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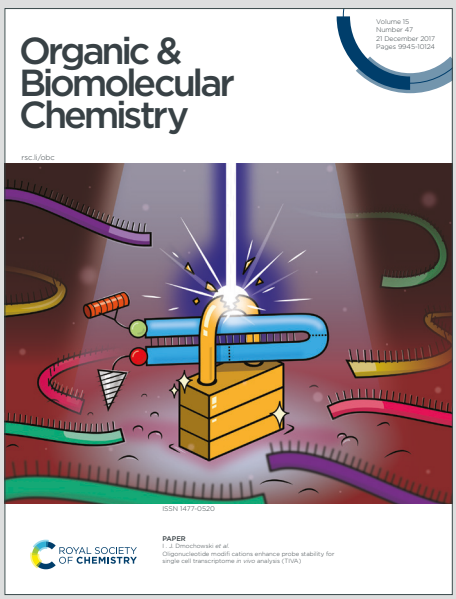

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ARTICLE

Synthesis of Cyclopentaquinolinone and Cyclopentapyridinone from *ortho*-alkynyl-N-arylaldehyde *via* Superbase-promoted C-N, C-O and C-C Bonds Formation

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An environmentally benign, transition metal-free, superbase-mediated intramolecular annulation of *o*-alkynylaldehydes with primary amines forms highly functionalized amino-subsituted cyclopentaquinolinones and cyclopentapyridinones *via* C-N, C-C, and C=O bond formation. Contrary to the traditional approaches of ring closures, a different mode of annulation is disclosed. The protocol involves the in-situ generations of imine intermediate followed by potassium hydroxide-promoted intramolecular cyclization and subsequent dimethyl sulfoxide induced dehydrogenation leads to the formation of *N*-heterocycles. X-ray crystallographic studies support the assigned structures of the amino-fused N-heterocycles.

Introduction

Superbase-mediated reactions have emerged as a potent tool for the synthesis of heterocyclic compounds[1] due to fascinating selectivity and unique ability to activate π-systems, especially carbon-carbon triple bonds, towards inter- and intramolecular cyclization.[2] Base-promoted intramolecular cyclization[3] of *ortho*-alkynyl-N-arylaldehyde derived (2-alkynyl)-arylaldimines having dual-functional groups is a significant challenge due to the chemoselectivity between imines and alkyne functional groups. Despite the significant achievements already accomplished, we have utilized the KOH-DMSO chemistry for the synthesis of 3*H*-cyclopentaquinolinone and 7*H*-cyclopentapyridinone *via* the intermolecular nucleophilic hydroxylation onto alkyne followed by intramolecular ring closure.

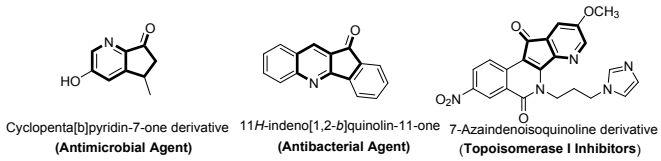
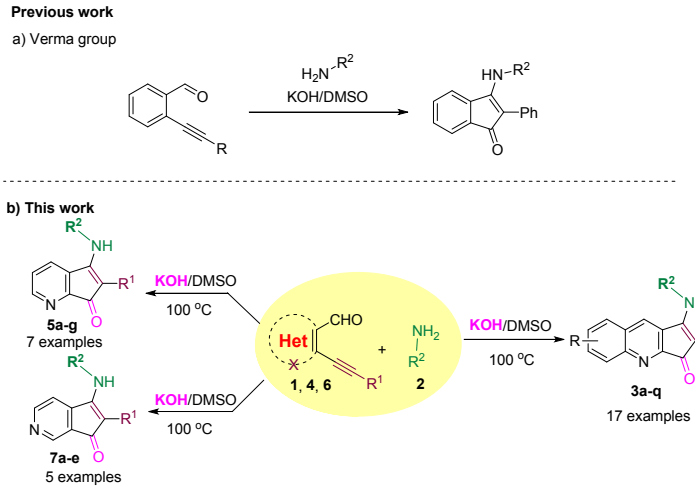


Fig 1. Biologically active compounds containing pyridinone and quinolinone cores

Base-mediated nucleophilic addition reactions of alkynes[4] are essential devices for the assembly of a wide variety of natural products,[5] pharmaceuticals,[6] and agrochemicals.[7] The cyclopenta-quinolinone and cyclopentapyridinone core moieties have been found to exhibit medicinal activity, such as cyclopenta[b]pyridin-7-one and 11*H*-indeno[1,2-b]quinolin-11-one derivative, which have antimicrobial, antibacterial activity respectively,[8] as well as 7-azaindenoisoquinoline derivative used as Topoisomerase I Inhibitors.[9] Due to the medicinal importance of these compounds, over the past decades, significant effort has been made[10] and are still demanding for the developments of the efficient approach for the synthesis.



Scheme 1 Synthetic approaches for utilizing *ortho*-alkynylaldehyde

In recent years, various research groups have reported the metal-catalyzed synthesis of heterocycles.[11-13] In 2016, the Singh group reported the Pd-catalyzed synthesis of 3-alkylsulfanyl-2- aryl-cyclopenta[b]quinolin-1-ones.[14] Transition metal-free synthesis has a broad scope in synthetic

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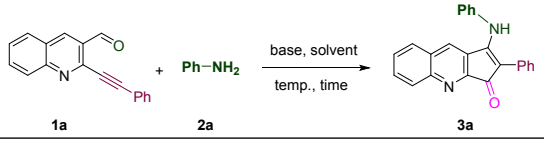
chemistry;[15,16] therefore, recently we have reported the transition metal-free synthesis of amino-indinones *via* intramolecular cyclization.[17] In continuation of our ongoing metal-free research on tandem cyclization, herein, we report a superbase-mediated tandem approach[18] for the synthesis of 3*H*-cyclopentaquinolinones and 7*H*-cyclopentapyridinones by the reaction *ortho*-alkynyl-hetero-aldehydes with primary amines.

