DOI 10.1007/s10593-016-1856-0

Chemistry of Heterocyclic Compounds **2016**, *52*(3), 200–205

General and efficient one-pot synthesis of *N*-substituted 7-bromo-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-ones

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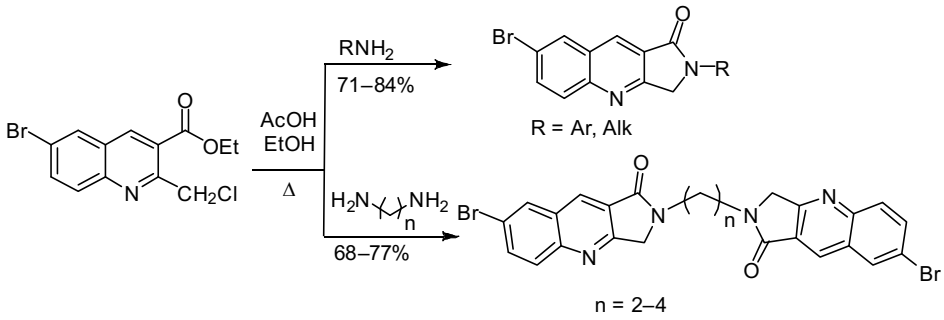
Published in Khimiya Geterotsiklicheskikh Soedinenii, 2016, *52*(3), 200–205

Submitted January 29, 2016
Accepted March 31, 2016



A simple and general synthesis of a series of quinoline-based isoindolin-l-ones, namely *N*-substituted 7-bromo-2,3-dihydro-1*H*-pyrrolo-[3,4-*b*]quinolin-1-ones through a one-pot reaction of ethyl 6-bromo-2-(chloromethyl)quinoline-3-carboxylate with various amines in refluxing EtOH–AcOH (v/v, 10:1) solvent system was described. A mechanism involving consecutive Williamson-type reaction of the 2-chloromethyl group with amine followed by intramolecular C–N bond cyclization process is proposed.

Keywords: amine, isoindolin-l-one, quinoline, intramolecular cyclization, Williamson-type reaction.

Isoindolin-1-ones constitute an exceptional class of structural motifs which have been found widely present in natural products like cichorine[1] and vitedoamine,[2] and also in pharmacologically important synthetic molecules such as indoprofen[3] and lenalidomide[4] (Fig. 1). Moreover, this benzolactam system is also used as important synthon to access various drugs and natural products.[5–7] Consequently attention has been increasingly paid to the use of the isoindolin-1-one molecular template for further modification and functionalization by both organic and medicinal chemists aiming to find new applications for these compounds.[8–10]

On the other hand, functionalized quinolines and their hetero-fused analogs represent an important class of organic molecules that have attracted a great deal of attention from synthetic as well as medicinal chemists.[11,12] It is well established that bioactive heterocyclic compounds when linked with quinoline moiety in fused or bonded forms usually results in new hybrids with potent pharmacological properties.[13,14] For example, Guo et al. have recently found that rhodanine derivatives upon bearing a quinoline moiety are interesting scaffolds for the development of novel Gram-positive antibacterial agents.[15] Very recently, a review concerning the chemistry and biological activity of heterocycle-fused quinolinone derivatives has been published by Shiro et al.[16]

Thus, in light of the combination principles for drug design,[17] it would be of synthetic importance to construct

