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Concise Report

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Palladium Iodide-Catalyzed Selective Carbonylative Double Cyclization of 4-(2-Aminophenyl)-3-yn-1-ols to Dihydrofuroquinolinone Derivatives

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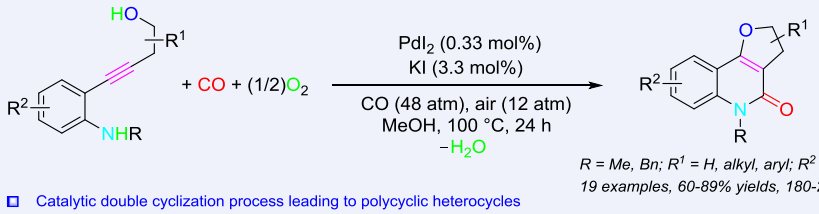
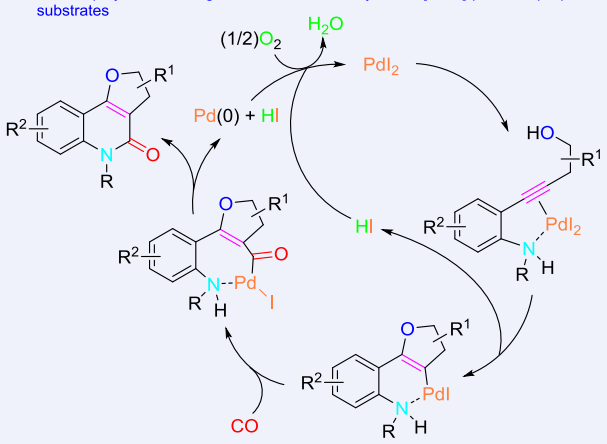
Keywords

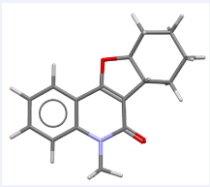
Carbonylation | Cyclization | Heterocycles | Palladium | Polycyclic heterocycles

Comprehensive Summary



- Catalytic double cyclization process leading to polycyclic heterocycles
- Selective 5-*endo*-*dig* *O*-cyclization followed by *N*-cyclocarbonylation
- One-step synthesis of high value added 2,3-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-ones from simple substrates





Molecular strucutre of a newly synthesized tetracyclic product confirmed by X-ray diffraction analysis

The PdI_2/KI-catalyzed oxidative carbonylation of 4-(2-aminophenyl)-3-yn-1-ols, bearing two potential nucleophilic groups in suitable position selectively leads to dihydrofuroquinolinone derivatives in fair to high yields (60%—89%) and excellent turnover numbers (180—267 mol of product per mol of Pd) over 19 examples, through a mechanistic pathway involving initial *O*-cyclization followed by *N*-cyclocarbonylation. In such process, the selective catalytic construction of two rings and three new bonds is achieved in one synthetic step to afford high value added fused heterocyclic structures starting from readily available materials.

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Background and Originality Content

The possibility to synthesize functionalized polycyclic heterocyclic derivatives in one step by sequential double cyclization of readily available acyclic substrates under catalytic conditions represents an important current goal in organic synthesis.[1] In fact, polycyclic heterocycles are molecular motifs of particular importance, owing to the significant various biological activities that present many of their derivatives.[2] The development of direct, step-economical approaches to their formation by the catalytic construction of two new rings in one step and in a selective manner is therefore of enormous synthetic interest.

