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New formal (3+3) cycloaddition of enaminones for forming tetracyclic indolo[2,3-*b*]quinolines under microwave irradiation

Meng-Yuan Li, Hai-Wei Xu, Wei Fan, Qin Ye, Xue Wang, Bo Jiang *, Shu-Liang Wang, Shu-Jiang Tu *

School of Chemistry and Chemical Engineering, and Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Jiangsu Normal University, Xuzhou 221116, Jiangsu, PR China

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ABSTRACT

Concise and efficient base-promoted domino formal (3+3) cycloaddition has been established for the formation of tetracyclic indolo[2,3-*b*]quinoline derivatives under microwave heating. The present methodology shows attractive properties, such as the maximum efficiency of a process, short reaction periods, and operational simplicity, and it can avoid time-consuming and costly syntheses, tedious work-up and isolation of intermediate. This chemistry provides a facile and promising synthetic strategy to construction of tetracyclic indolo[2,3-*b*]quinoline skeleton.

1. Introduction

The efficient construction of multicyclic skeletons with chemical and biomedical importance is an active theme in organic synthesis. Among these skeletons, the structurally diverse pyrido[2,3-*b*]indole (α-carboline I, Fig. 1) commonly exist in nature,[1–3] represented by grossularine-1 (II), grossularine-2 (III), mescengricin (IV), which exhibit a broad range of biological activities.[4] Furthermore, indolo[2,3-*b*]quinoline unit is the precursor to cryptotakieine (V) (also known as neocryptolepine) alkaloid,[5] one of the major metabolites out of the thirteen characterized alkaloids from *Cryptolepis sanguinolenta*,[6] which exhibited antitumor activity and DNA binding properties.[7] Because of their unique chemical and biological characteristics, many methodologies for the synthesis of indolo[2,3-*b*]quinolines have been developed. Most of them involved reduction cyclization of *o*,*o*′-dinitro-α-cyanodibenzyl,[8] thermal decomposition of adequate triazole,[9] annelation of indoles[10] and other methods.[11] Despite these limited indolo[2,3-*b*]quinoline syntheses, an exploration of a facile protocol for the direct formation of the indolo[2,3-*b*]quinoline skeleton and its multi-functionalizations would be highly favorable.

Modern organic synthesis has benefited from the development of high-efficient synthetic strategy for the selective construction of potentially useful target compounds. Domino reactions, being one of the most effective methods to improve chemical efficiency, can implement reaction cascades and generate the structural diversity of biologically important molecules by simultaneous combination of multiple transformations in a single pot.[12] Often mild and environmentally friendly, domino reactions also provide a shortened and atom-economical synthesis, thereby minimizing the generation of waste and rendering the transformations green.[13] In recent years, various domino reactions toward the formation of polycyclic fused azaheterocycles have been extensively studied.[14] In the past

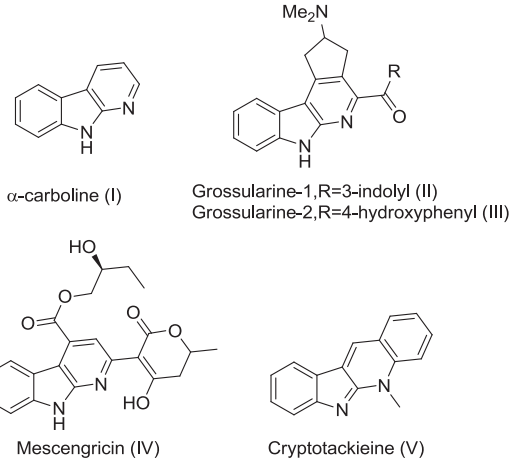

Fig. 1. Natural products with indole subunits.

* Corresponding authors. E-mail address: laotu@jsnu.edu.cn (S.-J. Tu).

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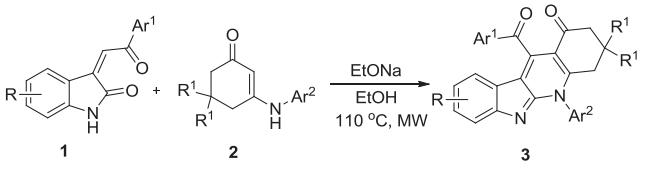
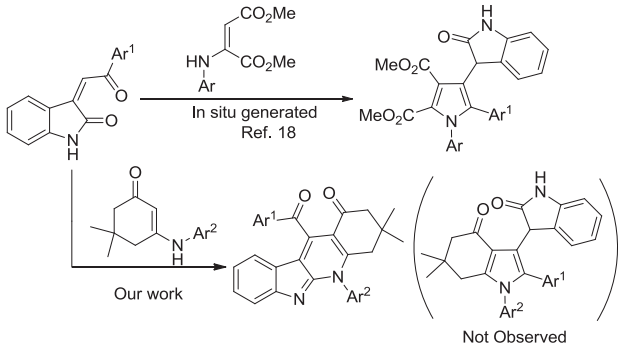
several years, we have developed a series of domino reactions for the construction of multiple functional ring structures of chemical and pharmaceutical importance.[15,16] As a continue of our works on this project, we now developed domino [3+3] heterocyclization of 3-aroylidene-2-oxindoles **1** with enaminones **2** leading to the formation of polyfunctionalized indolo[2,3-*b*]quinoline derivatives **3** in good yields (Scheme 1). The present work represents the special example for selective construction of these types of tetracyclic indolo[2,3-*b*]quinolines through decarbonylation of lactams.



Scheme 1. Domino synthesis of indolo[2,3-*b*]quinoline derivatives.

2. Results and discussion

3-Aroylidene-2-oxindoles are versatile and readily obtainable reagents, and their chemistry has received considerable attention in recent years.[17] It has been reported that when a mixture of 3-aroylidene-2-oxindoles and in situ generated β-enamino ester was refluxed in HOAc, pentasubstituted pyrroles were produced (Scheme 2).[18] During this project, we found that when β-enamino ester employed in the above literature were replaced by enaminones **2** at 110 °C used HOAc as a promoter under microwave irradiation, the reaction did not proceed. When the reaction condition was changed to basic condition, the reaction occurred in another direction to form multifunctionalized indolo[2,3-*b*]quinolines that are important scaffolds for organic synthesis and drug design in pharmaceutical sciences (Scheme 2).[19] Encouraged by this initial result, we then made many efforts on optimizing reaction conditions.



Scheme 2. The reaction of 3-aroylidene-2-oxindoles.

