12.0. HRMS (ESI) m/z: calculated for $C_{19}H_{15}NNaO^+$ $[M + Na]^+$: 296.1046, found: 296.1037.

7-methoxy-1-methyl-2-phenyl-3*H*-pyrrolo[1,2-a]indol-3-one 3w. Yellow solid (26.0 mg, 45% yield). m.p. 137–138 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57 – 7.53 (m, 2H), 7.51 – 7.44 (m, 2H), 7.43 – 7.36 (m, 1H), 7.12 – 7.09 (d, J = 2.4 Hz, 1H), 6.93 – 6.87 (dd, J = 8.6, 2.5 Hz, 1H), 6.77 (s, 1H), 3.77 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.7, 155.8, 143.3, 140.7, 134.8, 132.0, 130.5, 128.9, 128.4, 128.3, 128.1, 114.5, 112.0, 107.0, 106.7, 55.5, 12.0. HRMS (ESI) m/z: calculated for $C_{19}H_{16}NO_2^+$ $[M + H]^+$: 290.1176, found: 290.1180.

methyl 1-methyl-3-oxo-2-phenyl-3*H*-pyrrolo[1,2-a]indole-7-carboxylate 3x. Yellow solid (55.2 mg, 87% yield). m.p. 194–196 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.17 (s, 1H), 7.97 – 7.90 (d, J = 8.4 Hz, 1H), 7.70 – 7.64 (d, J = 8.3 Hz, 1H), 7.60 – 7.53 (m, 2H), 7.53 – 7.46 (t, J = 7.6 Hz, 2H), 7.45 – 7.39 (t, J = 7.2 Hz, 1H), 6.98 (s, 1H), 3.86 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.1, 163.9, 143.6,

141.6, 136.2, 133.9, 132.6, 130.1, 129.0, 128.5, 128.4, 124.5, 124.5, 111.4, 106.7, 52.1, 12.1. HRMS (ESI) m/z: calculated for $C_{20}H_{16}NO_3^+$ $[M + H]^+$: 318.1125, found: 318.1121.

2-(hydroxy(phenyl)methyl)-1-methyl-3H-pyrrolo[1,2-a]indol-3-one 3y. Yellow solid (43.4 mg, 75% yield). m.p. 85–87 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 – 7.46 (m, 2H), 7.46 – 7.42 (d, J = 7.6 Hz, 2H), 7.37 – 7.31 (t, J = 7.6 Hz, 2H), 7.28 – 7.21 (q, J = 7.4 Hz, 2H), 7.11 – 7.05 (t, J = 7.6 Hz, 1H), 6.76 – 6.70 (m, 1H), 5.85 (s, 1H), 5.61 (s, 1H), 2.18 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.0, 143.0, 142.6, 141.8, 136.1, 133.6, 133.6, 128.2, 127.1, 127.0, 126.0, 123.0, 111.3, 106.4, 66.4, 11.3. HRMS (ESI) m/z: calculated for $C_{19}H_{15}NNaO_2^+$ $[M + Na]^+$: 312.0995, found: 312.0986.

2-((4-fluorophenyl)(hydroxy)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3za. Yellow solid (41.8 mg, 68% yield). m.p. 156–158 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 – 7.45 (m, 4H), 7.28 – 7.23 (m, 1H), 7.19 – 7.13 (m, 2H), 7.11 – 7.06 (m, 1H), 6.75 (s, 1H), 5.91 (d, J = 4.1 Hz, 1H), 5.61 (d, J = 4.0 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.9, 161.2 (d, J = 242.4 Hz), 142.6, 141.9, 139.1 (d, J = 2.7 Hz), 135.8, 133.6, 133.6, 127.9 (d, J = 8.1 Hz), 127.1, 123.1, 114.9 (d, J = 21.3 Hz), 111.3, 106.5, 65.9, 11.2. ^{19}F NMR (471 MHz, DMSO-d_6) δ -115.928 ppm. HRMS (ESI) m/z: calculated for $C_{19}H_{14}FNNaO_2^-$ $[M + Na]^+$: 330.0901, found: 330.0910.