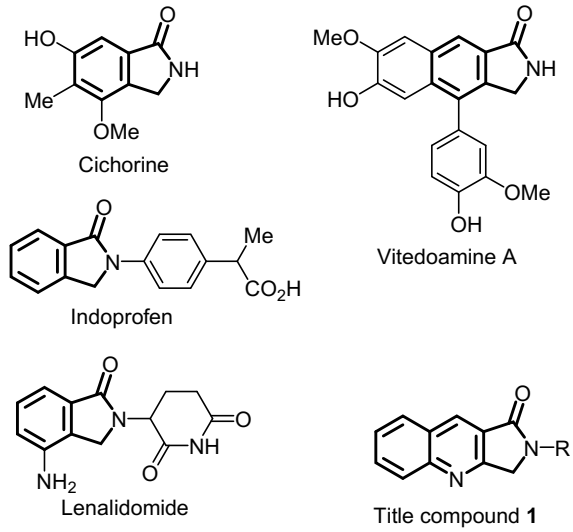
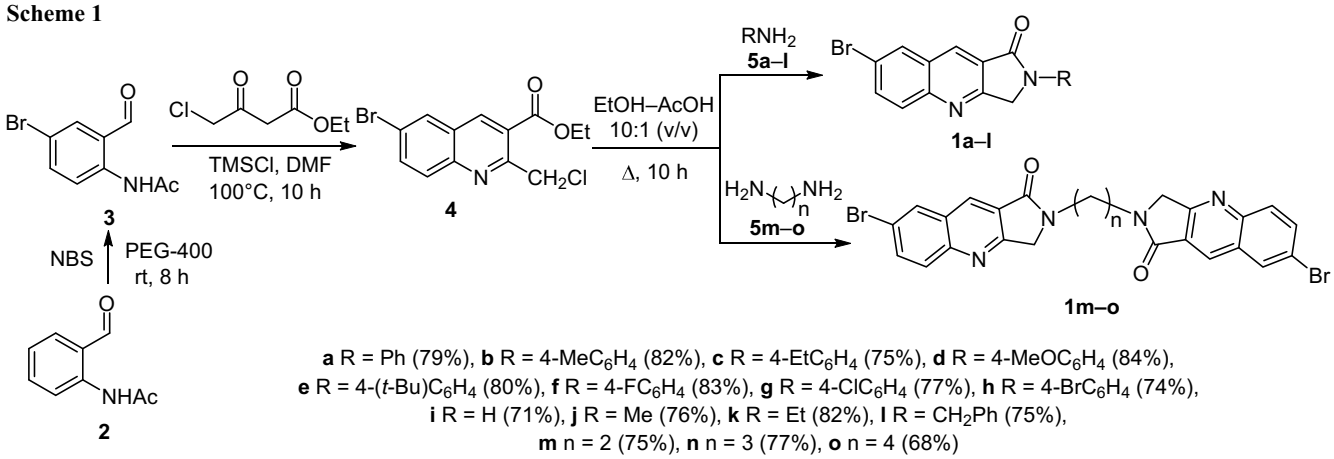


Figure 1. Structures of isoindolin-1-one-containing molecules and the title compound **1**.

Scheme 1



a R = Ph (79%), **b** R = 4-MeC_6H_4 (82%), **c** R = 4-EtC_6H_4 (75%), **d** R = 4-$MeOC_6H_4$ (84%), **e** R = 4-(*t*-Bu)C_6H_4 (80%), **f** R = 4-FC_6H_4 (83%), **g** R = 4-ClC_6H_4 (77%), **h** R = 4-BrC_6H_4 (74%), **i** R = H (71%), **j** R = Me (76%), **k** R = Et (82%), **l** R = CH_2Ph (75%), **m** n = 2 (75%), **n** n = 3 (77%), **o** n = 4 (68%)

quinoline-based isoindolin-l-one derivatives **1** as shown in Figure 1, wherein the benzene ring is replaced by quinoline moiety. A literature survey revealed that there are several examples reported concerning the synthesis of quinoline-based isoindolin-l-one derivatives.[18–20] For example, Anzini et al. previously reported the synthesis of 4-phenyl-quinoline-based isoindolin-l-one through the reaction of ethyl 6-chloro-2-(chloromethyl)-4-phenylquinoline-3-carboxylate with methylamine.[18] In this regard, Cappelli et al. described this type of synthesis involving the reaction of ethyl 2-chloromethylquinoline-3-carboxylate with aniline or 4-chloroaniline.[19] Recently, Bose et al. also reported a similar synthesis by using both *S*-phenylalaninol and *R*-phenethylamine as substrates in refluxing acetonitrile.[20] Although some achievements have been made, these reports are of individual and scattered syntheses, and no efforts have been made to develop a general synthetic approach. As such, the development of a more general method towards such compounds is of significant interest. Thus, we wish to report a general synthesis of quinoline-based isoindolin-l-one, namely, *N*-substituted 7-bromo-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-ones **1** through the one-pot reaction of ethyl 6-chloro-2-(chloromethyl)-quinoline-3-carboxylate with various amines.

We have been engaged in exploring the reactivity and synthetic applications of 2-halomethylquinoline-3-carboxaldehyde derivatives as an ideal starting material for the flexible synthesis of a large range of quinoline derivatives. In recent papers we have reported on the reaction of 2-halomethylquinoline with phenols,[21,22] salicylaldehydes,[23] aromatic aldehydes,[24] and quinolin-8-ols[25] for the synthesis of novel heterocycle-containing quinolines. Building on the evolving expertise, we envisaged that reacting ethyl 6-bromo-2-(chloromethyl)quinoline-3-carboxylate (**4**) with various amines **5** might produce the corresponding quinoline-based isoindolin-l-one derivatives through a cascade Williamson-type condensation reaction and subsequent intramolecular C–N bond cyclization in a single synthetic operation. Thus, according to that the first stage in this strategy involved the preparation of the substrate **4**, which could be easily obtained *via* Friedländer annulation reaction of *N*-(4-bromo-2-formylphenyl)acetamide (**3**) with ethyl 4-chloro-3-oxobutanoate according to the method described in the literature,[26] using chlorotrimethylsilane (TMSCl) as a promoter and water-acceptor agent (Scheme 1). In our synthesis, the C-6 position of the quinoline ring was occupied by a derivatizable bromo group in consideration of the fact that the functional group could provide ample opportunity for further synthetic manipulation, for example, for cross-coupling reactions, and thus would make the targeted products particularly appealing.