Results and discussion

In preliminary experiments, a number of bases were examined using 2-(phenylethynyl)quinoline-3-carbaldehyde **1a** and aniline **2a** as model substrates (Table 1). The reaction of **1a** and **2a** with K_2CO_3 and $NaHCO_3$ at 100 °C for 4 h, did not give a positive result (Table 1, entries 1 and 2). Instead of carbonate bases, we next tried the hydroxide bases and gave fruitful results. KOH-DMSO at 120 °C, provided 60% yield of desired product **3a** (entry 3). On increasing the amount of base from 1 equiv to 2 equiv, the yield of the desired cyclized product increased from 60% to 90% (entry 4). When the reaction proceeds at 100 °C for 45 min, the yield remains unchanged (entry 5). It is noteworthy that no desired product **3a** was obtained in other polar organic solvents like DMF and THF (entries 6 and 7). NaOH as the base also provided the desired product **3a** but in lower yield (entry 8). However, LiOH gave only a trace amount of product (entry 9).

Table 1. Optimization of the reaction conditions[a]

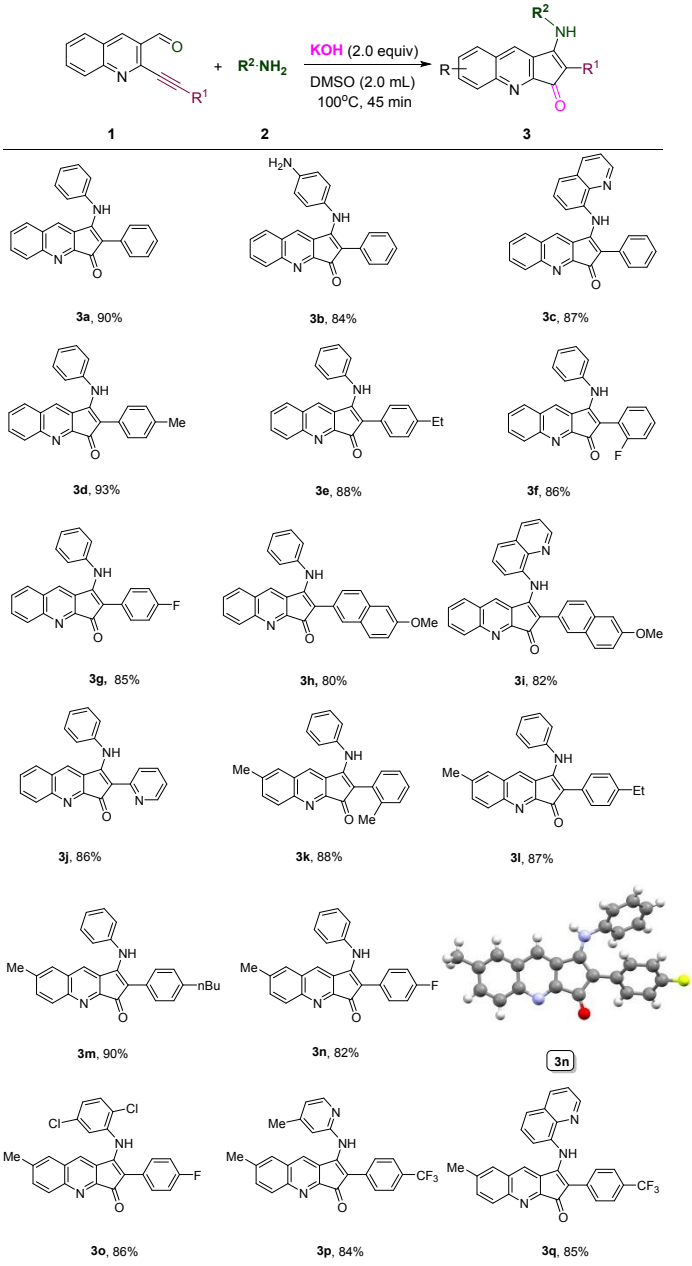


1a 2a 3a

entry	base (equiv)	solvent	time	yield (%)[b] 3a
1	K_2CO_3 (1.0)	DMSO	4 h	00
2	$NaHCO_3$ (1.0)	DMSO	4 h	00
3[c]	KOH (1.0)	DMSO	30 min	60
4[c]	KOH (2.0)	DMSO	30 min	90
5	KOH (2.0)	DMSO	45 min	90
6	KOH (2.0)	DMF	45 min	00
7	KOH (2.0)	THF	45 min	00
8	NaOH (2.0)	DMSO	4 h	42
9	LiOH (2.0)	DMSO	4 h	trace

[a]Unless otherwise noted all reactions were carried out using 2-(phenylethynyl)quinoline-3-carbaldehyde **1a** (0.50 mmol), aniline **2a** (0.50 mmol), and KOH (2.0 equiv) in 2 mL solvent at 100 °C, [b]Isolated yield, [c] 120 °C.

With optimized conditions in hand, we explored the scope and generality of the developed reaction by using a variety of *o*-alkynylquinolinaldehyde **1a-l** and various aryl and heteroaryl amines **2a-e** (Scheme 2). The reaction of substrate **1a**, with aniline **2a**, provided the desired product **3a** in 90% yield. 4-aminoaniline **2b** and 8-aminoquinolene **2c** performed well in the reaction, providing the cyclized product **3b-c** in 84% and 87% yield, respectively. The reaction of electron-donating group-bearing substrates **1b**–**c**, such as *p*-Me, *p*-Et on the benzene ring of the alkyne, afforded the corresponding products **3d**–**e** in 88–93% yield. Electron-withdrawing substrates having substituents such as 2-fluoro and 4-fluoro provided the desired products **3f-g** in good yield. A bulky group such as 6-methoxynaphthalene-substituted aldehyde **1f** reacted smoothly with aniline **2a,** and 8-aminoquinolene **2c**, and afforded the corresponding heterocycles **3h-i** in 80% and 82% yields, respectively. It was interesting to note that under the optimized reaction conditions, electron-deficient heteroaromatic alkyne **1g** provided the targeted product **3j** in 86% yield.



Scheme 2. Scope of *o*-alkynylquinolinaldehyde and primary amines.