2-((4-chlorophenyl)(hydroxy)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3zb. Yellow solid (47.9 mg, 74% yield). m.p. 176–178 °C. ^{1}H NMR (600 MHz, DMSO-d_6)

δ 7.51 – 7.47 (m, 2H), 7.47 – 7.44 (d, *J* = 8.5 Hz, 2H), 7.41 – 7.37 (d, *J* = 8.5 Hz, 2H), 7.28 – 7.23 (m, 1H), 7.11 – 7.06 (m, 1H), 6.76 (s, 1H), 5.97 (d, *J* = 4.1 Hz, 1H), 5.61 (d, *J* = 4.0 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 163.9, 142.5, 142.3, 141.9, 135.6, 133.62, 133.56, 131.5, 128.1, 127.8, 127.2, 123.1, 111.3, 106.6, 65.7, 11.2. HRMS (ESI) m/z: calculated for $C_{19}H_{13}ClNO_2^-$ [M - H]$^-$: 322.0640, found: 322.0644.

2-((4-bromophenyl)(hydroxy)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3zc. Yellow solid (39.8 mg, 54% yield). m.p. 170–172 ^{o}C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.56 – 7.51 (d, *J* = 8.4 Hz, 2H), 7.51 – 7.45 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.36 (d, *J* = 8.4 Hz, 2H), 7.29 – 7.22 (t, *J* = 7.7 Hz, 1H), 7.12 – 7.04 (m, 1H), 6.76 (s, 1H), 5.97 (d, *J* = 4.0 Hz, 1H), 5.59 (d, *J* = 3.9 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ 163.9, 142.5, 142.34, 142.26, 135.5, 133.6, 133.5, 131.0, 128.1, 127.2 123.1, 120.0, 111.3, 106.6, 65.7, 11.2. HRMS (ESI) m/z: calculated for $C_{19}H_{13}BrNO_2^-$ [M - H]$^-$: 366.0135, found: 336.0136.

2-(hydroxy(4-iodophenyl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3zd. Yellow solid (51.5 mg, 62% yield). m.p. 148–150 ^{o}C. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 7.72 – 7.68 (d, *J* = 8.3 Hz, 2H), 7.51 – 7.45 (m, 2H), 7.29 – 7.23 (m, 3H), 7.11 – 7.06 (t, *J* = 7.6 Hz, 1H), 6.77 – 6.74 (d, *J* = 0.5 Hz, 1H), 5.93 (d, *J* = 4.1 Hz, 1H), 5.56 (d, *J* = 4.0 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ 163.9, 142.8, 142.5, 142.2, 136.9, 135.5, 133.6, 133.6, 128.3, 127.2, 123.1, 111.3, 106.6, 92.8, 65.8, 11.2. HRMS (ESI) m/z: calculated for $C_{19}H_{13}INO_2^-$ [M - H]$^-$: 413.9996, found: 413.9997.

2-(hydroxy(4-(trifluoromethyl)phenyl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3ze. Yellow solid (59.3 mg, 83% yield). m.p. 191–193 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 – 7.62 (q, J = 8.4 Hz, 4H), 7.52 – 7.45 (m, 2H), 7.30 – 7.22 (t, J = 7.7 Hz, 1H), 7.12 – 7.04 (t, J = 7.6 Hz, 1H), 6.80 – 6.76 (d, J = 2.7 Hz, 1H), 6.12 – 6.08 (d, J = 4.0 Hz, 1H), 5.70 (d, J = 3.6 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.8, 147.6, 142.7, 142.4, 135.2, 133.6, 133.5, 127.5 (q, J = 31.6 Hz) ,127.2, 126.6, 125.1, 125.0, 124.3 (q, J = 271.9 Hz) 123.1, 111.3, 106.8, 65.7, 11.2. ^{19}F NMR (471 MHz, DMSO-d_6) δ -60.781 ppm. HRMS (ESI) m/z: calculated for $C_{20}H_{13}F_3NO_2^-$ [M - H]$^-$: 356.0904, found: 356.0912.