We started this study by subjecting a preformed 3-*p*-methoxyphenacylideneoxindole **1a** and 5,5-dimethyl-3-(4-methylpheny lamino)cyclohex-2-enone **2a** in ethanol at 80 °C under microwave irradiation, using different bases (1.0 equiv). The incomplete reaction was observed using various bases, such as K_2CO_3, NaOH, *t*-BuOK, and EtONa as a base catalyst. Sodium ethylate (EtONa) was proven to be the best base (Table 1, entry 4). Subsequently, the reaction catalyzed by NaOEt was performed and repeated many times in different temperatures in a sealed vessel under microwave irradiation for 12 min. The best yield of product **3a** (85%) was obtained in ethanol as the reaction temperature was increased to 110 °C (Table 1, entry 6). A further increase in reaction temperature failed to improve the yield of the desired product **3a** (Table 1, entry 7). Subsequently, the same reaction was investigated under classical heating (CH) conditions at 110 °C for 120 min, providing the product **3a** in 72% yield (Table 1, entry 8).

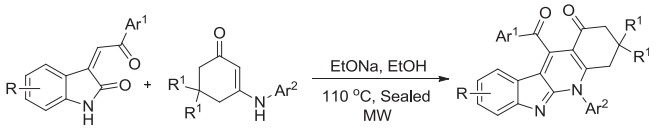
Table 1
Optimization of the catalysts for compound **3a**

Entry	Base/equiv	*T*/°C	Time/min	Yield/%
1	K_2CO_3 (1.0)	80	12	43
2	NaOH (1.0)	80	12	52
3	*t*-BuOK (1.0)	80	12	32
4	EtONa (1.0)	80	12	68
5	EtONa (1.0)	100	12	75
6	EtONa (1.0)	110	12	85
7	EtONa (1.0)	120	12	83
8	EtONa (1.0)	110	2 h[a]	72

[a] Conventional heating.

With this result in hand, a library of new multi-functionalized indolo[2,3-*b*]quinoline derivatives **3** was synthesized in order to evaluate the scope of the protocol (Table 2). The effect of different groups bound to enaminones was evaluated at first, reacting **1a** with structurally diverse enaminones. The electronic characteristics of the substituent attached to the *para* position of the aromatic ring (electron-donating or electron-withdrawing) did not affect performance of the transformation, and the corresponding indolo [2,3-*b*]quinolines were obtained in very high yield. Notably, when *N*-aryl enaminones with two MeO groups at the 3,4-positions was employed, the respective product was obtained in 73% yield. Furthermore, steric effects did not significantly affect the reaction. Using *ortho*-bromo- and *ortho*-iodophenyl enaminones, the corresponding products **3h** and **3j** were delivered in good yield,

Table 2
Domino synthesis of indolo[2,3-*b*]quinoline **3** under MW[a]



Entry	3	Ar^1	R	Ar^2	R^1	Time/min	Yield/%[b]
1	**3a**	4-$MeOC_6H_4$ (**1a**)	H	4-MeC_6H_4 (**2a**)	Me	12	85
2	**3b**	4-$MeOC_6H_4$ (**1a**)	H	4-$MeOC_6H_4$ (**2b**)	Me	8	83
3	**3c**	4-$MeOC_6H_4$ (**1a**)	H	3,4-$(MeO)_2C_6H_3$ (**2c**)	Me	16	73
4	**3d**	4-$MeOC_6H_4$ (**1a**)	H	C_6H_5 (**2d**)	Me	15	75
5	**3e**	4-$MeOC_6H_4$ (**1a**)	H	4-FC_6H_4 (**2e**)	Me	9	80
6	**3f**	4-$MeOC_6H_4$ (**1a**)	H	4-ClC_6H_4 (**2f**)	Me	8	81
7	**3g**	4-$MeOC_6H_4$ (**1a**)	H	4-BrC_6H_4 (**2g**)	Me	8	86
8	**3h**	4-$MeOC_6H_4$ (**1a**)	H	2-BrC_6H_4 (**2h**)	Me	10	83
9	**3i**	4-$MeOC_6H_4$ (**1a**)	H	2-IC_6H_4 (**2i**)	Me	12	81
10	**3j**	4-MeC_6H_4 (**1b**)	H	4-BrC_6H_4 (**2g**)	Me	12	85
11	**3k**	4-MeC_6H_4 (**1b**)	H	2-BrC_6H_4 (**2h**)	Me	10	78
12	**3l**	4-MeC_6H_4 (**1b**)	H	2-IC_6H_4 (**2i**)	Me	15	76
13	**3m**	4-MeC_6H_4 (**1c**)	5-Me	4-MeC_6H_4 (**2a**)	Me	10	80
14	**3n**	4-MeC_6H_4 (**1c**)	5-Me	4-BrC_6H_4 (**2g**)	Me	9	84
15	**3o**	4-FC_6H_4 (**1d**)	H	4-ClC_6H_4 (**2f**)	Me	11	82
16	**3p**	4-FC_6H_4 (**1d**)	H	4-BrC_6H_4(**2g**)	Me	10	86
17	**3q**	4-FC_6H_4 (**1d**)	H	2-IC_6H_4 (**2i**)	Me	10	81
18	**3r**	4-ClC_6H_4 (**1e**)	H	4-MeC_6H_4 (**2a**)	Me	13	83
19	**3s**	4-ClC_6H_4 (**1e**)	H	4-BrC_6H_4 (**2g**)	Me	11	84
20	**3t**	4-MeC_6H_4 (**1b**)	H	4-ClC_6H_4 (**2j**)	H	14	76
21	**3u**	4-MeC_6H_4 (**1b**)	H	4-BrC_6H_4 (**2k**)	H	14	78
22	**3v**	4-MeC_6H_4 (**1c**)	5-Me	4-BrC_6H_4 (**2k**)	H	16	73
23	**3w**	4-$MeOC_6H_4$ (**1a**)	H	4-FC_6H_4 (**2l**)	H	11	83
24	**3x**	4-$MeOC_6H_4$ (**1a**)	H	4-ClC_6H_4 (**2j**)	H	13	78
25	**3y**	4-$MeOC_6H_4$ (**1a**)	H	4-BrC_6H_4 (**2k**)	H	12	80
26	**3z**	4-$MeOC_6H_4$ (**1a**)	H	2-IC_6H_4 (**2m**)	H	14	79