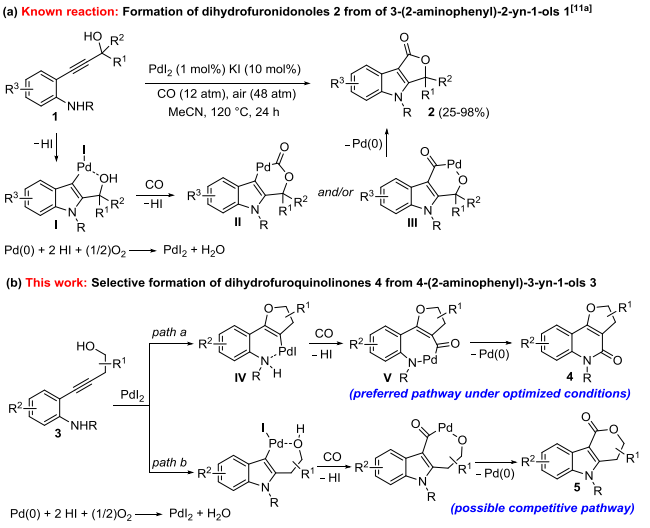
In this field, palladium catalysis plays a major role, as Pd-based catalysts may be able to efficiently promote different kinds of heterocyclizations, including processes occurring with the insertion of simple molecules (such as carbon monoxide) into the final cycle.[3] When the same palladium catalyst is capable to promote heterocyclization coupled with carbonylation,[4] formation of two new rings with incorporation of CO as a carbonyl function in a single synthetic operation may take place, with direct formation of carbonylated fused heterocycles.[1p-q,5-6]

We have recently reported that the simple catalytic system PdI_2/KI,[7] proposed by our research group as an efficient catalyst for the oxidative carbonylation of alkynes in 1992[8] and since then used for promoting many carbonylative heterocyclization processes,[7,9-10] is able to catalyze the sequential oxidative heterocyclization – cyclocarbonylation of different suitably difunctionalized acetylenic derivatives with formation of carbonylated polycyclic heterocycles.[11] In particular, we were able to synthesize high value added 3,4-dihydro-1*H*-furo[3,4-*b*]indol-1-ones **2** in one step starting from 3-(2-aminophenyl)-2-yn-1-ols **1**, as shown in Scheme 1.[11a] The catalytic process was initiated by triple bond activation (through coordination to the metal center) followed by 5-*endo-dig* *N*-cyclization (via intramolecular nucleophilic attack of the amino group on coordinated triple bond). This led to the formation of β-indolylpalladium iodide intermediate **I**, stabilized by coordination of the hydroxyl group. This intermediate then underwent carbon monoxide insertion with formation of palladacycles **II** and/or **III** followed by reductive elimination. Pd(0) was then oxidized back to PdI_2 in the presence of O_2 (from air) as external oxidant (Scheme 1a; anionic iodide ligands are omitted for clarity).[11a]

In the present work, we have studied the reactivity of the higher homologues of **1**, namely, 4-(2-aminophenyl)-3-yn-1-ols **3**, bearing the triple bond substituted with a hydroxyethyl rather than hydroxymethyl chain. We have found that, under the optimized conditions, 3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one derivatives **4** can be selectively obtained in high yields. This result is noteworthy, since, different from 3-(2-aminophenyl)-2-yn-1-ols **1**, substrates **3** could in principle undergo divergent mechanistic pathways under PdI_2/KI-catalyzed oxidative carbonylation conditions, to give isomeric double cyclization fused heterocycles **4** and **5**. In fact, with substrates **3**, an initial *O*-cyclization (by intramolecular 5-*endo-dig* nucleophilic attack by the hydroxyl group on coordinated triple bond) becomes possible, with formation of a stable 5-membered ring intermediate **IV**. With substrates **1**, this kind of reactivity was hindered by the shortness of the chain, which would have led to the formation of an unstable four-membered ring intermediate. Intermediate **IV** would then undergo carbon monoxide insertion to give palladacycle **V** followed by reductive elimination to yield **4** (Scheme 1b, path a). On the other hand, isomeric 4,5-dihydropyrano[4,3-*b*]indol-1(3*H*)-ones **5** could still be formed through a reaction pathway similar to that seen in Scheme 1a for the formation of dihydrofuroindolones **2** from **1**, as shown in Scheme 1b, path b.

The possibility to selectively obtain 3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-ones **4** in one step from simple building blocks is of particular interest, in view of the importance of this class of fused heterocycles, whose core is present in several compounds (including natural products) displaying significant biological activities;[12] a couple of examples are shown in Figure 1.