We further extended the scope of the developed protocol with electron-rich substitution on the quinoline ring **1h-l**. 6-Methyl

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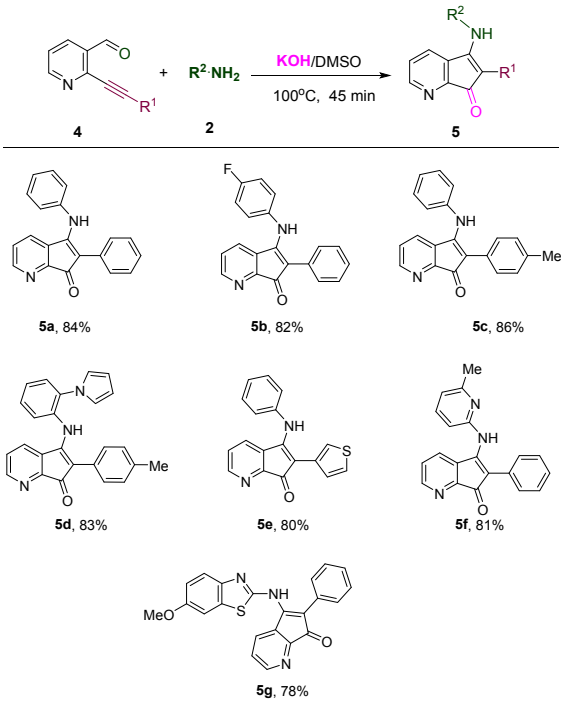
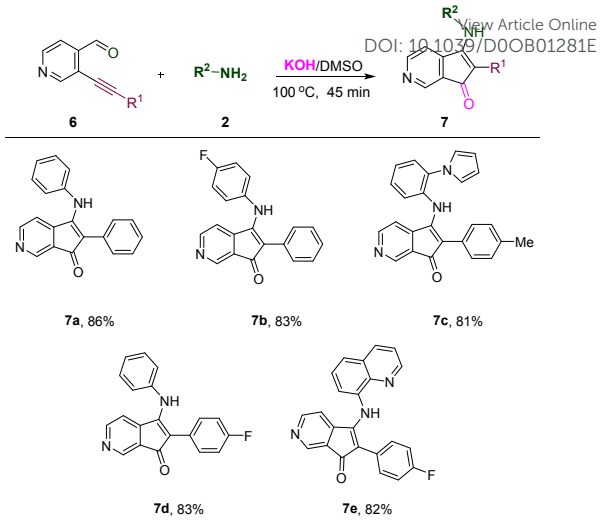
substituted quinoline **1h**-**1l** provided the desired products **3k**-**3q** in good yields with electron-donating and electron-withdrawing group substituted aryl-alkynes. The regioselectivity of the products was clearly assigned by X-ray crystallographic study[19] of compound **3n**.



Scheme 3. Scope of *o*-alkynylpyridinaldhyde

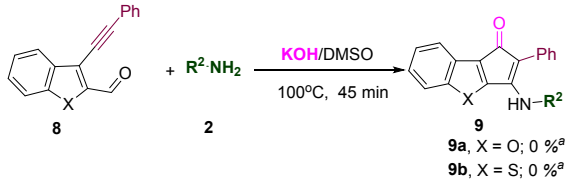
Encouraged by the above results, we explored the scope of *ortho*-alkynylnicotinaldehydes for the synthesis of cyclopentapyridinone derivatives (Scheme 3). The reaction of 2-(phenylethynyl)nicotinaldehyde **4a**, with aniline **2a** or electron-withdrawing 4-fluoroaniline **2f**, provided the desired products **5a-b** in good yields. Electron donating group-bearing aryl alkyne **4b** gave the desired products **5c-d** in 86% and 83% yields, respectively. It is worth noting that the reaction of substrate **4c** having an electron-rich thiophene-substituted alkyne provided the desired product **5e** in 80% yield. Notably, the heterocyclic amine such as 6-methylpyridin-2-amine **2h** and 6-methoxybenzo[d]thiazol-2-amine **2i** effectively gave the corresponding cyclopenta[b]pyridin-7-ones **5f-g** in good yields.

The scope of this base-mediated intramolecular annulation was further investigated by using *ortho*-alkynyl isonicotinaldehyde **6a-c** (Scheme 4). Reaction of 3-(phenylethynyl)isonicotinaldehyde **6a** with aniline **2a** and **2f** were successful and provided the cyclized amino-fused products **7a-b** in 86% and 83% yields respectively. Interestingly, electron-rich and electron-poor alkyne-substituted aldehydes **6b** and **6c** afforded the desired products **7c-e** in 81-84% yields.



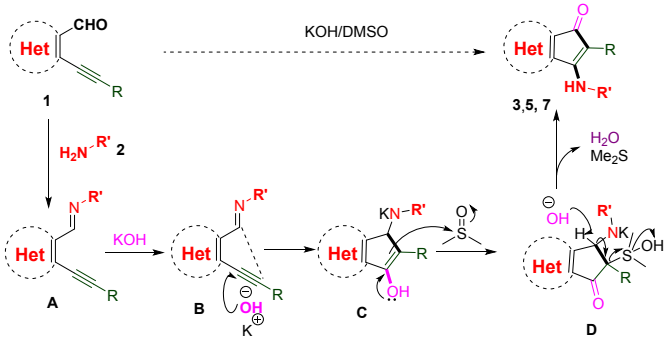
Scheme 4. Scope of Isonicotinaldehyde

To further check the generality of the developed protocol, we extended the chemistry on substrates *ortho*-alkynyl benzo[*b*]thiophen-2-carbaldehyde and *ortho*-alkynyl benzo[*b*]furan-2-carbaldehyde **8a–b**; both of the substrates failed to provide the desired products **9a-b** (Scheme 5).



Scheme 5. Scope of O/S heterocycles; [a] reaction decomposed.

Based on the literature reports,[20] a plausible reaction pathway has been proposed in Scheme 6. The mechanism starts with the aldehyde-amine reaction, which results in the formation of species **A**. Regioselective intramolecular annulation promoted by hydroxide would produce species **C**. Nucleophilic attack of the enol **C** on dimethyl sulfoxide and subsequent proton transfer would generate the species **D**. Finally base-mediated elimination of dimethyl sulfide produces the desired products.