[a] Reagents and conditions: 110 °C, EtOH (1.5 mL) microwave heating.
[b] Isolated yield.

respectively. Next, the influence of the 3-aroylidene-2-oxindoles was evaluated, employing **2** with different functionalities attached at the *para* position of the phenyl ring, including methyl, fluoro, and chloro groups. The results indicated that both electron-withdrawing and electron-donating groups are suitable substrates, affording the corresponding products **3j**–**s** in 76–86% yield. As an extension of the above study, 5,5-unsubstituted enaminones was subjected with diverse 3-aroylidene-2-oxindoles to investigate the possibility of this transformation. Substituents on the phenyl ring of **1** and **2** were all successfully engaged in this reaction, leading to the final products with good yields (**3t**–**z**). Furthermore, groups like bromide and chloride were well tolerated. These functional groups provide ample opportunity for further functional group manipulations, for example, such as modern cross-coupling reactions. It can be noted that the results exhibit the scope and generality of the domino reaction with respect to a range of enaminone and 3-aroylidene-2-oxindole substrates.

The structures of the indolo[2,3-*b*]quinolin were fully characterized by ^{1}H and ^{13}C NMR, HRMS, IR spectra, and the structure of compound **3w** was further confirmed by single crystal X-ray diffraction (Fig. 2).

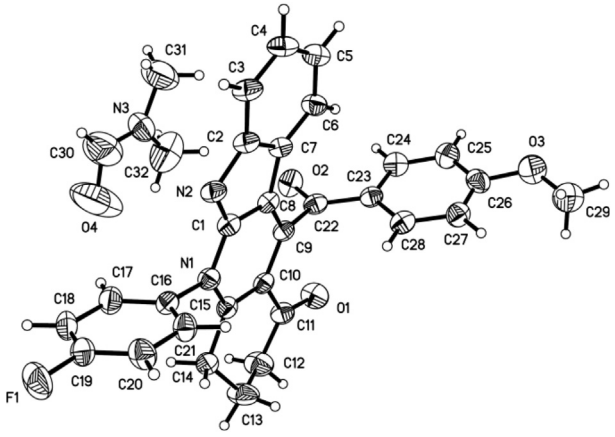
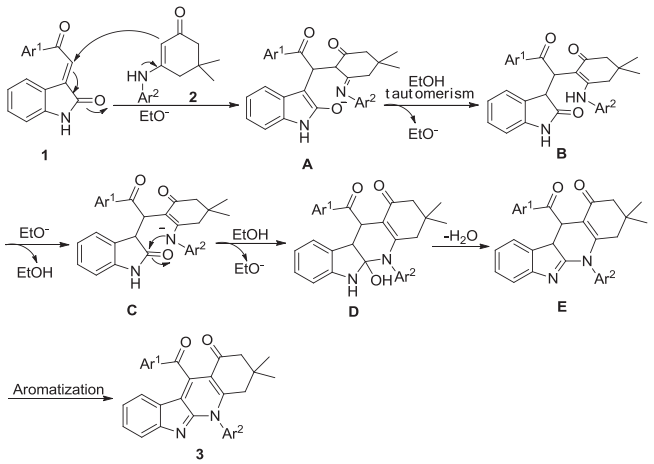


Fig. 2. ORTEP drawing of **3w**.[20]

On the basis of literature reports[18] and observations of the above results, a possible mechanism has been proposed for the formation of indolo[2,3-*b*]quinoline derivatives as shown in Scheme 3. The reaction involves the ring closure cascade reactions that consist of initial Michael addition (**1** to **A**), tautomerism (**A** to **B**), intramolecular cyclization (**C** to **D**), and subsequent dehydration and aromatization (**D** to **3**). This type of hydrogen loss is well precedented.[21]



Scheme 3. The reasonable mechanism for the formation of **3**.

3. Conclusion

In summary, an operationally simple and highly efficient base-promoted formal (3+3) cycloaddition strategy for the formation of tetracyclic indolo[2,3-*b*]quinoline derivatives has been developed in this work. The mild conditions, the maximum efficiency of a process and short reaction periods as well as operational simplicity are clearly represented in this one-pot transformation that provides an elegant methodology for the synthesis of highly functionalized indolo[2,3-*b*]quinolines. Further investigations to evaluate the applicability of this process to a broad range of substrates, synthesizing more complex products and testing their biological activity is an ongoing goal of research in our laboratory.

4. Experimental section

4.1. General

Microwave irradiation was carried out with Initiator from Biotage Company, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on a FT-IR-Tensor 27 spectrometer in KBr pellets and reported in cm^{-1}. ^{1}H NMR spectra were measured on a Bruker DPX 400 MHz spectrometer in DMSO-d_6 with chemical shift (δ) given in parts per million relative to TMS as internal standard. HRMS (ESI) was determined by using microTOF-Q II HRMS/MS instrument (Bruker). X-ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

4.2. Typical procedure for the preparation of 11-(4-methoxy benzoyl)-3,3-dimethyl-5-(*p*-tolyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3a)

Typically, 5,5-dimethyl-3-(4-methylphenylamino)cyclohex-2-enone (**2a**, 1.1 mmol, 1.1 equiv) was introduced in a 10-mL Initiator™ reaction vial, 3-*p*-methoxyphenacylideneoxindole (**1a**, 1.0 mmol, 1.0 equiv), EtONa (1.0 mmol, 1.0 equiv), and EtOH (1.5 mL) were successively added. Subsequently, the reaction vial was capped and then pre-stirred for 20 s. The mixture was irradiated (Time: 12 min, Temperature: 110 °C; Absorption Level: High; Fixed Hold Time) until TLC (petroleum ether: acetic ether 3:1) revealed that conversion of the starting material **1a** was complete. The reaction mixture was cooled to room temperature. Next, the system was diluted with cold water (20 mL) and neutralized by diluted acidic solution. The resulting precipitate was collected by filtration and was purified by flash column chromatography to afford the desired pure product **3a**.