methyl 4-(hydroxy(1-methyl-3-oxo-3*H*-pyrrolo[1,2-a]indol-2-yl)methyl)benzoate 3zf. Yellow solid (53.5 mg, 77% yield). m.p. 184–185 ^{o}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.96 – 7.92 (d, J = 8.4 Hz, 2H), 7.61 – 7.57 (d, J = 8.2 Hz, 2H), 7.52 – 7.47 (d, J = 7.9 Hz, 2H), 7.29 – 7.24 (m, 1H), 7.11 – 7.07 (m, 1H), 6.77 (s, 1H), 6.05 (d, J = 4.1 Hz, 1H), 5.68 (d, J = 4.1 Hz, 1H), 3.84 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.1, 163.8, 148.4, 142.7, 142.4, 135.4, 133.6, 133.5, 129.1, 128.2, 127.2, 126.1, 123.1, 111.3, 106.8, 65.7, 52.1, 11.2. HRMS (ESI) m/z: calculated for $C_{21}H_{16}NO_4^-$ [M - H]$^-$: 346.1085, found: 346.1084.

2-(hydroxy(thiophen-3-yl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3zh. Yellow solid (20.1 mg, 34% yield). m.p. 96–99 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.52 – 7.49 (d, J = 8.4 Hz, 2H), 7.44 – 7.42 (dd, J = 4.9, 1.3 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.12 – 7.08 (m, 1H), 7.00 – 6.98 (m, 1H), 6.98 – 6.95 (m, 1H), 6.80 (s, 1H), 6.17

(d, J = 4.3 Hz, 1H), 5.81 (d, J = 4.2 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.8, 147.1, 142.5, 142.3, 135.4, 133.6, 133.6, 127.3, 126.8, 125.0, 123.8, 123.1, 111.4, 106.9, 63.1, 11.4. HRMS (EI) calculated for $C_{17}H_{13}NO_2S$ $[M]^+$ 295.0677, found 295.0676.

2-(benzofuran-2-yl(hydroxy)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3zi. Yellow oil (48.7 mg, 74% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.62 – 7.58 (d, J = 7.2 Hz, 1H), 7.55 – 7.49 (m, 3H), 7.30 – 7.24 (m, 2H), 7.24 – 7.20 (td, J = 7.5, 0.8 Hz, 1H), 7.13 – 7.09 (m, 1H), 6.87 (s, 1H), 6.83 (s, 1H), 6.25 (d, J = 4.8 Hz, 1H), 5.72 (d, J = 4.7 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.7, 157.8, 154.3, 144.5, 142.4, 133.7, 133.6, 132.7, 127.9, 127.4, 124.1, 123.3, 123.2, 122.9, 121.1, 111.4, 111.1, 107.2, 103.3, 60.9, 11.4. HRMS (ESI) m/z: calculated for $C_{21}H_{14}NO_3^-$ $[M - H]^-$: 328.0979, found: 328.0982.

2-(hydroxy(naphthalen-2-yl)methyl)-1-methyl-3*H*-pyrrolo[1,2-a]indol-3-one 3zj. Yellow oil (43.4 mg, 64% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.99 (s, 1H), 7.95 – 7.92 (m, 1H), 7.90 – 7.86 (d, J = 8.6 Hz, 2H), 7.57 – 7.54 (dd, J = 8.6, 1.6 Hz, 1H), 7.51 – 7.47 (m, 4H), 7.28 – 7.23 (td, J = 7.7, 1.0 Hz, 1H), 7.11 – 7.05 (m, 1H), 6.76 (s, 1H), 6.01 (d, J = 4.1 Hz, 1H), 5.78 (d, J = 4.0 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.1, 142.6, 142.3, 140.4, 135.9, 133.6, 133.6, 132.8, 132.2, 127.9, 127.8, 127.5, 127.12, 126.14, 125.8, 124.6, 124.03, 123.06, 111.3, 106.5, 66.38, 11.3. HRMS (ESI) m/z: calculated for $C_{23}H_{16}NO_2^-$ $[M – H]^-$: 338.1187, found: 338.1184.