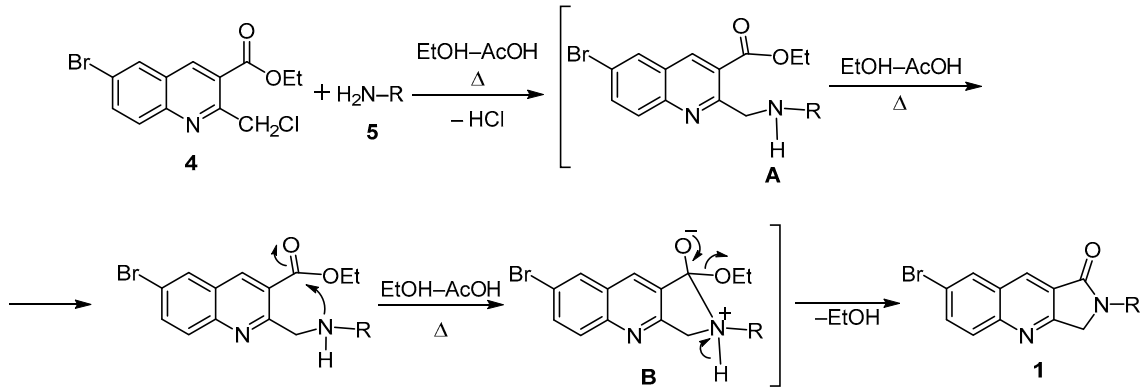
Subsequently, our attention was transferred to the reaction of ethyl 6-bromo-2-(chloromethyl)quinoline-3-carboxylate (**4**) with a series of aromatic amines for building the desired isoindolin-l-one system. At this stage, we first took up the synthesis of 7-bromo-2-phenyl-2,3-dihydro-1*H*-pyrrolo-[3,4-*b*]quinolin-1-one (**1a**). Our initial investigation was conducted using ethanol as solvent in accordance with the reaction conditions described in the literature.[19] However, the result was less satisfactory, and the expected pyrrolo-[3,4-*b*]quinolin-1-one **1a** was obtained in a moderate yield of 61% (Table 1, entry 1). Accordingly, to further improve the yield of this synthetic approach, various solvents were

Table 1. Reaction conditions and yields of *N*-phenylpyrrolo[3,4-*b*]quinolin-1-one **1a***

Entry	Solvent	Temperature, °C	Time, h	Yield, %
1	EtOH	Δ	24	61
2	MeOH	Δ	24	50
3	$CHCl_3$	Δ	24	42
4	DMF	85	24	33
5	Dioxane	85	24	29
6	H_2O	Δ	24	0
7	Solvent-free	rt	3	0
8	EtOH–AcOH (20:1, v/v)	Δ	10	67
9	EtOH–AcOH (15:1, v/v)	Δ	10	74
10	**EtOH–AcOH (10:1, v/v)**	Δ	**10**	**79**
11	EtOH–AcOH (5:1, v/v)	Δ	12	67
12	EtOH–AcOH (2:1, v/v)	Δ	24	44

* Reaction conditions: compound **4** (0.5 mmol), aniline **5a** (0.5 mmol), solvent (5 ml).

Scheme 2



applied to promote this transformation. The results summarized in Table 1 show that the choice of the solvent was critical for this reaction. These attempts using MeOH, $CHCl_3$, DMF, THF, and dioxane as solvent were unfruitful, and no further improvement of the yields was observed (entries 2–5). Upon switching the solvent to H_2O or solvent-free conditions, no desired product was detected (entries 6, 7), and the starting materials were recovered unchanged. After many attempts, we were delight to find that the use of EtOH–AcOH solvent system described in the literature[27] afforded a significant amelioration in our synthesis (entry 9), and the most striking yield (79%) was obtained when the volume ratio of EtOH–AcOH was 10:1 (entry 10). Due to the good yield obtained and in order to retain the simplicity of the procedure, no further optimization in the reaction conditions was necessary and the above-mentioned conditions were chosen for the following work.