Scheme 1 Known knowledge and conceptual advance of this contribution



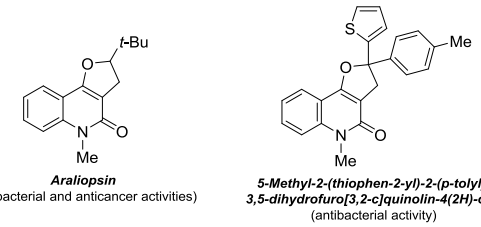


Figure 1 Examples of bioactive 3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one derivatives.[12]

Results and Discussion

4-(2-(Methylamino)phenyl)but-3-yn-1-ol **3a**, easily synthesized by Sonogashira coupling between 2-iodo-*N*-methylaniline and but-3-yn-1-ol (see the Supporting Information for details) was used as model substrate. Carbonylation of **3a** was initially carried out under conditions similar to those employed for the synthesis of 3,4-dihydro-1*H*-furo[3,4-*b*]indol-1-ones **2** (Scheme 1),[11a] namely, 40 atm of a 1 : 7 mixture of CO-air,[13] 5 mol% of PdI_2, 50 mol% of KI, MeCN as the solvent (initial **3a** concentration = 0.10 mmol of **3a** per mL of MeCN) at 100 °C. After 15 h, substrate conversion was quantitative, and two carbonylation products were separated from the reaction mixture, corresponding to isomeric 5-methyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one **4a** and 5-methyl-4,5-dihydropyrano[4,3-*b*]indol-1(3*H*)-one **5a** (21% and 45% yields, respectively; Table 1, entry 1). The structure of **5a** was confirmed by XRD analysis (Figure 2; see the Supporting Information for full XRD data). This preliminary result was in agreement with the possible divergent pathways shown in Scheme 1.

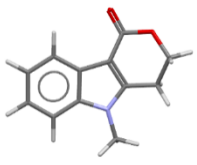
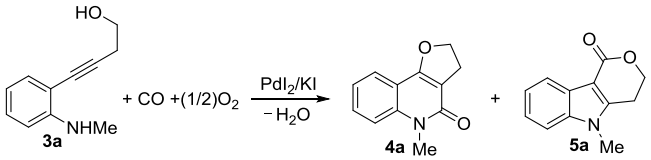


Figure 2 X-ray molecular structure of 5-methyl-4,5-dihydropyrano-[4,3-*b*]indol-1(3*H*)-one **5a**.

A lower total yield of the two isomers was observed under more diluted conditions (yields of **4a** and **5a** were 17% and 33%, respectively; Table 1, entry 2). The two products were formed in *ca*. equimolar amounts when the process was carried out under more concentrated conditions (Table 1, entry 3) or at 80 °C (with a lower total yield; Table 1, entry 4). Interestingly, product selectivity turned out to be in favor of dihydrofuroquinolinone **4a** by using 1,2-dimethoxyethane (DME) as the solvent (yields of **4a** and **5a** = 38% and 19%, respectively; Table 1, entry 5). When the reaction was carried out in dioxane, only **4a** could be isolated, although in modest yield (34%, Table 1, entry 6). This yield improved to 50% in MeOH as the reaction medium, still without formation of **5a** (Table 1, entry 7). The effect of pressure on the reaction outcome was then investigated, both in MeCN (where a mixture of the two isomers was consistently formed) and MeOH (where only **4a** was obtained). In MeCN, under the same conditions as those of the first experiment (Table 1, entry 1), but under 20 atm of a 4 : 1 mixture of CO-air, the formation of dihydropyranoindolone **5a** was still favored, even though to a minor extent with respect to the parent reaction (Table 1, entry 8). With the same 4 : 1 mixture of CO-air, but under a total pressure of 40 atm, similar results were observed (Table 1, entry 9), while almost equimolar amounts of the two isomers were formed under 60 atm (36% of **4a** and 39% of **5a**; Table 1, entry 10). On the other hand, in MeOH as the solvent and under 60 atm of a 4 : 1 mixture of CO-air), only **4a** was obtained, and in a higher yield (65%; Table 1, entry 11) with respect to the experiment carried out under 5 : 35 atm of CO/air (50%; Table 1, entry 7). The high selectivity toward **4a** observed in MeOH with respect to MeCN is likely due to a diminished nucleophilicity of the amino group of **3a** in the protic solvent, which disfavors pathway *b* leading to **5a** with respect to pathway *a* leading to **4a** (Scheme 1b).[14]