2-(hydroxy(phenyl)methyl)-1-methyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one

5a. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 – 7.91 (m, 0.42H), 7.88 - 7.82 (d, J = 7.1 Hz, 0.61H), 7.60 – 7.48 (m, 2H), 7.46 – 7.42 (d, J = 7.6 Hz, 1H), 7.41 – 7.31 (m, 2H), 7.29 – 7.21 (m, 3H), 6.35 (s, 1H), 5.91 – 5.87 (m, 0.43H), 5.62 – 5.58 (m, 0.62H), 5.41 – 5.36 (t, J = 3.8 Hz, 0.44H), 5.16 – 5.11 (d, J = 2.6 Hz, 0.64H), 4.04 – 3.98 (dd, J = 8.4, 3.8 Hz, 0.43H), 3.82 – 3.87 (m, 0.64H), 3.68 – 3.57 (m, 0.45H), 3.52 - 3.46 (d, J = 8.4 Hz, 0.64H), 1.64 - 1.56 (d, J = 7.2 Hz, 1.88H), 1.16 - 1.12 (d, J = 7.3 Hz, 1.28H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.4, 171.0, 150.0, 149.9, 144.0, 143.7, 134.9, 134.9, 129.6, 129.6, 127.9, 127.5, 126.49, 126.45, 126.3, 125.8, 123.79, 123.5, 122.8, 122.5, 120.7, 120.5, 112.9, 98.2, 97.2, 70.3, 69.7, 56.2, 55.2, 35.7, 30.8, 30.5, 16.5, 13.4. HRMS (EI) calculated for $C_{19}H_{17}NO_2$ $[M]^+$ 291.1259, found 291.1257.

(*Z*)-3-(1*H*-indol-2-yl)-1-(pyrrolidin-1-yl)but-2-en-1-one 5b

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.50 (s, 1H), 7.59 – 7.55 (d, J = 7.9 Hz, 1H), 7.48 – 7.43 (m, 1H), 7.18 – 7.12 (m, 1H), 7.03 – 6.97 (m, 1H), 6.82 (d, J = 0.6 Hz, 1H), 6.16 (s, 1H), 3.61 - 3.54 (t, J = 6.8 Hz, 2H), 3.50 - 3.43 (t, J = 6.8 Hz, 2H), 2.36 (s, 3H), 1.96 – 1.87 (m, 2H), 1.86– 1.77 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.1, 138.2, 136.1, 135.8, 127.3, 123.2, 120.8, 119.4, 116.6, 111.8, 105.2, 47.2, 46.16, 25.7, 24.1, 23.9. HRMS (ESI) m/z: calculated for $C_{16}H_{19}N_2O^+$ $[M + H]^+$: 255.1492, found: 255.1485.

ASSOCIATED CONTENT

Supporting Information.

The Supporting Information is available free of charge on the

ACS Publications website at DOI: xxxxx.

X-ray crystal structure of compound **3a** (CIF)

^{1}H and ^{13}C NMR spectra data (PDF)

Author Information

Corresponding Authors

E-mail: hliu@simm.ac.cn.

E-mail: jianli@ecust.edu.cn

Notes

The authors declare no competing financial interests.

Acknowledgments

We gratefully acknowledge financial support from the National Natural Science Foundation of China (81620108027, 21632008, 91229204 and 81220108025）the Major Project of Chinese National Programs for Fundamental Research and Development (2015CB910304), and National S&T Major Projects (2014ZX09507002-001).