Scheme 6. Plausible reaction pathway

Conclusions

In summary, we have demonstrated the transition metal-free, superbase-promoted intramolecular cyclization of readily accessible *ortho*-alkynyl-hetero-aldehydes with a wide range of anilines for the synthesis of substituted cyclopentaquinolinones and cyclopentapyridinones with good yields. A wide variety of readily available ortho-alkynyl-hetero-aldehydes were utilised including electron-withdrawing and electron-donating alkynyl-aldehydes. We expect that the protocol will be useful for the synthesis of highly-substituted cyclopentanone-fused quinoline and pyridine derivatives, which could find application in the synthesis of pharmaceutically active compounds.

Experimental Section

General Procedure for the Synthesis of Starting Substrate 1, 4, 6 and **9**: To a solution of substituted 2-halo-aldehyde (1.0 mmol) in MeCN (5 mL), 3 mol% of $Pd(PPh_3)_2Cl_2$ was added. The reaction vial was then sealed and flushed with nitrogen. Then, 1.5 equiv of Et_3N and 1.05 mmol of alkyne were added to the reaction mixture. Afterwards the reaction was stirred at 70 °C until TLC revealed complete conversion of the starting material. After complete of the reaction, the reaction mixture was allowed to cool, diluted with H_2O, and finally extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated under vacuum, and purified by column chromatography using 100–200 mesh sized silica gel (hexane: ethyl acetate) to afford the corresponding product. The structure and purity of known starting materials **1, 4, 6** and **9** were confirmed by comparison of their physical and NMR-spectral data (^{1}H NMR and ^{13}C NMR) with those reported in the literature.[21]

General experimental procedure for the synthesis of cyclopenta[b]quinolin-3-one, cyclopenta[b]pyridin-7-one 3, 5, 7: To a solution of *ortho*-alkynylaldehyde (0.5 mmol), amine **2** (0.5 mmol) in DMSO (2.0 mL), 2.0 equiv of KOH was added. The reaction was then stirred at 100 °C temperature until TLC revealed a complete conversion of the starting material. The reaction mixture was allowed to cool, diluted with H_2O, and finally extracted with EtOAc (2 × 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated under vacuum, and purified by column chromatography using 100–200 mesh size silica gels (hexane: ethyl acetate) to afford the corresponding product.

2-Phenyl-1-(phenylamino)-3*H*-cyclopenta[b]quinolin-3-one (3a). The product was obtained as a red needles, mp: 171–173 °C (156.6 mg, 90%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 8.33 (s, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.90–7.87 (m, 1H), 7.74–7.70 (m, 1H), 7.62–7.58 (m, 1H), 7.02–6.93 (m, 8H), 6.92–6.88 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.8, 155.8, 155.5, 148.5, 138.3, 132.3, 131.2, 130.7, 130.6, 129.6, 128.7, 128.5, 128.45, 127.5, 126.5, 125.4, 125.2, 124.2, 114.5; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{24}H_{16}N_2O]$ 349.1341, found 349.1333.

1-((4-Aminophenyl)amino)-2-phenyl-3H-cyclopenta[b]quinolin-3-one (3b). The product was obtained as a red needles, mp: 160–162 °C (152.4 mg, 84%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (s, 1H), 8.04 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 3.9 Hz, 1H), 7.73–7.69 (m, 1H), 7.60–7.56 (m, 1H), 7.18–6.99 (m, 6H), 6.66 (d, J = 5.5 Hz, 2H), 6.35–6.26 (m, 2H), 5.04 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.7, 156.6, 148.4, 147.3, 132.5, 130.6, 130.5, 129.8, 129.6, 128.5, 128.3, 127.5, 126.8, 125.9, 125.4, 116.1, 113.6; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{24}H_{17}N_3O]$ 364.1450, found 364.1471.

2-Phenyl-1-(quinolin-8-ylamino)-3H-cyclopenta[b]quinolin-3-one (3c). The product was obtained as a red needles, mp: 175–177 °C (173.5 mg, 87%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (br s, 1H), 8.94 (dd, J = 4.2, 1.6 Hz, 1H), 8.31 (d, J = 8.4 Hz, 1H), 8.23 (dd, J = 8.4, 1.6 Hz, 1H), 7.89 (s, 1H), 7.77 (dd, J = 8.0, 1.2 Hz, 1H), 7.73–7.68 (m, 1H), 7.59–7.53 (m, 2H), 7.50 (dd, J = 8.3, 1.0 Hz, 1H), 7.43–7.41 (m, 2H), 7.29–7.23 (m, 3H), 7.19-7.15 (m, 1H), 6.82 (dd, J = 7.6, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.9, 154.9, 153.2, 149.3, 148.7, 139.9, 136.6, 133.6, 131.4, 130.6, 130.2, 129.6, 128.7, 128.4, 128.34, 128.2, 127.5, 126.0, 124.6, 122.6, 122.2, 119.8, 118.7; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{17}N_3O]$ 400.1450, found 400.1464.

1-(phenylamino)-2-(*p*-tolyl)-3H-cyclopenta[b]quinolin-3-one (3d). The product was obtained as a red needles, mp: 278–280 °C (168.3 mg, 93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.2 Hz, 1H), 7.67 (s, 1H), 7.65–7.59 (m, 1H), 7.46–7.43 (m, 2H), 7.42–7.32 (m, 5H), 7.24 (d, J = 7.0 Hz, 2H), 7.20 (d, J = 7.8 Hz, 2H), 7.01 (s, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.4, 157.1, 156.0, 148.3, 137.8, 137.5, 131.0, 130.1, 129.7, 129.4, 128.9, 128.5, 128.0, 127.7, 127.1, 126.9, 125.8, 117.9, 21.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{25}H_{18}N_2O]$ 363.1497, found 363.1500.