Table 1 PdI_2/KI-catalyzed oxidative carbonylation of 4-(2-(methylamino)-phenyl)but-3-yn-1-ol **3a** under different conditions[a]



Entry[a]	Solvent	T/°C	p_{CO}/atm	P_{air}/atm	**3a** Concn.[b]	Yield of **4a**[c]/%	Yield of **5a**[c]/%
1	MeCN	100	5	35	0.10	21	45
2	MeCN	100	5	35	0.05	17	33
3	MeCN	100	5	35	0.22	36	34
4	MeCN	80	5	35	0.10	28	25
5	DME	100	5	35	0.10	38	19
6	dioxane	100	5	35	0.10	34	
7	MeOH	100	5	35	0.10	50	
8	MeCN	100	16	4	0.10	31	38
9	MeCN	100	32	8	0.10	33	40
10	MeCN	100	48	12	0.10	36	39
11	MeOH	100	48	12	0.10	65	

[a] All reactions were carried out for 15 h in the presence of 5 mol% of PdI_2 and 50 mol% of KI. Substrate conversion was quantitative in all cases. [b] mmol of **3a** per mL of solvent. [c] Isolated yield based on starting **3a**.

Having identified MeOH as a suitable solvent to make the process selective toward the formation of a single isomer (dihydrofuroquinolinone **4a**, in particular) in an acceptable yield, the next experiments were aimed at assessing the possibility to improve the process catalyticity in this solvent. Quite interestingly, the yield of **4a** turned out to be higher when the reaction was carried out for 24 h with a lower catalyst loading (1 mol% of PdI_2 and 10 mol% of KI). In fact, under these conditions, the yield of **4a** was 70% (Table 2, entry 1), to be compared with 65% obtained with 5 mol% of PdI_2 and 50 mol% of KI (Table 1, entry 11). This unexpected result could be due to the occurrence of side reactions, leading to an increase of the amount of unidentified byproducts (chromatographically immobile materials), promoted by the catalytic system when present in an excessive amount with respect to that required for the formation of the desired carbonylation product. This trend was consistently observed when the catalyst loading was further decreased to 0.5 mol% (yield of **4a**, 72%; Table 2, entry 2) and to 0.33% (yield of **4a**, 75%; Table 2, entry 3), with the achievement of an excellent TON of 225 mol of **4a**/mol of Pd. On the other hand, a further reduction of the catalyst loading to 0.2% led to a decrease of the **4a** yield to 55%, also due to the formation of isomer **5a** in 10% yield (Table 2, entry 4). Reducing the amount of catalyst under a lower CO pressure (5 atm of CO and 35 atm of air) led to inferior results with respect to the reaction performed under 48 atm of CO and 12 atm of air, as shown in Table 2, entry 5 (to be compared with entry 2).

The final optimized conditions therefore corresponded to those of Table 2, entry 3, involving the use of MeOH as the solvent (substrate concentration = 0.10 mmol per mL of solvent) at 100 °C for 24 h, in the presence of 0.33 mol% of PdI_2 in conjunction with 3.3 mol% of KI and under 60 atm of a 4 : 1 mixture of CO-air. Under these conditions, other differently substituted 4-(2-aminophenyl)-3-yn-1-ols **3b–s** were smoothly and selectively converted into the corresponding dihydrofuroquinolinone derivatives **4b–s** with yields ranging from 60% to 89% (Table 2, entries 6—23). When nitrogen was substituted with ethyl (substrate **3b**) or benzyl (substrate **3c**), the yields of the corresponding dihydrofuroquinolinones **4b** and **4c** were practically the same as that observed with *N*-methyl substitution (72% and 73%, respectively; Table 2, entries 6 and 7).[15] An electron-donating as well as an electron-withdrawing substituent (such as Me or Cl, respectively) in *para* position to either the triple bond or the amino group (substrates **3d–g**) were perfectly compatible (Table 2, entries 8—11). Alkyl substitution α to the hydroxyl group (as in substrates **3h–m**) led to high yields of the corresponding dihydrofuroquinolinones, also in the presence of an additional substituent on the aromatic ring (Table 2, entries 12—17). α-Aryl substitution (with the simple phenyl group, sterically demanding 2,3,5-trimethylphenyl, or electron-deficient 4-cyanophenyl, substrates **3n–p**) was also tolerated (Table 2, entries 18—20), as well as α,α-dialkyl (substrate **3q**) (Table 2, entry 21) and α-alkyl,α-aryl disubstitution (substrate **3r**) (Table 2, entry 22). Finally, we tested α,β-disubstituted substrate **3s**, still with good results (Table 2, entry 23). The structure of tetrycyclic product **4s**, including the *trans* junction between the fused dihydrofuran and cyclohexane rings, was confirmed by X-ray diffraction analysis (Figure 3; see the Supporting Information for full X-ray data).