Thereafter, we investigated the scope and limitations by extending the reaction to various aromatic amines **5b**–**h** for building differently substituted analogs as shown in Scheme 1. Our results demonstrated that the reaction proceeded smoothly with aromatic amines and the expected products **1b**–**h** were obtained in good yields ranging from 74 to 84%. Moreover, in this series of reactions the effect of substitution groups is not very strong; both the electron-donating (*e.g.*, Me, Et, OMe, *t*-Bu) and slightly electron-withdrawing groups (*e.g.*, F, Cl, Br) worked well, showing little distinction. However, it is noteworthy that when a strong electron-withdrawing groups such as NO_2 and CN were present, the reaction scarcely proceeded and the desired product was detected in negligible amount that did not warrant isolation. A possible reason is that the presence of the strong electron-withdrawing group might render the aromatic amines highly electron-deficient and thus retard the reaction process.

Further, due to the simplicity of the one-pot synthesis, we decided to extend its scope to some aliphatic amines **5i**–**l** and aliphatic diamines **5m**–**o** with the aim of diversifying our work on new quinoline-based isoindolin-l-one derivatives. To our delight, these amines were equally amenable to the reaction process without any experimental difficulties, successfully furnishing the corresponding pyrrolo-[3,4-*b*]quinolin-1-ones **1i**–**o** in comparable yields of 68–82% (Scheme 1).

To the best of our knowledge, all the newly synthesized quinoline-based isoindolin-l-ones **1a**–**o** have never been reported and their structures were easily confirmed by their spectroscopic and analytical data, which were in good agreement with the compounds expected (see Experimenta). The IR spectrum of compound **1a** exhibited the disappearance of the ester carbonyl group at 1711 cm^{-1}, and the appearance of the lactam C=O stretching frequency at a decreased wave number of 1685 cm^{-1}, which were clear evidence for cyclization having occurred. The main feature of the ^1H NMR spectrum of compound **1a** was the presence of a singlet sharp line at 5.65 ppm, readily recognizable as arising from methylene protons, supporting the signal of its ^{13}C NMR spectrum at 51.7 ppm. Moreover, the presence of 9 aromatic protons in the range of the aromatic region of 7.51–9.55 ppm exactly matches its structure as well. Further, the structure assigned to compound **1a** was fully supported by its elemental analysis, which established its molecular formula in accordance with the suggested molecular structure. The other synthesized compounds exhibited similar spectral characteristics, except the substituents, which exhibited characteristic signals with appropriate chemical shifts.

On the basis of the obtained results, a mechanistic proposal portraying the probable sequence of events for the formation of the title compounds **1** is outlined in Scheme 2. The one-pot reaction might start with the nucleophilic attack of amine **5** to 2-(chloromethyl)quinoline **4** to give the intermediate **A**, which undergoes subsequent intramolecular nucleophilic cyclization in the presence of acetic acid with participation of the nitrogen atom and the ester C=O group to form a five-membered cyclic system **B**. At this point, we reason that the presence of the catalytic amount of acetic acid might play an important role in pushing the cyclization reaction forward, though the detailed pathway remains to be elucidated. Importantly, it is pertinent to note that this type of acetic acid-promoted intramolecular cyclization has been already reported by Hu et al.[27,28] But in both literatures no detailed mechanistic studies were carried out to explain the catalytic activity of acetic acid, and at the current stage there is no consensus of opinion regarding the role of acetic acid. After this cyclization, the elimination of an equivalent of EtOH led to the formation of pyrrolo[3,4-*b*]quinolin-1-one ring. The whole reactions

occurred effectively in one pot. It is worthy to mention that an example that is particularly relevant to the present discussion is described in the literature,[29] wherein 7-isopropyl-1-methylazulen-4-amine undergoes intramolecular ring annulation reactions with ester group at position 3 to yield tricyclic δ-lactams with the elimination of ethanol without the need for a catalyst.

In summary, we have provided an easy access to biologically intriguing quinoline-based isoindolin-l-ones in one-pot synthesis in relatively environmentally benign EtOH–AcOH solvent system. These newly synthesized compounds would likely possess significant biological activities and could also be potentially applied as useful synthetic building blocks for the development of biologically and pharmaceutically important drugs. Currently, the studies concerning their application are underway.

Experimental

IR spectra were recorded on a Shimadzu FTIR-8400S infrared spectrophotometer using samples in thin layer. ^{1}H and ^{13}C NMR spectra were recorded on a Brucker Avance II 400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ using TMS as internal standard. (The abbreviation H Quino corresponds to the protons of the quinoline ring.) Mass spectra were obtained on a Finnigan-MAT 8430 mass spectrometer (electron ionization, 70 eV). The elemental analyses were performed using an Elementar Vario EL-III element analyzer. The progress of reactions was monitored by thin layer chromatography (TLC) on silica gel GF254 using petroleum ether–EtOAc, 4:1, as eluent. Melting points (uncorrected) were determined by using WRS-1B melting points apparatus. All chemicals (AR graded) were commercially available and used without further purification.