2-(4-Ethylphenyl)-1-(phenylamino)-3*H*-cyclopenta[b]quinolin-3-one (3e). The product was obtained as a red needles, mp: 258–260 °C (165.4 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.2 Hz, 1H), 8.08 (br s, 1H), 7.62–7.58 (m, 1H), 7.45–7.39 (m, 2H), 7.33–7.24 (m, 5H), 7.18–7.16 (m, 3H), 7.11 (d, J = 7.8 Hz, 2H), 2.55 (q, J = 7.5 Hz, 2H), 1.16 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.7, 157.2, 156.1, 148.3, 143.7, 137.8, 130.9, 130.1, 129.1, 129.0, 128.9, 128.8, 128.3, 128.1, 127.9, 126.8, 126.6, 125.6, 117.5, 28.8, 15.7; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{20}N_2O]$ 377.1654, found 377.1649.

2-(2-Fluorophenyl)-1-(phenylamino)-3*H*-cyclopenta[b]quinolin-3-one (3f). The product was obtained as a yellow needles, mp: 221–223 °C (157.3 mg, 86%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.49 (s, 1H), 8.49 (s, 1H), 8.12 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 7.8 Hz, 1H), 7.80–7.76 (m, 1H), 7.69–7.65 (m, 1H), 7.17–7.08 (m, 2H), 7.03–6.92 (m, 6H), 6.74–6.69 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.0, 159.2 (d, $J_{C\text{-}F}$ = 244.7 Hz), 156.5, 155.8, 148.5, 137.5, 132.0, 130.8, 129.8, 129.5, 129.4, 128.8, 128.3, 128.2, 125.7, 125.6, 124.4, 124.0, 121.1 (d, $J_{C\text{-}F}$ = 16.4 Hz), 114.9 (d, $J_{C\text{-}F}$ = 22.2 Hz), 108.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{24}H_{15}FN_2O]$ 367.1247, found 367.1257.

2-(4-Fluorophenyl)-1-(phenylamino)-3H-cyclopenta[b]quinolin-3-one (3g). The product was obtained as a yellow needles, mp: 282–284 °C (155.3 mg, 85%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.36 (s, 1H), 8.38 (s, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.93–7.89 (m, 1H), 7.75–7.70 (m, 1H), 7.63–7.59 (m, 1H), 7.06–6.95 (m, 5H), 6.91-6.86 (m, 2H), 6.83–6.78 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.8, 161.0 (d, $J_{C\text{-}F}$ = 243.7 Hz), 155.8, 155.7, 148.5, 138.2, 131.4 (d, $J_{C\text{-}F}$ = 7.7 Hz), 131.1, 130.8, 130.7, 129.7, 128.8, 128.6, 128.5, 125.4 (d, $J_{C\text{-}F}$ = 21.2 Hz), 124.4, 114.3 (d, $J_{C\text{-}F}$ = 21.2 Hz), 113.4; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{24}H_{15}FN_2O$] 367.1247, found 367.1251.

2-(6-Methoxynaphthalen-2-yl)-1-(phenylamino)-3*H*-cyclopenta[b] quinolin-3-one (3h). The product was obtained as a yellow needles, mp: 217–219 °C (171.1 mg, 80%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.36 (s, 1H), 8.34 (s, 1H), 8.11 (d, J = 8.2 Hz, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.77–7.73 (m, 1H), 7.65–7.61 (m, 1H), 7.56–7.52 (m, 2H), 7.44 (d, J = 8.2 Hz, 1H), 7.14–7.12 (m, 2H), 7.03 (d, J = 8.2 Hz, 1H), 6.97–6.93 (m, 4H), 6.85–6.83 (m, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.0, 157.6, 155.9, 155.5, 148.5, 138.4, 133.1, 131.3, 130.8, 130.6, 129.9, 129.6, 128.7, 128.5, 128.3, 128.1, 127.4, 125.6, 125.3, 125.1, 124.2, 118.7, 114.6, 106.1, 55.6; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{29}H_{20}N_2O_2$] 429.1603, found 429.1596.

2-(6-Methoxynaphthalen-2-yl)-1-(quinolin-8-ylamino)-3H-cyclopenta[b]quinolin-3-one (3i). The product was obtained as a red needles, mp: 265–267 °C (196.1 mg, 82%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 8.96–8.95 (m, 1H), 8.56 (s, 1H), 8.19–8.17 (m, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.76–7.72 (m, 1H), 7.64–7.60 (m, 1H), 7.54–7.51 (m, 1H), 7.42 (d, J = 8.2 Hz, 1H), 7.22–7.15 (m, 4H), 7.01–6.96 (m, 2H), 6.91–6.87 (m, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.0, 157.5, 157.3, 156.2, 150.6, 148.5, 142.5, 136.7, 135.4, 132.9, 131.4, 130.8, 130.6, 129.7, 129.4, 128.7, 127.9, 127.7, 127.4, 126.0, 125.9, 125.6, 125.4, 125.2, 122.5, 118.6, 115.2, 105.9, 55.6; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{32}H_{21}N_3O_2$] 480.1712, found 480.1703.

1-(Phenylamino)-2-(pyridin-2-yl)-3*H*-cyclopenta[b]quinolin-3-one (3j). The product was obtained as a red needles, mp: 284–286 °C (149.9 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.39 (br s, 1H), 8.90 (d, J = 8.3 Hz, 1H), 8.43 (d, J = 4.2 Hz, 1H), 8.20 (d, J = 8.3 Hz, 1H), 7.77–7.73 (m, 1H), 7.63–7.60 (m, 1H), 7.56–7.47 (m, 5H), 7.43–7.36 (m, 2H), 7.08–7.05 (m, 1H), 6.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.5, 163.0, 157.2, 154.7, 148.9, 146.4, 138.1, 136.9, 130.9, 130.6, 129.6, 129.2, 129.1, 128.1, 127.9, 127.8, 127.0, 122.2, 120.2, 109.0; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{23}H_{15}N_3O$] 350.1293, found 350.1302.