Notes and References

1. (a) Pindur, U.; Lem*ster, T. Curr. Med. Chem.* **2001**, *8,* 1681. (b) Ramirez, A.; Garcia-Rubio, S. Curr. M*ed. Chem.* **2003**, *10*, 1891. (c) Somei, M.; Yamada, F. *Nat. Prod. Rep.* **2005**, *22*, 73. (d) Kawasaki, T.；Higuchi, K. *Nat. Prod. Rep.* **2005**, *22*, 761.

(e) Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489.

2. (a) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (b) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2011**, *111*, PR215. (c) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875. (d) Bandini, M.; Eichholzer, A. *Angew. Chem. Int. Ed.* **2009**, *48*, 9608. (e) Joucla, L.; Djakovitch, L. *Adv. Synth. Catal.* **2009**, *351*, 673. (f) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (g) Sandtorv, A. H. *Adv. Synth. Catal.* ***2015****, 357, 2403*. (h) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281. (i) Yang, F.; Ackermann, L. *J. Org. Chem.* 2014, *79*, 12070.

3. For the palladium-catalyzed direct C-H bond functionalization of indoles, see: (a) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972. (b) Q. Liu, Q.; Li, Q.; Ma, Y.; Jia, Y. *Org. Lett.* **2013**, *15*, 4528. For the rhodium-catalyzed direct C-H bond functionalization of indoles, (c) Schipper, D. J.; Hutchinson, M.; Fagnou, K. *J. Am. Chem. Soc.* **2010**, *132*, 6910. (d) Patureau, F. W.; Besset, T.; Glorius, F. *Angew. Chem. Int. Ed.* **2011**, *50*, 1064. (e) Qin, X.; Liu, H.; Qin, D.; Wu, Q.; You, J.; Zhao, D.; Guo, Q.; Huang, X.; Lan, *J. Am. Chem. Sci.* **2013**, *4*, 1964. (f) Xie, F.; Qi, Z.; Yu, S.; Li, X. *J. Am. Chem. Soc.* **2014**, *136*, 4780.

4. For the ruthenium-catalyzed direct C-H bond functionalization of indoles, see: (a) Manikandan, R.; Jeganmohan, M. *Org. Biomol. Chem.* **2015**, *13*, 10420. (b) (c) Zhang, Z.; Jiang, H.; Huang, Y. *Org. Lett*. **2014**, *16*, 5976. (b) Zhang, W.; Wei, J.; Fu, S.; Lin, D.; Jiang, H.; Zeng, W. *Org. Lett.* **2015**, *17*, 1349. (c) Yang, F.; Ackermann, L., *J. Org. Chem.* **2014**, *79*, 12070. (d) Lanke, V.; Ramaiah Prabhu, K. *Org. Lett.* **2013**, *15*, 6262. For the iridium-catalyzed direct C-H bond functionalization of indoles, (e)Paul, S.;

Chotana, G. A.; Holmes, D.; Reichle, R. C.; Maleczka, R. E.; Smith, M. R. *J. Am. Chem. Soc.* **2006**, *128*, 15552. (f) Robbins, D. W.; Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 4068.

5. Transition metal-catalyzed *N*-fused indole synthesis via C-H activation: (a) Lopez, S. L.; Greaney, M. F. *Chem. Comm.* **2011**, *47*, 7992. (b) Davis, T. A.; Hyster, T. K.; Rovis, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 14181. (c) Ackermann, L.; Wang, L.; Lygin, A. V. *Chem. Sci.* **2012**, *3*, 177. (d) Zhang, Y.; Zheng, J.; Cui, S. *J. Org. Chem.* **2014**, *79*, 6490. (e) Wang, X.; Tang, H.; Feng, H.; Li, Y.; Yang, Y.; Zhou, B. *J. Org. Chem.* **2015**, *80*, 6238. (f) Yokoyama, Y.; Unoh, Y.; Bohmann, R. A.; Satoh, T.; Hirano, K.; Bolm, C.; Miura, M. *Chem. Lett.* **2015**, *44*, 1104. (g) Yi, C. S.; Yun, S. Y.; Guzei, L. A. *J. Am. Chem. Soc.* **2005**, *127*, 5782. (h) Ackermann, L.; Wang, L.; Lygin, A. V. *Chem. Sci.* **2012**, *3*, 177.