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2957, 1671, 1668, 1600, 1510, 1415, 1304, 1261, 1246, 1166, 1075, 1020, 856, 793, 622 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.94 (d, J=7.2 Hz, 1H, ArH), 7.78–7.62 (m, 1H, ArH), 7.50 (d, J=8.0 Hz, 1H, ArH), 7.39 (s, 1H, ArH), 7.23 (s, 1H, ArH), 7.03 (s, 1H, ArH), 6.95 (d, J=7.4 Hz, 1H, ArH), 3.85 (s, 3H, OCH_3), 2.74 (s, 2H, CH_2), 2.53 (s, 3H, CH_3), 2.49 (s, 2H, CH_2), 1.10 (s, 6H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm) 194.0, 193.9, 163.8, 160.5, 155.8, 154.4, 151.2, 140.5, 135.2, 131.4, 131.2, 130.9, 129.4, 128.7, 127.1, 126.9, 122.8, 121.2, 119.2, 114.3, 113.4, 55.5, 50.5, 42.5, 33.1, 28.4, 27.9, 21.5.

HRMS (ESI) *m*/*z*: calcd for $C_{32}H_{29}N_2O_3$: 489.2178 $[M+H]^+$; found: 489.2173.

4.3. 11-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3b)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 3415, 2956, 1673, 1656, 1599, 1511, 1412, 1304, 1264, 1231, 1144, 1022, 857, 826, 741 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.94 (d, *J*=8.4 Hz, 2H, ArH), 7.69 (d, *J*=8.0 Hz, 1H, ArH), 7.49 (d, *J*=7.6 Hz, 1H, ArH), 7.45–7.34 (m, 2H, ArH), 7.28 (s, 1H, ArH), 7.18 (t, *J*=8.0 Hz, 2H, ArH), 7.02 (t, *J*=6.4 Hz, 1H, ArH), 6.94 (d, *J*=8.4 Hz, 2H, ArH), 3.94 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 2.74 (s, 2H, CH_2), 2.48 (d, *J*=7.2 Hz, 2H, CH_2), 1.10 (s, 3H, CH_3), 1.08 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 194.0, 193.9, 163.9, 160.6, 151.5, 130.9, 130.3, 130.2, 129.4, 128.8, 128.5, 128.3, 125.5, 125.1, 122.8, 121.4, 119.1, 115.9, 114.3, 55.7, 55.5, 50.5, 42.6, 33.1, 28.5, 27.9.

HRMS (ESI) *m*/*z*: calcd for $C_{32}H_{29}N_2O_4$: 505.2127 $[M+H]^+$; found: 505.2126.

4.4. 5-(3,4-Dimethoxyphenyl)-11-(4-methoxybenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3c)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 3069, 2956, 1666, 1619, 1600, 1518, 1441, 1305, 1264, 1161, 1015, 871, 763 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.94 (d, *c* 2H, ArH), 7.71 (d, *J*=8.4 Hz, 1H, ArH), 7.49 (d, *J*=6.8 Hz, 1H, ArH), 7.39 (t, *J*=8.0 Hz, 1H, ArH), 7.13 (t, *J*=8.0 Hz, 1H, ArH), 7.13–6.97 (m, 2H, ArH), 6.94 (d, *J*=7.6 Hz, 3H, ArH), 4.03 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 2.76 (d, *J*=10.4 Hz, 2H, CH_2), 2.48 (d, *J*=8.4 Hz, 2H, CH_2), 1.11 (s, 3H, CH_3), 1.09 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 194.0, 193.8, 163.9, 155.9, 154.5, 151.5, 150.4, 140.9, 130.9, 130.4, 129.4, 128.8, 122.8, 121.3, 119.8, 119.5, 119.2, 114.3, 114.3, 113.4, 112.0, 111.8, 110.2, 110.1, 56.2, 56.2, 55.5, 50.5, 42.4, 33.0, 28.5, 27.7.

HRMS (ESI) *m*/*z*: calcd for $C_{33}H_{31}N_2O_5$: 535.2227 $[M+H]^+$; found: 535.2215.

4.5. 11-(4-Methoxybenzoyl)-3,3-dimethyl-5-phenyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3d)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2950, 1670, 1621, 1599, 1523, 1505, 1412, 1337, 1293, 1246, 1166, 1024, 857, 766 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.95 (d, *J*=7.2 Hz, 2H, ArH), 7.80–7.69 (m, 2H, ArH), 7.66 (d, *J*=7.6 Hz, 2H, ArH), 7.50 (s, 2H, ArH), 7.38 (s, 2H, ArH), 7.04 (t, *J*=7.6 Hz, 1H, ArH), 6.95 (d, *J*=8.4 Hz, 2H, ArH), 3.86 (s, 3H, OCH_3), 2.71 (s, 2H, CH_2), 2.48 (d, *J*=8.4 Hz, 2H, CH_2), 1.10 (s, 3H, CH_3), 1.08 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 193.9, 193.8, 163.9, 155.7, 154.5, 150.9, 141.0, 137.9, 130.9, 130.8, 130.6, 130.3, 129.5, 128.8, 127.6, 127.4, 122.8, 121.3, 119.2, 114.3, 113.5, 55.5, 50.5, 42.6, 33.1, 28.5, 27.9.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{27}N_2O_3$: 475.2022 $[M+H]^+$; found: 475.2029.

4.6. 5-(4-Fluorophenyl)-11-(4-methoxybenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3e)

Yellow solid, mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 3416, 2951, 1671, 1620, 1601, 1575, 1510, 1411, 1248, 1153, 1026, 860, 848, 764, 625 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.94 (d, *J*=7.7 Hz, 1H, ArH), 7.66 (d, *J*=8.2 Hz, 1H, ArH), 7.50 (s, 1H, ArH), 7.46–7.33 (m, 2H, ArH), 7.03 (s, 1H, ArH), 6.95 (d, *J*=8.2 Hz, 1H, ArH), 3.86 (s, 3H, OCH_3), 2.71 (s, 2H, 2H, CH_2), 2.61–2.33 (m, 2H, CH_2), 1.11 (s, 3H, CH_3), 1.09 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 193.8, 193.7, 163.9, 163.2($^1J_{CF}$=249.5 Hz), 155.8, 154.4, 150.8, 140.9, 130.9, 129.5($^3J_{CF}$=8.8 Hz), 129.4, 129.2, 129.0, 123.1, 122.9 ($^4J_{CF}$=2.1 Hz), 121.5, 119.2, 118.0 ($^2J_{CF}$=22.9 Hz), 117.9, 117.7, 114.3, 113.5, 55.5, 50.4, 42.6, 33.1, 28.5, 27.9.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}FN_2O_3$: 493.1927 $[M+H]^+$; found: 493.1954.