Synthesis of ethyl 6-bromo-2-(chloromethyl)quinoline-3-carboxylate (4). *N*-(4-Bromo-2-formylphenyl)acetamide (**3**) (4.84 g, 20 mmol) and ethyl 4-chloro-3-oxobutanoate (3.3 g, 20 mmol) were placed in a 50-ml reaction kettle and dissolved in DMF (20 ml). To the solution thus obtained, TMSCl (8.7 g, 80 mmol) was carefully added dropwise. The kettle was sealed and heated at 100°C for 10 h. After cooling, the kettle was opened and the mixture was poured into H_2O (1000 ml) and the mixture thus obtained was allowed to stand at room temperature in ultrasonic bath for 1 h. The resulting precipitate was filtered off and purified by column chromatography on silica gel using hexane–EtOAc, 10:1, as eluent, affording the pure product **4** in 64% yield. Mp 127–130°C. IR spectrum, ν, cm^{-1}: 1711 (C=O), 1609, 1583, 1558, 1478, 1440, 1072. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.48 (3H, t, *J* = 7.2, $OCH_2C\underline{H}_3$); 4.50 (2H, q, *J* = 7.2, $OC\underline{H}_2CH_3$); 5.28 (2H, s, CH_2Cl); 7.91 (1H, d, *J* = 8.4, H Quino); 8.05 (1H, d, *J* = 8.4, H Quino); 8.10 (1H, s, H Quino); 8.75 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 14.2; 45.9; 62.2; 119.4; 122.1; 124.1; 127.8, 130.4; 130.6; 135.7; 140.1; 156.0; 165.1. Found, %: C 47.75; H 3.62; N 4.11. $C_{13}H_{11}BrClNO_2$. Calculated, %: C 47.52; H 3.37; N 4.26.

Synthesis of 7-bromo-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]-quinolin-1-ones 1a–o (General method). A mixture of ethyl 6-bromo-2-(chloromethyl)quinoline-3-carboxylate (**4**) (0.328 g, 1.0 mmol) and the respective amine **5a**–**l** (1.0 mmol) or diamine **5m**–**o** (0.5 mmol) in EtOH–AcOH (10 ml, 10:1 v/v) solvent system was stirred at refluxing temperature for 10 h. After the reaction was complete (monitored by TLC), the reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel using hexane–EtOAc, 9:1, as eluent, giving the pure products **1a**–**o**.

7-Bromo-2-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one (1a). Mp 252–254°C. IR spectrum, ν, cm^{-1}: 3053, 2939, 1685 (C=O), 1609 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.65 (2H, s, CH_2); 7.51–7.64 (5H, m, H Ph); 8.36 (1H, d, *J* = 8.0, H Quino); 8.46 (1H, d, *J* = 8.0, H Quino); 8.71 (1H, s, H Quino); 9.55 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 51.7; 121.5; 123.1; 126.3; 127.1; 128.9; 129.6; 129.7; 132.9; 134.7; 137.4; 141.8; 142.9; 156.6; 164.0. Mass spectrum, *m*/*z* (I_{rel}, %): 340 $[M+H]^+$ (100). Found, %: C 60.47; H 3.10; N 8.45. $C_{17}H_{11}BrN_2O$. Calculated, %: C 60.20; H 3.27; N 8.26.

7-Bromo-2-(4-methylphenyl)-2,3-dihydro-1*H*-pyrrolo-[3,4-*b*]quinolin-1-one (1b). Mp 266–267°C. IR spectrum, ν, cm^{-1}: 3044, 2964, 1679 (C=O), 1619 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.15 (3H, s, CH_3); 5.31 (2H, s, CH_2); 7.10 (2H, d, *J* = 7.6, H Ar); 7.21 (2H, d, *J* = 7.6, H Ar); 8.07 (1H, d, *J* = 8.4, H Quino); 8.42 (1H, s, H Quino); 8.47 (1H, d, *J* = 8.4, H Quino); 9.24 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 18.9; 51.7; 121.6; 123.0; 126.9; 129.2; 129.3; 130.0; 131.7; 136.9; 138.6; 138.9; 140.2; 142.7; 156.5; 163.9. Mass spectrum, *m*/*z* (I_{rel}, %): 354 $[M+H]^+$ (100). Found, %: C 60.99; H 3.88; N 8.11. $C_{18}H_{13}BrN_2O$. Calculated, %: C 61.21; H 3.71; N 7.93.