7-Methyl-1-(phenylamino)-2-(*o*-tolyl)-3H-cyclopenta[b]quinolin-3-one (3k). The product was obtained as a red needles, mp: 268–270 °C (165.4 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 1H), 7.47 (dd, J = 8.5, 1.8 Hz, 1H), 7.36–7.30 (m, 3H), 7.26 (s, 2H), 7.23–7.15 (m, 6H), 7.05 (s, 1H), 2.45 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 157.9, 155.4, 146.7, 138.2, 138.1, 137.5, 132.2, 130.8, 130.75, 130.5, 130.1, 129.2, 128.5, 128.4, 128.3, 128.0, 127.0, 126.3, 126.2, 125.7, 118.4, 116.3, 21.6, 20.5; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{26}H_{20}N_2O$] 377.1654, found 377.1655.

2-(4-Ethylphenyl)-7-methyl-1-(phenylamino)-3*H*-cyclopenta[b]quinolin-3-one (3l). The product was obtained as a red needles, mp: 153–155 °C (169.6 mg, 87%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (br s, 1H), 8.04 (d, J = 8.2 Hz, 1H), 7.41 (d, J = 8.2 Hz, 1H), 7.29–7.23 (m, 5H), 7.20 (s, 1H), 7.16–7.13 (m, 3H), 7.07 (d, J = 7.3 Hz, 2H), 2.54 (q, J = 7.5 Hz, 2H), 2.40 (s, 3H), 1.15 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0, 157.1, 155.2, 146.7, 143.5, 138.1, 137.8, 132.0, 130.6, 129.0, 128.3, 128.2, 128.17, 126.6, 126.2, 125.4, 117.1, 28.8, 21.5, 15.7; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{27}H_{22}N_2O$] 391.1810, found 391.1786.

2-(4-Butylphenyl)-7-methyl-1-(phenylamino)-3*H*-cyclopenta[b]quinolin-3-one (3m). The product was obtained as a red needles, mp: 251–253 °C (188.1 mg, 90%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.42 (dd, J = 8.5, 1.6 Hz, 1H), 7.29–7.23 (m, 5H), 7.20 (s, 1H), 7.17–7.13 (m, 3H), 7.06 (d, J = 8.1 Hz, 2H), 2.49 (t, J = 7.6 Hz, 2H), 2.39 (s, 3H), 1.54–1.46 (m, 2H), 1.34–1.25 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0, 157.0, 155.2, 146.7, 142.1, 138.1, 137.8, 132.0, 130.6, 129.0, 128.9, 128.7, 128.3, 128.2, 128.17, 126.6, 126.1, 125.4, 117.0, 35.5, 33.6, 22.3, 21.5, 14.0; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{29}H_{26}N_2O$] 419.2123, found 419.2148.

2-(4-Fluorophenyl)-7-methyl-1-(phenylamino)-3*H*-cyclopenta[b] quinolin-3-one (3n). The product was obtained as a red needles, mp: 155–157 °C (155.9 mg, 82%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 8.23 (s, 1H), 7.94 (d, J = 8.5 Hz, 1H), 7.63 (s, 1H), 7.53 (dd, J = 8.5, 1.8 Hz, 1H), 7.05–7.02 (m, 2H), 6.99–6.93 (m, 3H), 6.90–6.88 (m, 2H), 6.83–6.77 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.9, 161.0 (d, $J_{C\text{-}F}$ = 242.8 Hz), 155.6, 154.9, 146.9, 138.6, 138.2, 132.5, 131.4 (d, $J_{C\text{-}F}$ = 7.7 Hz), 131.2, 130.5, 128.7, 128.6, 128.4, 125.5, 124.8, 124.4, 114.3 (d, $J_{C\text{-}F}$ = 21.2 Hz), 113.1, 21.6; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{25}H_{17}FN_2O$] 381.1403, found 381.1403.

1-((2, 5-Dichlorophenyl)amino)-2-(4-fluorophenyl)-7-methyl-3H-cyclopenta[b]quinolin-3-one (3o). The product was obtained as a yellow needles, mp: 321–323 °C (192.6 mg, 86%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1H), 8.36 (s, 1H), 7.97 (d, J = 8.7 Hz, 1H), 7.71 (s, 1H), 7.57 (d, J = 8.7 Hz, 1H), 7.30 (d, J = 8.7 Hz, 1H), 7.17-7.11 (m, 2H), 6.93–6.83 (m, 4H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.2, 161.1 (d, $J_{C\text{-}F}$ = 243.7 Hz), 156.5, 154.7, 146.8, 138.8, 137.0, 132.6, 132.0, 131.3 (d, $J_{C\text{-}F}$ = 7.7 Hz), 131.1, 130.8, 130.6, 128.8, 128.4, 128.1 (d, $J_{C\text{-}F}$ = 6.7 Hz), 124.9, 116.6, 116.2, 114.4 (d, $J_{C\text{-}F}$ = 21.2 Hz), 114.3, 21.6; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{25}H_{15}Cl_2FN_2O$] 449.0624, found 449.0620.

7-Methyl-1-((4-methylpyridin-2-yl)amino)-2-(4-(trifluoromethyl) phenyl)-3H-cyclopenta[b]quinolin-3-one (3p). The product was obtained as a yellow needles, mp: 148–150 °C (186.9 mg, 84%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.80 (br s, 1H), 8.40 (s, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 5.1 Hz, 1H), 7.69 (s, 1H), 7.57 (dd, J = 8.5, 1.8 Hz, 1H), 7.38 (d, J = 8.2 Hz, 2H), 7.17 (d, J = 7.8 Hz, 2H), 6.76 (d, J = 4.9 Hz, 1H), 6.59 (s, 1H), 2.47 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.2, 156.0, 154.2, 151.1, 148.7, 147.8, 146.9, 138.9, 137.6, 132.8, 131.1, 130.6, 129.5, 128.9, 128.5, 126.8 (q, $J_{C\text{-}F}$ = 31.8 Hz), 125.9, 124.8 (q, $J_{C\text{-}F}$ = 271.7 Hz), 124.4 (q, $J_{C\text{-}F}$ = 2.9 Hz), 121.3, 119.0, 114.4, 21.6, 20.5; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{26}H_{18}F_3N_3O$] 446.1480, found 446.1506.