4.7. 5-(4-Fluorophenyl)-11-(4-methoxybenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3f)

Yellow solid, mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2957, 2871, 1672, 1624, 1602, 1520, 1510, 1432, 1305, 1245, 1109, 1016, 855, 821, 770 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.92 (d, *J*=8.4 Hz, 2H, ArH), 7.67 (t, *J*=8.0 Hz, 3H, ArH), 7.48 (d, *J*=7.6 Hz, 1H, ArH), 7.44 (d, *J*=8.4 Hz, 1H, ArH), 7.39 (t, *J*=7.6 Hz, 1H, ArH), 7.32 (d, *J*=8.4 Hz, 1H, ArH), 7.03 (t, *J*=7.6 Hz, 1H, ArH), 6.92 (d, *J*=8.4 Hz, 2H, ArH), 3.83 (s, 3H, OCH_3), 2.70 (s, 2H, CH_2), 2.44 (d, *J*=7.2 Hz, 2H, CH_2), 1.08 (s, 3H, CH_3), 1.06 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 193.9, 193.7, 163.9, 155.6, 154.4, 150.6, 140.9, 136.5, 136.1, 131.1, 131.0, 130.9, 129.4, 129.0, 129.0, 128.8, 123.1, 122.9, 122.9, 121.5, 119.2, 114.3, 113.6, 55.5, 50.4, 42.6, 33.2, 28.5, 27.9.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}ClN_2O_3$: 509.1632 $[M+H]^+$; found: 509.1628.

4.8. 5-(4-Bromophenyl)-11-(4-methoxybenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3g)

Yellow solid, mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2957, 1671, 1624, 1602, 1518, 1510, 1409, 1304, 1227, 1148, 1013, 854, 821 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.93 (d, *J*=8.4 Hz, 2H, ArH), 7.85 (t, *J*=8.4 Hz, 2H, ArH), 7.66 (d, *J*=8.0 Hz, 1H, ArH), 7.48 (d, *J*=7.6 Hz, 1H, ArH), 7.39 (t, *J*=8.4 Hz, 2H, ArH), 7.24 (s, 1H, ArH), 7.03 (t, *J*=8.0 Hz, 1H, ArH), 6.94 (d, *J*=8.4 Hz, 2H, ArH), 3.85 (s, 3H, OCH_3), 2.71 (s, 2H, CH_2), 2.48 (d, *J*=8.8 Hz, 2H, CH_2), 1.11 (s, 3H, CH_3), 1.09 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 193.9, 193.7, 163.9, 155.5, 154.4, 150.6, 141.0, 136.7, 134.1, 133.9, 130.9, 129.3, 129.1, 129.03, 124.7, 123.1, 122.9, 121.5, 119.2, 114.3, 113.6, 55.5, 50.4, 42.6, 33.2, 28.5, 27.9.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}BrN_2O_3$: 553.1121 $[M+H]^+$; found: 553.1159.

4.9. 5-(2-Bromophenyl)-11-(4-methoxybenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3h)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2948, 1667, 1624, 1599, 1509, 1439, 1412, 1305, 1257, 1222, 1166, 1022, 856, 774, 765 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.92 (t, *J*=7.2 Hz, 3H, ArH), 7.71–7.63 (m, 2H, ArH), 7.61–7.46 (m, 3H, ArH), 7.39 (t, *J*=7.6 Hz, 1H, ArH), 7.04 (t, *J*=7.6 Hz, 1H, ArH), 6.94 (t, *J*=7.6 Hz, 2H, ArH), 3.85 (s, 3H, OCH_3), 2.71–2.55 (m, 2H, CH_2), 2.49 (d, *J*=9.6 Hz, 2H, CH_2), 1.12 (s, 3H, CH_3), 1.10 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm) 193.8, 193.7, 163.9, 163.8, 150.7, 140.8, 137.1, 134.7, 134.5, 131.9, 130.9, 129.9, 129.6, 129.4, 129.2, 129.0, 122.9, 121.4, 119.2, 114.4, 114.3, 55.5, 50.6, 42.0, 33.0, 29.2, 27.5.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}BrN_2O_3$: 553.1121 $[M+H]^+$; found: 553.1113.

4.10. 5-(2-Iodophenyl)-11-(4-methoxybenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3i)

Yellow solid; mp>300 °C.

IR (KBr, *v*, cm^{-1}): 2948, 1668, 1623, 1600, 1523, 1507, 1412, 1338, 1294, 1242, 1166, 1022, 856, 743 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.16 (d, *J*=7.2 Hz, 1H, ArH), 7.98–7.86 (m, 2H, ArH), 7.75–7.65 (m, 2H, ArH), 7.50 (m, 2H, ArH), 7.40 (s, 2H, ArH), 7.05 (d, *J*=6.8 Hz, 1H, ArH), 6.93 (t, *J*=7.4 Hz, 2H, ArH), 3.84 (s, 3H, OCH_3), 2.63 (m, 2H, CH_2), 2.49 (d, *J*=10.0 Hz, 2H, CH_2), 1.15 (s, 3H, CH_3), 1.13 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 193.9, 193.7, 163.9, 163.8, 154.7, 154.6, 150.5, 141.1, 140.8, 131.8, 130.9, 130.5, 129.0, 128.8, 128.6, 122.9, 121.4, 119.3, 114.4, 114.2, 97.5, 55.5, 50.6, 42.2, 32.96, 29.3, 27.8.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}IN_2O_3$: 601.0988 $[M+H]^+$; found: 601.0963.

4.11. 5-(4-Bromophenyl)-3,3-dimethyl-11-(4-methylbenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3j)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2949, 1665, 1620, 1579, 1567, 1487, 1366, 1327, 1280, 1109, 885, 825, 758 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ ppm): 7.86 (d, *J*=8.0 Hz, 2H, ArH), 7.74–7.61 (m, 3H, ArH), 7.53–7.43 (m, 2H, ArH), 7.40 (t, *J*=7.2 Hz, 1H, ArH), 7.35–7.30 (m, 1H, ArH), 7.27 (s, 1H, ArH), 7.25 (s, 1H, ArH), 7.03 (t, *J*=7.6 Hz, 1H, ArH), 2.71 (s, 2H, CH_2), 2.48 (d, *J*=7.6 Hz, 2H, CH_2), 2.41 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 1.09 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 194.7, 193.8, 155.5, 154.4, 150.4, 144.5, 140.8, 136.6, 134.1, 133.9, 133.8, 129.7, 129.3, 129.1, 128.6, 124.7, 123.2, 122.8, 121.5, 119.2, 113.6, 50.3, 42.6, 33.2, 28.5, 27.9, 21.8.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}BrN_2O_2$: 537.1178 $[M+H]^+$; found: 537.1187.