7-Bromo-2-(4-ethylphenyl)-2,3-dihydro-1*H*-pyrrolo-[3,4-*b*]quinolin-1-one (1c). Mp 248–250°C. IR spectrum, ν, cm^{-1}: 3046, 2960, 1681 (C=O), 1613 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.08 (3H, t, *J* = 7.6, $C\underline{H}_3CH_2$); 2.53 (2H, q, *J* = 7.6, $CH_3C\underline{H}_2$); 5.39 (2H, s, CH_2); 7.20 (2H, d, *J* = 7.6, H Ar); 7.30 (2H, d, *J* = 7.6, H Ar); 8.12 (1H, d, *J* = 8.4, H Quino); 8.23 (1H, d, *J* = 8.4, H Quino); 8.48 (1H, s, H Quino); 9.31 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 13.4; 27.7; 51.8; 110.0; 121.4; 123.2; 126.1; 127.0; 129.0; 129.6; 131.9; 132.7; 137.2; 141.6; 142.7; 146.7; 156.7; 164.0. Mass spectrum, *m*/*z* (I_{rel}, %): 368 $[M+H]^+$ (100). Found, %: C 62.32; H 3.97; N 7.75. $C_{19}H_{15}BrN_2O$. Calculated, %: C 62.14; H 4.12; N 7.63.

7-Bromo-2-(4-methoxyphenyl)-2,3-dihydro-1*H*-pyrrolo-[3,4-*b*]quinolin-1-one (1d). Mp 269–271°C. IR spectrum, ν, cm^{-1}: 3037, 2984, 1671 (C=O), 1618 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.94 (3H, s, OCH_3); 5.51 (2H, s, CH_2); 7.11 (2H, d, *J* = 7.6, H Ar); 7.54 (2H, d, *J* = 7.6, H Ar); 8.24 (1H, d, *J* = 8.4, H Quino); 8.35 (1H, d, *J* = 8.4, H Quino); 8.61 (1H, s, H Quino); 9.43 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 56.0 (2C); 116.1; 122.2; 122.6; 125.9; 128.8; 130.5; 131.4; 133.7 (2C); 138.1; 138.3; 142.6; 143.6; 157.3; 159.2; 164.3. Mass spectrum, *m*/*z* (I_{rel}, %): 370 $[M+H]^+$ (100). Found, %: C 58.68; H 3.63; N 7.44. $C_{18}H_{13}BrN_2O_2$. Calculated, %: C 58.56; H 3.55; N 7.59.

7-Bromo-2-[4-(*tert*-butyl)phenyl]-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one (1e). Mp 255–257°C. IR spectrum, ν, cm^{-1}: 3042, 2945, 1674 (C=O), 1614 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.37 (9H, s, $(CH_3)_3C$); 5.60 (2H, s, CH_2); 7.52 (2H, d, *J* = 7.6, H Ar); 7.63 (2H, d, *J* = 7.2, H Ar); 8.32 (1H, d, *J* = 8.4, H Quino); 8.43 (1H, d, *J* = 8.4, H Quino); 8.68 (1H, s, H Quino); 9.51 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 29.6; 34.2; 52.0; 110.0; 121.6; 122.9; 126.3; 126.8; 127.2; 129.8; 131.8; 132.9; 137.4; 141.8; 142.8; 153.7; 156.8; 164.5. Mass spectrum, *m*/*z* (I_{rel}, %): 396 $[M+H]^+$ (19), 260 $[M–Br–(CH_3)_3C]^+$ (100). Found, %: C 64.00; H 4.89; N 6.91. $C_{21}H_{19}BrN_2O$. Calculated, %: C 63.81; H 4.84; N 7.09.

7-Bromo-2-(4-fluorophenyl)-2,3-dihydro-1*H*-pyrrolo-[3,4-*b*]quinolin-1-one (1f). Mp 234–236°C. IR spectrum, ν, cm^{-1}: 3034, 2895, 1666 (C=O), 1611 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.57 (2H, s, CH_2); 7.20 (2H, t, *J* = 7.6, H Ar); 7.61 (2H, t, *J* = 7.6, H Ar); 8.29 (1H, d, *J* = 8.4, H Quino); 8.40 (1H, d, *J* = 8.4, H Quino); 8.66 (1H, s, H Quino); 9.49 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 51.7; 110.0; 116.4; 116.6; 121.5; 124.8; 125.2; 125.3; 126.3; 126.9; 129.7; 132.8; 137.4; 141.8; 142.9; 156.5; 163.9. Mass spectrum, *m*/*z* (I_{rel}, %): 358 $[M+H]^+$ (100). Found, %: C 57.42; H 3.12; N 7.92. $C_{17}H_{10}BrFN_2O$. Calculated, %: C 57.17; H 2.82; N 7.84.