7-Methyl-1-(quinolin-8-ylamino)-2-(4-(trifluoromethyl)phenyl)-3H-cyclopenta[b]quinolin-3-one (3q). The product was obtained as a yellow needles, mp: 149–151 °C (204.1 mg, 85%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.80 (s, 1H), 8.84–8.83 (m, 1H), 8.48 (s, 1H), 8.20 (dd, J = 8.4, 1.6 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.70 (s, 1H), 7.63 (dd, J = 8.2, 1.0 Hz, 1H), 7.58 (dd, J = 8.5, 1.8 Hz, 1H), 7.48–7.45 (m, 1H), 7.36–7.34 (m, 1H), 7.24 (t, J = 7.8 Hz, 1H), 6.95 (d, J = 8.2 Hz, 2H), 6.79 (d, J = 8.1 Hz, 2H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.3, 158.5, 155.2, 150.7, 147.0, 142.4, 138.7, 136.7, 136.6, 135.5, 132.7, 130.9, 130.5, 129.4, 128.9, 128.8, 128.5, 126.9, 126.4, 126.1, 126.07, 125.5, 123.3 (q, $J_{C\text{-}F}$ = 2.9 Hz), 122.5, 113.4, 21.6; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{29}H_{18}F_3N_3O]$ 482.1480, found 482.1473.

6-Phenyl-5-(phenylamino)-7*H*-cyclopenta[b]pyridin-7-one (5a). The product was obtained as a yellow needles, mp: 164–166 °C (124.9 mg, 84%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.14 (s, 1H), 8.48 (dd, J = 5.1, 1.2 Hz, 1H), 7.97 (d, J = 6.9 Hz, 1H), 7.38 (dd, J = 7.5, 5.2 Hz, 1H), 7.02–6.90 (m, 8H), 6.88–6.86 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.4, 154.8, 154.2, 150.1, 138.2, 135.5, 132.3, 129.6, 128.4, 127.4, 126.5, 126.1, 125.2, 124.1, 108.3; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{14}N_2O]$ 299.1184, found 299.1186.

5-((4-Fluorophenyl)amino)-6-phenyl-7*H*-cyclopenta[b]pyridin-7-one (5b). The product was obtained as a red needles, mp: 153–155 °C (129.5 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.12 (s, 1H), 8.48 (dd, J = 5.2, 1.1 Hz, 1H), 7.98 (d, J = 7.3 Hz, 1H), 7.39–7.36 (m, 1H), 6.98 (dd, J = 6.0, 3.6 Hz, 3H), 6.91–6.87 (m, 4H), 6.82–6.78 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.4, 159.8 (d, J = 242.8 Hz, 1C), 155.2, 154.3, 150.2, 135.4, 134.7, 132.3, 129.8, 127.5, 126.4, 126.3, 126.2 (d, J = 4.8 Hz, 1C), 125.3, 115.1 (d, J = 23.1 Hz, 1C), 108.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{13}FN_2O]$ 317.1090, found 317.1086.

5-(Phenylamino)-6-(*p*-tolyl)-7*H*-cyclopenta[b]pyridin-7-one (5c). The product was obtained as a red needles, mp: 170–172 °C (134.1 mg, 86%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.06 (s, 1H), 8.46–8.44 (m, 1H), 7.90–7.88 (m, 1H), 7.35 (dd, J = 7.5, 5.2 Hz, 1H), 7.04–7.00 (m, 2H), 6.96–6.92 (m, 1H), 6.89–6.87 (m, 2H), 6.84–6.79 (m, 4H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.6, 154.6, 154.2, 150.0, 138.4, 135.6, 135.2, 129.5, 129.4, 128.5, 128.1, 126.5, 125.3, 125.2, 124.2, 108.6, 21.3; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{21}H_{16}N_2O]$ 313.1341, found 313.1321.

5-((2-(1H-pyrrol-1-yl)phenyl)amino)-6-(p-tolyl)-7H-cyclopenta[b]pyridin-7-one (5d). The product was obtained as a yellow needles, mp: 163–165 °C (156.4 mg, 83%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35–8.34 (m, 1H), 7.65 (s, 1H), 7.31–7.28 (m, 1H), 7.26–7.22 (m, 1H), 7.15–7.11 (m, 1H), 7.09–7.06 (m, 2H), 7.04–6.97 (m, 5H), 6.81–6.80 (m, 2H), 6.31–6.30 (m, 2H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.2, 155.2, 154.3, 149.6, 136.9, 135.5, 133.8, 132.4, 129.2, 128.8, 127.5, 127.3, 127.2, 126.5, 124.3, 121.7, 112.6, 110.6, 21.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{25}H_{19}N_3O]$ 378.1606, found 378.1600.

5-(Phenylamino)-6-(thiophen-3-yl)-7H-cyclopenta[b]pyridin-7-one (5e). The product was obtained as a red needles, mp: 171–173 °C (121.5 mg, 80%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1H), 8.45–8.43 (m, 1H), 7.84–7.82 (m, 1H), 7.33 (dd, J = 7.5, 5.2 Hz, 1H), 7.16–7.14 (m, 1H), 7.12–7.08 (m, 2H), 7.04–7.00 (m, 1H), 6.97–6.96 (m, 1H), 6.94–6.91 (m, 2H), 6.73–6.71 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.5, 154.4, 154.2, 150.0, 138.4, 135.7, 132.0, 128.7, 126.7, 125.4, 125.3, 124.1, 124.0, 123.2, 104.8; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_{12}N_2OS]$ 305.0749, found 305.0739.

5-((6-Methylpyridin-2-yl)amino)-6-phenyl-7H-cyclopenta[b]pyridin-7-one (5f). The product was obtained as a red needles, mp: 258–260 °C (126.7 mg, 81%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.45 (br s, 1H), 8.47–8.46 (m, 1H), 8.01–7.99 (m, 1H), 7.38 (dd, J = 7.5, 5.2 Hz, 1H), 7.33–7.29 (m, 1H), 7.21–7.18 (m, 1H), 7.07–7.01 (m, 2H), 6.98–6.95 (m, 2H), 6.71 (d, J = 7.4 Hz, 1H), 6.67 (d, J = 8.1 Hz, 1H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.4, 159.6, 156.9, 153.9, 150.9, 150.0, 138.0, 136.2, 133.2, 129.0, 127.6, 127.1, 126.3, 118.9, 114.2, 111.3, 105.5, 23.7; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{15}N_3O]$ 314.1293, found 314.1294.