4.12. 5-(2-Bromophenyl)-3,3-dimethyl-11-(4-methylbenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3k)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2952, 1674, 1669, 1620, 1604, 1513, 1440, 1404, 1336, 1224, 1144, 1012, 856, 846, 776, 763 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.92 (t, *J*=6.8 Hz, 1H, ArH), 7.88–7.79 (m, 2H, ArH), 7.68 (t, *J*=8.8 Hz, 2H, ArH), 7.57 (t, *J*=8.0 Hz, 1H, ArH), 7.54–7.45 (m, 2H, ArH), 7.40 (t, *J*=7.6 Hz, 1H, ArH), 7.28 (s, 1H, ArH), 7.24 (s, 1H, ArH), 7.04 (t, *J*=7.6 Hz, 1H, ArH), 2.77–2.54 (m, 2H, CH_2), 2.48 (d, *J*=7.2 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.10 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 194.7, 193.9, 150.7, 144.5, 134.7, 134.5, 133.8, 131.9, 129.9, 129.8, 129.7, 129.4, 129.2, 129.0, 128.6, 122.9, 122.8, 121.6, 121.4, 119.2, 50.5, 41.9, 41.8, 33.0, 30.9, 29.1, 28.7, 27.9, 27.5, 21.8.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}BrN_2O_2$: 537.1178 $[M+H]^+$; found: 537.1179.

4.13. 5-(2-Iodophenyl)-3,3-dimethyl-11-(4-methylbenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3l)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2951, 1671, 1662, 1620, 1603, 1519, 1440, 1403, 1292, 1224, 1178, 1145, 1024, 856, 774, 761 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.14 (d, *J*=7.6 Hz, 1H, ArH), 7.84 (t, *J*=8.8 Hz, 2H, ArH), 7.69 (s, 2H, ArH), 7.58–7.44 (m, 2H, ArH), 7.39 (d, *J*=5.6 Hz, 2H, ArH), 7.27 (s, 1H, ArH), 7.24–7.16 (m, 1H, ArH), 7.04 (t, *J*=7.2 Hz, 1H, ArH), 2.77–2.52 (m, 2H, CH_2), 2.47 (d, *J*=8.4 Hz, 2H, CH_2), 2.39 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 1.12 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 194.7, 193.9, 154.6, 150.4, 150.3, 144.4, 140.8, 133.9, 131.8, 130.7, 130.5, 129.8, 129.7, 129.0, 128.7, 128.7, 128.6, 123.0, 122.8, 121.4, 119.3, 113.8, 97.5, 50.5, 42.2, 33.0, 29.2, 28.8, 28.2, 27.8, 21.8.

HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{26}IN_2O_2$: 585.1039 $[M+H]^+$; found: 585.1038.

4.14. 3,3,8-Trimethyl-11-(4-methylbenzoyl)-5-(*p*-tolyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3m)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2957, 1670, 1664, 1621, 1604, 1524, 1468, 1416, 1370, 1317, 1239, 1152, 1012, 820, 753 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.86 (d, *J*=7.6 Hz, 2H, ArH), 7.56 (d, *J*=8.4 Hz, 1H, ArH), 7.49 (t, *J*=8.4 Hz, 2H, ArH), 7.37 (d, *J*=8.4 Hz, 1H, ArH), 7.28 (s, 2H, ArH), 7.25–7.15 (m, 3H, ArH), 2.71 (s, 2H, CH_2), 2.52 (s, 3H, CH_3), 2.45 (d, *J*=5.6 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.07 (s, 3H, CH_3).

HRMS (ESI) *m*/*z*: calcd for $C_{33}H_{31}N_2O_3$: 487.2386 $[M+H]^+$; found: 487.2384.

4.15. 5-(4-Bromophenyl)-3,3,8-trimethyl-11-(4-methylbenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3n)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2952, 1674, 1671, 1620, 1604, 1514, 1440, 1402, 1336, 1224, 1142, 1012, 848, 846, 776, 763 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.84 (t, *J*=7.2 Hz, 4H, ArH), 7.57 (d, *J*=8.4 Hz, 1H, ArH), 7.41 (d, *J*=8.4 Hz, 1H, ArH), 7.27 (s, 2H, ArH), 7.26–7.18 (m, 3H, ArH), 2.70 (s, 2H, CH_2), 2.46 (d, *J*==5.2 Hz, 2H, CH_2), 2.41 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.08 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 194.8, 193.7, 155.2, 152.5, 150.2, 144.4, 140.5, 136.7, 134.0, 133.9, 131.0, 130.5, 129.7, 129.3, 129.1, 128.7, 124.6, 123.2, 122.8, 118.8, 113.5, 50.4, 42.6, 33.1, 28.5, 27.9, 21.8, 21.5.

HRMS (ESI) *m*/*z*: calcd for $C_{32}H_{28}BrN_2O_2$: 551.1334 $[M+H]^+$; found: 551.1349.

4.16. 5-(4-Chlorophenyl)-11-(4-fluorobenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3o)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2959, 1672, 1619, 1597, 1521, 1505, 1434, 1412, 1305, 1292, 1228, 1147, 1075, 858, 765, 751 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.99 (m, 2H, ArH), 7.72 (d, *J*=7.6 Hz, 1H, ArH), 7.50 (t, *J*=7.2 Hz, 2H, ArH), 7.47–7.34 (m, 3H, ArH), 7.24 (s, 1H, ArH), 7.15 (t, *J*=8.4 Hz, 2H, ArH), 7.05 (t, *J*=7.6 Hz, 1H, ArH), 2.75 (d, *J*=4.4 Hz, 2H, CH_2), 2.49 (d, *J*=6.4 Hz, 2H, CH_2), 1.10 (s, 3H, CH_3), 1.08 (s, 3H, CH_3).

HRMS (ESI) *m*/*z*: calcd for $C_{30}H_{23}ClFN_2O_2$: 497.1432 $[M+H]^+$; found: 497.1431.