7-Bromo-2-(4-chlorophenyl)-2,3-dihydro-1*H*-pyrrolo-[3,4-*b*]quinolin-1-one (1g). Mp 223–225°C. IR spectrum, ν, cm^{-1}: 3035, 2938, 1681 (C=O), 1609 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.66 (2H, s, CH_2); 7.57 (2H, d, *J* = 8.0, H Ar); 7.68 (2H, d, *J* = 7.6, H Ar); 8.37 (1H, d, *J* = 8.4, H Quino); 8.48 (1H, d, *J* = 8.4, H Quino); 8.73 (1H, s, H Quino); 9.57 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 51.2; 112.8; 115.6; 121.6; 123.8; 126.4; 126.9; 129.8; 132.9 (2C); 133.5; 135.0; 137.5; 141.9; 142.9; 156.4; 163.8. Mass spectrum, *m*/*z* (I_{rel}, %): 376 $[M+H]^+$ (30), 374 $[M+H]^+$ (100). Found, %: C 54.40; H 2.60; N 7.64. $C_{17}H_{10}BrClN_2O$. Calculated, %: C 54.65; H 2.70; N 7.50.

7-Bromo-2-(4-bromophenyl)-2,3-dihydro-1*H*-pyrrolo-[3,4-*b*]quinolin-1-one (1h). Mp 240–241°C. IR spectrum, ν, cm^{-1}: 3028, 2946, 1672 (C=O), 1608 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.65 (2H, s, CH_2); 7.61 (2H, d, *J* = 8.4, H Ar); 7.72 (2H, d, *J* = 8.0, H Ar); 8.37 (1H, d, *J* = 8.8, H Quino); 8.48 (1H, d, *J* = 8.4, H Quino); 8.73 (1H, s, H Quino); 9.56 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 51.2; 111.3; 113.6; 121.7; 122.5; 124.0; 126.5; 127.1; 129.9; 133.0; 133.1; 134.2; 137.6; 142.0; 143.1; 156.5; 163.8. Mass spectrum, *m*/*z* (I_{rel}, %): 419 $[M+H]^+$ (100), 417 $[M+H]^+$ (92). Found, %: C 48.63; H 2.52; N 6.79. $C_{17}H_{10}Br_2N_2O$. Calculated, %: C 48.84; H 2.41; N 6.70.

7-Bromo-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one (1i). Mp 263–265°C. IR spectrum, ν, cm^{-1}: 3412 (NH), 3042, 2956, 1684 (C=O), 1615 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.34 (2H, s, CH_2); 8.38 (1H, d, *J* = 8.0, H Quino); 8.51 (1H, d, *J* = 8.4, H Quino); 8.75 (1H, s, H Quino); 8.97 (1H, s, H Quino); 9.59 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 40.1; 110.8; 116.5; 122.2; 127.0; 130.3; 133.8; 138.4; 142.8; 144.3; 162.7. Mass spectrum, *m*/*z* (I_{rel}, %): 264 $[M+H]^+$ (100). Found, %: C 50.06; H 2.82; N 10.78. $C_{11}H_7BrN_2O$. Calculated, %: C 50.22; H 2.68; N 10.65.

7-Bromo-2-methyl-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one (1j). Mp 192–193°C. IR spectrum, ν, cm^{-1}: 3034, 2934, 1694 (C=O), 1634 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.24 (3H, s, CH_3); 5.00 (2H, s, CH_2); 8.07 (1H, d, *J* = 8.4, H Quino); 8.21 (1H, d, *J* = 8.4, H Quino); 8.46 (1H, s, H Quino); 9.23 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 24.1; 46.1; 116.4; 121.2; 121.7; 124.5; 127.8; 132.1; 136.6; 137.3; 151.9; 159.9. Mass spectrum, *m*/*z* (I_{rel}, %): 278 $[M+H]^+$ (100). Found, %: C 52.22; H 3.34; N 9.86. $C_{12}H_9BrN_2O$. Calculated, %: C 52.01; H 3.27; N 10.11.

7-Bromo-2-ethyl-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one (1k). Mp 237–238°C. IR spectrum, ν, cm^{-1}: 3048, 2960, 1681 (C=O), 1631 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 (3H, t, *J* = 7.2, $CH_2C\underline{H}_3$); 3.65 (2H, q, *J* = 7.2, $C\underline{H}_2CH_3$); 4.65 (2H, s, CH_2); 7.98 (1H, d, *J* = 8.4, H Quino); 8.03 (1H, d, *J* = 8.4, H Quino); 8.47 (1H, s, H Quino); 8.69 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 13.6; 37.0; 50.8; 120.0; 125.4; 128.9; 131.2; 131.4; 132.1; 134.6; 148.0; 156.9; 162.2. Mass spectrum, *m*/*z* (I_{rel}, %): 292 $[M+H]^+$ (100). Found, %: C 53.85; H 3.90; N 9.54. $C_{13}H_{11}BrN_2O$. Calculated, %: C 53.63; H 3.81; N 9.62.