6.Elmegeed, G. A.; Baiuomy, A. R.; Abdel-Salam, O. M. E. *Eur. J. Med. Chem.* **2007**, *42*, 1285.

7. Protter, A. A.; Chakravarty, S. Patent, WO2012/112961A1, 2012.

8. Wilson, R. M.; Thalji, R. K.; Bergman, R. G.; Ellman, J. A. *Org. Lett.* **2006**, *8*, 1745.

9. (a) Liang, L.; Fu, S.; Lin, D.; Zhang, X. Q.; Deng, Y.; Jiang, H.; Zeng, W. *J. Org. Chem*. **2014**, *79*, 9472. (b) Ikemoto, H.; Yoshino, T.; Sakata, K.; Matsunaga, S.; Kanai, M. *J. Am. Chem. Soc.* **2014**, *136*, 5424. (c) Arockiam, P. B.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H.; *Angew. Chem. Int. Ed*. **2010**, *49*, 6629. (d) Simmons, E. M.; Hartwig, J. F. *Angew. Chem. Int. Ed*. **2012**, *51*, 3066. (e) Dwight, T. A.; Rue, N. R.;

Charyk, D.; Josselyn, R.; DeBoef, B. *Org. Lett.* **2007**, *9*, 3137. (f) Ackermann, L.; Tonin, M.; Zell, D.; Müller, V. *Synthesis.* **2016**, *49*, 127. (j) Kandukuri, S. R.; Schiffner, J. A.; Oestreich, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 1265.

10. (a) Wu, X.; Wang, B.; Zhou, S.; Zhou, Y.; Liu, H. *ACS Catal.* 2017, *7*, 2494. (b) Wu, X.; Wang, B.; Zhou, Y.; Liu, H. *Org. Lett.* 2017, *19*, 1294. (c) Peng, P.; Wang, J.; Jiang, H.; Liu, H. *Org. Lett.* 2016, *18*, 5376. (d) Wu, X.; Zhang, D.; Zhou, S.; Gao, F.; Liu, H. *Chem. Commun.* 2015, *51*, 12571.

11. For details, see the Supporting Information. CCDC 1521413 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

12. (a) Ackermann, L.; Vicente, R.; Althammer, A. *Org. Lett.* 2008, *10*, 2299. (b) Ackermann, L.; Vicente, R.; Potukuchi, H. K.; Pirovano, V. *Org. Lett.* 2010, *12*, 5032. (c) Flegeau, E. F.; Bruneau, C.; Dixneuf, P. H.; Jutand, A. *J. Am. Chem. Soc.* **2011**, *133*, 10161.

12. Zheng, J.; Zhang, Y.; Cui, S. *Org. Lett.* **2014,** *16*, 3560.

13. Stuart, D. R.; Bertrand-Laperle, M.; Burgess, K. M. N.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130*, 16474.

14. Jaimes, M. C. B.; Ahrens, A.; Rudolph, M.; Hashmi, A. S. K. *Chem. Eur. J.* **2015**, *21*, 427.

15. Alyson, E. G.; Alexandra, D. B.; Kristine, A. N. *Tetrahedron Lett.* **2013**, *54*, 459.

16. José, A. F.; Andrew, J. E.; David, J. P. *J. Am. Chem. Soc.* **2016**, *138*, 790.

17. Lenden, P.; Entwistle, D. A.; Willis, M. C. *Angew. Chem. Int. Ed.* **2011**, *50*, 10657.

18. Sevov, C. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 2116.