4.17. 5-(4-Bromophenyl)-11-(4-fluorobenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3p)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2959, 1671, 1619, 1597, 1522, 1505, 1434, 1412, 1304, 1292, 1224, 1147, 1075, 859, 765, 755 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm) :8.06–7.89 (m, 2H, ArH), 7.85 (t, *J*=7.6 Hz, 2H, ArH), 7.67 (d, *J*=8.0 Hz, 1H, ArH), 7.49–7.32 (m, 4H, ArH), 7.14 (t, *J*=7.6 Hz, 1H, ArH), 7.09–6.99 (m, 2H, ArH), 2.72 (s, 2H, CH_2), 2.49 (d, *J*=7.2 Hz, 2H, CH_2), 1.10 (s, 6H, CH_3). HRMS (ESI) *m*/*z*: calcd for $C_{30}H_{23}BrF_2N_2O_2$: 541.0927 $[M+H]^+$; found: 541.0901.

4.18. 11-(4-Fluorobenzoyl)-5-(2-iodophenyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3q)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2957, 1670, 1614, 1597, 1524, 1505, 1434, 1416, 1304, 1290, 1224, 1147, 1075, 859, 765, 748 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 8.15 (d, *J*=7.6 Hz, 1H, ArH), 8.03–7.87 (m, 2H, ArH), 7.79–7.63 (m, 2H, ArH), 7.61–7.45 (m, 2H, ArH), 7.45–7.36 (m, 2H, ArH), 7.20–7.10 (m, 1H, ArH), 7.06 (t, *J*=8.0 Hz, 1H, ArH), 6.94 (d, *J*=8.0 Hz, 1H, ArH), 2.76–2.55 (m, 2H, CH_2), 2.55–2.42 (m, 2H, CH_2), 1.15 (s, 3H, CH_3), 1.13 (s, 3H, CH_3).

HRMS (ESI) *m*/*z*: calcd for $C_{30}H_{23}FIN_2O_2$: 589.0788 $[M+H]^+$; found: 589.0781.

4.19. 11-(4-Chlorobenzoyl)-3,3-dimethyl-5-(*p*-tolyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3r)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2950, 1676, 1664, 1623, 1604, 1513, 1440, 1404, 1359, 1304, 1231, 1176, 1104, 1012, 846, 776 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.90 (d, *J*=8.0 Hz, 2H, ArH), 7.69 (d, *J*=8.0 Hz, 1H, ArH), 7.50 (t, *J*=8.4 Hz, 2H, ArH), 7.48–7.42 (m, 3H, ArH), 7.41–7.34 (m, 2H, ArH), 7.24 (d, *J*=7.6 Hz, 1H, ArH), 7.04 (t, *J*=7.6 Hz, 1H, ArH), 2.73 (s, 2H, CH_2), 2.53 (s, 3H, CH_3), 2.47 (d, *J*=7.2 Hz, 2H, CH_2), 1.09 (s, 3H, CH_3), 1.07 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (*δ* ppm): 194.1, 194.0, 155.8, 154.6, 151.3, 140.6, 139.9, 135.1, 134.8, 131.5, 131.3, 129.9, 129.4, 129.1, 127.1, 126.9, 123.1, 122.5, 121.4, 119.5, 113.3, 50.3, 42.5, 33.2, 28.4, 28.0, 21.5.

HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{38}NO_8$: 528.2597 $[M+H]^+$; found: 528.2546.

4.20. 5-(4-Bromophenyl)-11-(4-chlorobenzoyl)-3,3-dimethyl-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3s)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2952, 1674, 1664, 1620, 1604, 1514, 1440, 1412, 1354, 1304, 1230, 1176, 1104, 1012, 864, 776 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.93–7.79 (m, 4H, ArH), 7.68 (d, *J*=8.0 Hz, 1H, ArH), 7.44 (d, *J*=8.4 Hz, 3H, ArH), 7.41–7.36 (m, 2H, ArH), 7.25 (s, 1H, ArH), 7.06 (t, *J*=7.6 Hz, 1H, ArH), 2.71 (s, 2H, CH_2), 2.47 (d, *J*=8.0 Hz, 2H, CH_2), 1.10 (s, 3H, CH_3), 1.08 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (*δ* ppm): 193.9, 193.8, 155.4, 154.5, 150.6, 140.0, 139.8, 136.5, 134.6, 134.1, 134.0, 129.8, 129.4, 129.2, 129.0, 124.8, 123.3, 122.6, 121.7, 119.4, 113.5, 50.3, 42.5, 33.2, 28.4, 27.9.

HRMS (ESI) *m*/*z*: calcd for $C_{30}H_{23}BrClN_2O_2$: 557.0626 $[M+H]^+$; found: 557.0624.

4.21. 5-(4-Chlorophenyl)-11-(4-methylbenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3t)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2952, 1674, 1668, 1619, 1604, 1513, 1440, 1404, 1367, 1304, 1224, 1176, 1144, 1012, 846, 776 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.87 (d, *J*=8.0 Hz, 2H, ArH), 7.75–7.58 (m, 3H, ArH), 7.53–7.43 (m, 2H, ArH), 7.44–7.32 (m, 2H, ArH), 7.27 (s, 1H, ArH), 7.25 (s, 1H, ArH), 7.03 (t, *J*=7.6 Hz, 1H, ArH), 2.86 (m, 2H, CH_2), 2.61 (m, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.17 (t, *J*=7.6 Hz, 2H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$) (*δ* ppm): 194.8, 193.8, 152.1, 144.5, 141.2, 136.6, 136.1, 133.8, 131.0, 130.8, 129.7, 129.1, 129.0, 128.8, 128.7, 123.4, 122.9, 122.8, 121.5, 119.2, 114.6, 36.9, 29.2, 21.8, 21.5.

HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{22}ClN_2O_2$: 465.1370 $[M+H]^+$; found: 465.1374.

4.22. 5-(4-Bromophenyl)-11-(4-methylbenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3u)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2963, 1667, 1638, 1619, 1604, 1520, 1505, 1413, 1340, 1287, 1228, 1174, 1069, 1008, 839, 762 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm) 7.93–7.77 (m, 4H, ArH), 7.66 (d, *J*=8.0 Hz, 1H, ArH), 7.46 (d, *J*=7.6 Hz, 1H, ArH), 7.44–7.35 (m, 2H, ArH), 7.33–7.28 (m, 2H, ArH), 7.25 (s, 1H, ArH), 7.02 (t, *J*=7.6 Hz, 1H, ArH), 2.85 (m, 2H, CH_2), 2.60 (m, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.25–1.94 (m, 2H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$) (*δ* ppm): 194.7, 193.8, 155.2, 154.5, 152.0, 144.5, 141.2, 136.7, 134.0, 133.8, 129.7, 129.3, 129.1, 128.8, 124.7, 123.4, 122.9, 122.8, 121.5, 119.2, 114.6, 36.9, 29.2, 21.8, 21.5.

HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{22}BrN_2O_2$: 509.0865 $[M+H]^+$; found: 509.0848.

4.23. 5-(4-Bromophenyl)-8-methyl-11-(4-methylbenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3v)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2950, 1672, 1668, 1605, 1520, 1487, 1467, 1409, 1327, 1285, 1237, 1199, 1124, 1045, 856, 830, 773 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.95–7.75 (m, 4H, ArH), 7.55 (d, *J*=8.0 Hz, 1H, ArH), 7.42 (d, *J*=8.0 Hz, 1H, ArH), 7.30 (s, 2H, ArH), 7.26–7.15 (m, 3H, ArH), 2.84 (d, *J*=5.6 Hz, 2H, CH_2), 2.60 (d, *J*=6.4 Hz, 2H, CH_2), 2.41 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 2.17 (s, 2H, CH_2).

HRMS (ESI) *m*/*z*: calcd for $C_{30}H_{24}BrN_2O_2$: 523.1016 $[M+H]^+$; found: 523.0997.

4.24. 5-(4-Fluorophenyl)-11-(4-methoxybenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3w)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2957, 1670, 1600, 1573, 1521, 1510, 1442, 1409, 1275, 1228, 1169, 857, 763 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.95 (d, *J*=8.0 Hz, 2H, ArH), 7.68 (d, *J*=8.0 Hz, 1H, ArH), 7.52 (s, 1H, ArH), 7.46 (d, *J*=7.6 Hz, 1H, ArH), 7.40 (s, 4H, ArH), 7.03 (t, *J*=7.6 Hz, 1H, ArH), 6.95 (d, *J*=8.4 Hz, 1H, ArH), 3.86 (s, 3H, OCH_3), 2.86 (d, *J*=5.6 Hz, 2H, CH_2), 2.62 (d, *J*=8.0 Hz, 2H, CH_2), 2.31–2.07 (m, 2H, CH_2).

HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{22}FN_2O_3$: 465.1614 $[M+H]^+$; found: 465.1613.

4.25. 5-(4-Chlorophenyl)-11-(4-methoxybenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3x)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2957, 1672, 1600, 1573, 1521, 1514, 1442, 1400, 1276, 1230, 1169, 857, 768 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.94 (d, *J*=8.4 Hz, 2H), 7.67 (t, *J*=7.2 Hz, 3H), 7.47 (t, *J*=7.2 Hz, 2H), 7.43–7.31 (m, 2H), 7.03 (t, *J*=7.2 Hz, 1H), 6.94 (d, *J*=8.4 Hz, 2H), 3.85 (s, 3H), 2.86 (s, 2H), 2.62 (d, *J*=8.0 Hz, 2H), 2.17 (s, 2H).

HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{22}ClN_2O_3$: 481.1319 $[M+H]^+$; found: 481.1330.

4.26. 5-(4-Bromophenyl)-11-(4-methoxybenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3y)

Yellow solid; mp: >300 °C.

IR (KBr, *v*, cm^{-1}): 2957, 1670, 1609, 1573, 1525, 1520, 1442, 1407, 1268, 1232, 1172, 855, 768 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.94 (d, *J*=8.4 Hz, 2H, ArH), 7.82–7.56 (m, 3H, ArH), 7.54–7.43 (m, 2H, ArH), 7.42–7.30 (m, 2H,

ArH), 7.03 (t, J=7.6 Hz, 1H, ArH), 6.94 (d, J=8.8 Hz, 2H, ArH), 3.85 (s, 3H, OCH_3), 2.86 (m, 2H, CH_2), 2.62 (m, 2H, CH_2), 2.39–1.95 (m, 2H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 193.7, 193.7, 163.9, 155.1, 152.0, 136.6, 134.0, 133.8, 131.0, 129.4, 129.3, 129.1, 124.7, 122.98, 122.8, 121.6, 119.2, 114.6, 114.3, 55.5, 37.0, 32.9, 29.2, 21.5.

HRMS (ESI) m/z: calcd for $C_{29}H_{22}BrN_2O_3$: 525.0808 $[M+H]^+$; found: 525.0798.

4.27. 5-(2-Iodophenyl)-11-(4-methoxybenzoyl)-2,3,4,5-tetrahydro-1*H*-indolo[2,3-*b*]quinolin-1-one (3z)

Yellow solid; mp: >300 °C.

IR (KBr, ν, cm^{-1}): 2957, 1672, 1610, 1573, 1527, 1520, 1486, 1407, 1258, 1232, 1172, 855, 744 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.14 (d, J=7.2 Hz, 1H, ArH), 7.94 (s, 2H, ArH), 7.77–7.60 (m, 2H, ArH), 7.51 (s, 2H, ArH), 7.39 (d, J=7.2 Hz, 2H, ArH), 7.05 (d, J=7.2 Hz, 1H, ArH), 6.94 (s, 2H, ArH), 3.85 (s, 3H, OCH_3), 2.78 (s, 2H, CH_2), 2.64 (s, 2H, CH_2), 2.18 (s, 2H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 194.0, 193.8, 163.9, 154.7, 154.3, 152.1, 141.1, 141.0, 140.7, 131.8, 131.7, 131.0, 130.7, 129.4, 129.0, 128.8, 128.6, 122.9, 121.4, 119.3, 114.4, 114.2, 97.5, 55.5, 37.1, 31.0, 28.7, 21.6.

HRMS (ESI) m/z: calcd for $C_{29}H_{22}IN_2O_3$: 573.0675 $[M+H]^+$; found: 573.0663.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.11.022.

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20. Crystal data for **3w**: $C_{32}H_{28}FN_3O_4$, crystal dimension 0.42×0.18×0.14 mm, Monoclinic, space group Cc, a=14.4352(13) Å, b=26.027(3) Å, c=9.3423(8) Å, α=90°, β=129.925(2)°, γ=90°, V=2691.7(4) Å^3, M_r=537.57, Z=4, D_c=1.327 Mg/m^3, γ=0.71073 Å, μ(Mo K_α)=0.093 mm^{-1}, F(000)=1128, R=0.0631, wR_2=0.1535, S=1.044, largest diff. Peak and hole: 0.346 and −0.245 e/Å^3
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