5-((6-Methoxybenzo[d]thiazol-2-yl)amino)-6-phenyl-7H-cyclopenta[b]pyridin-7-one (5g). The product was obtained as a yellow needles, mp: 180–182 °C (150.1 mg, 78%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.36 (br s, 1H), 8.52 (d, J = 4.7 Hz, 1H), 7.77 (d, J = 7.1 Hz, 1H), 7.59–7.50 (m, 1H), 7.43–7.32 (m, 2H), 7.21–7.01 (m, 4H), 6.99–6.94 (m, 1H), 6.82 (dd, J = 8.8, 2.5 Hz, 1H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.8, 169.7, 161.5, 156.6, 156.5, 151.5, 143.1, 132.7, 129.2, 128.6, 127.6, 127.0, 124.9, 121.6, 115.3, 114.8, 105.2, 56.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{22}H_{15}N_3O_2S]$ 386.0963, found 386.0959.

6-Phenyl-5-(phenylamino)-7*H*-cyclopenta[c]pyridin-7-one (7a). The product was obtained as a red needles, mp: 265–267 °C (128.1 mg, 86%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.50 (s, 1H), 7.72 (d, J = 4.7 Hz, 1H), 6.99–6.95 (m, 5H), 6.92–6.88 (m, 3H), 6.83–6.81 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.7, 155.0, 154.1, 148.7, 140.3, 138.2, 132.1, 129.7, 128.4, 127.5, 127.3, 126.4, 125.1, 123.8, 114.8, 108.5; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{14}N_2O]$ 299.1184, found 299.1185.

5-((4-Fluorophenyl)amino)-6-phenyl-7*H*-cyclopenta[c]pyridin-7-one (7b). The product was obtained as a red needles, mp: 267–269 °C (131.1 mg, 83%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 8.78 (d, J = 4.9 Hz, 1H), 8.52 (s, 1H), 7.74 (d, J = 4.9 Hz, 1H), 7.62–7.53 (m, 1H), 7.02–7.01 (m, 2H), 6.88–6.78 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.3, 159. 2 (d, $J_{C\text{-}F}$ = 242.5 Hz), 154.6, 154.1, 148.2, 139.9, 139.8, 134.2 (d, $J_{C\text{-}F}$ = 1.9 Hz), 131.6, 129.5, 127.1, 126.9, 126.1, 125.5 (d, $J_{C\text{-}F}$ = 7.7 Hz), 114.7 (d, $J_{C\text{-}F}$ = 23.0 Hz), 114.3, 107.8; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{13}FN_2O]$ 317.1090, found 317.1093.

5-((2-(1H-pyrrol-1-yl)phenyl)amino)-6-(p-tolyl)-7H-cyclopenta[c]pyridin-7-one (7c). The product was obtained as a red needles, mp: 226–228 °C (152.6 mg, 81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.50 (d, J = 4.9 Hz, 1H), 7.35 (dd, J = 7.8, 1.5 Hz, 1H), 7.25–7.21 (m, 1H), 7.14–7.06 (m, 6H), 6.94 (dd, J = 8.0, 1.2 Hz, 1H), 6.84–6.83 (m, 2H), 6.66–6.65 (m, 1H), 6.36–6.35 (m, 2H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 154.3, 153.2, 147.4, 141.2, 137.5, 134.7, 132.8, 129.3, 128.9, 127.5, 127.4, 126.9, 126.7, 126.6, 126.1, 121.8, 114.3, 113.9, 110.8; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{25}H_{19}N_3O]$ 378.1606, found 378.1615.

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6-(4-Fluorophenyl)-5-(phenylamino)-7H-cyclopenta[c]pyridin-7-one (7d). The product was obtained as a red needles, mp: 243–245 °C (131.1 mg, 83%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.16 (s, 1H), 8.79 (d, J = 4.6 Hz, 1H), 8.53 (s, 1H), 7.77 (d, J = 4.6 Hz, 1H), 7.05–7.01 (m, 2H), 6.99–6.95 (m, 1H), 6.93–6.89 (m, 2H), 6.85–6.79 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.6, 161.0 (d, $J_{C\text{-}F}$ = 243.7 Hz), 155.0, 154.2, 148.6, 140.3, 138.1, 131.5 (d, $J_{C\text{-}F}$ = 8.7 Hz), 128.5, 127.2, 125.3, 124.0, 114.7, 114.3 (d, $J_{C\text{-}F}$ = 21.2 Hz), 107.4; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{20}H_{13}FN_2O$] 317.1090, found 317.1091.

6-(4-Fluorophenyl)-5-(quinolin-8-ylamino)-7H-cyclopenta[c]pyridin-7-one (7e). The product was obtained as a red needles, mp: 257–259 °C (150.4 mg, 82%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 8.88-8.86 (m, 1H), 8.76 (s, 1H), 8.51 (s, 1H), 8.27–8.25 (m, 1H), 7.89 (d, J = 4.7 Hz, 1H), 7.64–7.62 (m, 1H), 7.51–7.48 (m, 1H), 7.20–7.12 (m, 2H), 6.65–6.60 (m, 2H), 6.55–6.49 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.6, 160.7 (d, $J_{C\text{-}F}$ = 243.7 Hz), 156.1, 155.1, 150.5, 148.6, 142.2, 140.2, 136.8, 135.3, 130.9 (d, $J_{C\text{-}F}$ = 7.7 Hz), 128.7, 128.3, 127.4, 126.1 (d, $J_{C\text{-}F}$ = 9.0 Hz), 125.5, 122.5, 116.2, 115.0, 113.8 (d, $J_{C\text{-}F}$ = 21.2 Hz), 108.2; HRMS (ESI) [M+H]$^+$ Calcd for [$C_{23}H_{14}FN_3O$] 368.1199, found 368.1199.

Conflicts of interest

There are no conflicts of interest to declare.

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Notes and references

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