2-Benzyl-7-bromo-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]-quinolin-1-one (1l). Mp 257–259°C. IR spectrum, ν, cm^{-1}: 3054, 2973, 2921, 1675 (C=O), 1632 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.57 (2H, s, CH_2Ph); 4.87 (2H, s, CH_2); 7.30–7.37 (5H, m, H Ph); 8.18 (1H, d, *J* = 8.4, H Quino); 8.30 (1H, d, *J* = 8.4, H Quino); 8.60 (1H, s, H Quino); 9.41 (1H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 46.0; 51.4; 120.1; 124.9; 127.7; 128.0; 128.1; 128.4; 128.9; 129.4; 131.1; 131.8; 132.0; 132.1; 132.2; 137.3; 148.1; 161.9. Mass spectrum, *m*/*z* (I_{rel}, %): 354 $[M+H]^+$ (100). Found, %: C 61.01; H 3.77; N 8.06. $C_{18}H_{13}BrN_2O$. Calculated, %: C 61.21; H 3.71; N 7.93.

2,2'-(Ethane-1,2-diyl)bis(7-bromo-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one) (1m). Mp >300°C. IR spectrum, ν, cm^{-1}: 3074, 2977, 1675 (C=O), 1629 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.71 (4H, d, *J* = 7.2, $2CH_2$); 5.28 (4H, s, $2CH_2N$); 8.30 (2H, d, *J* = 8.4, H Quino); 8.48 (2H, d, *J* = 8.4, H Quino); 8.72 (2H, s, H Quino); 9.46 (2H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 40.4; 49.2; 110.6; 113.4; 116.3; 119.1; 122.2; 126.3; 130.2; 133.5; 157.2; 162.1. Mass spectrum, *m*/*z* (I_{rel}, %): 553 $[M+H]^+$ (100). Found, %: C 52.52; H 2.84; N 10.34. $C_{24}H_{16}Br_2N_4O_2$. Calculated, %: C 52.20; H 2.92; N 10.15.

2,2'-(Propane-1,3-diyl)bis(7-bromo-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one) (1n). Mp >300°C. IR spectrum, ν, cm^{-1}: 3067, 2952, 1669 (C=O), 1617 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.33–2.40 (2H, m, CH_2); 3.98 (4H, t, *J* = 7.2, $2CH_2$); 5.28 (4H, s, $2CH_2N$); 8.23 (2H, d, *J* = 8.4, H Quino); 8.37 (2H, d, *J* = 8.4, H Quino); 8.61 (2H, s, H Quino); 9.38 (2H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 25.1; 40.3; 49.3; 115.5; 121.3; 126.1; 129.5; 132.7; 137.1; 141.6; 142.4; 157.0; 164.9. Mass spectrum, *m*/*z* (I_{rel}, %): 567 $[M+H]^+$ (100). Found, %: C 53.46; H 3.25; N 10.13. $C_{25}H_{18}Br_2N_4O_2$. Calculated, %: C 53.03; H 3.20; N 9.89.

2,2'-(Butane-1,4-diyl)bis(7-bromo-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one) (1o). Mp >300°C. IR spectrum, ν, cm^{-1}: 3041, 2637, 1689 (C=O), 1608 (C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.93–1.99 (4H, m, $2CH_2$); 3.93 (4H, t, *J* = 7.2, $2CH_2$); 5.24 (4H, s, $2CH_2N$); 8.24 (2H, d, *J* = 8.4, H Quino); 8.32 (2H, d, *J* = 8.4, H Quino); 8.44 (2H, s, H Quino); 9.35 (2H, s, H Quino). ^{13}C NMR spectrum, δ, ppm: 24.4; 43.5; 51.2; 118.3; 121.5; 126.7; 129.2; 136.8; 138.6; 138.8; 142.4; 156.9; 162.3. Mass spectrum, *m*/*z* (I_{rel}, %): 581 $[M+H]^+$ (100). Found, %: C 54.06; H 3.73; N 9.38. $C_{26}H_{20}Br_2N_4O_2$. Calculated, %: C 53.82; H 3.47; N 9.66.

Supplementary information file to this article containing ^1H and ^{13}C NMR spectra of syntesized compounds is available online at http://link.springer.com/journal/10593.

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