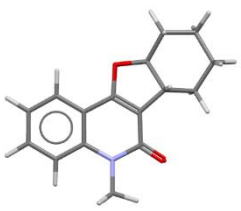
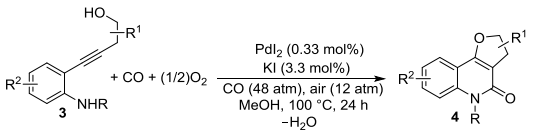
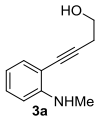
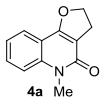
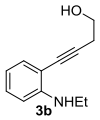
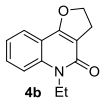
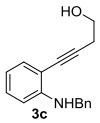
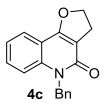
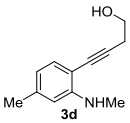
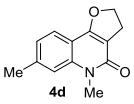
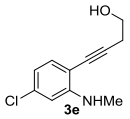
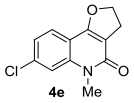
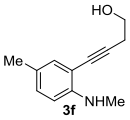
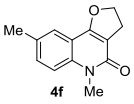
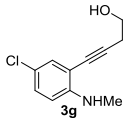
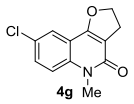
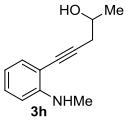
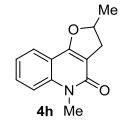
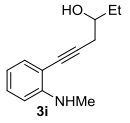
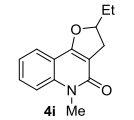
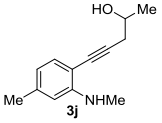
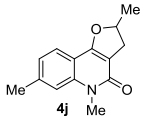
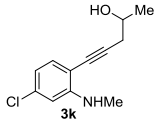
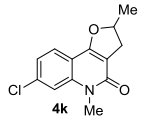


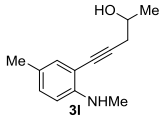
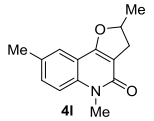
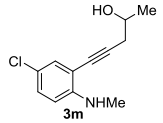
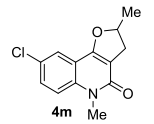
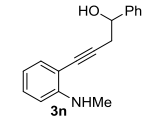
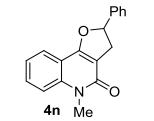
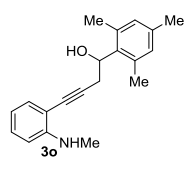
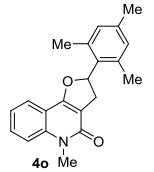
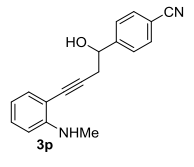
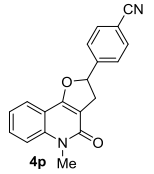
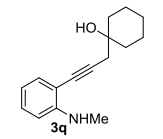
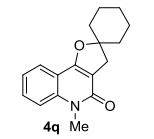
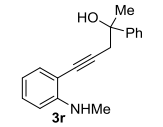
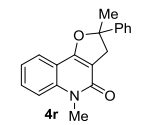
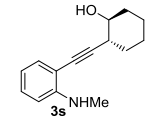
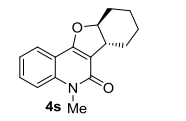
Figure 3 Molecular structure of (6b*RS*,10a*SR*)-5-methyl-6b,7,8,9,10,10a-hexahydrobenzofuro[3,2-*c*]quinolin-6(5*H*)-one **4s**.

Table 2 Synthesis of 3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-ones **4** by PdI_2/KI-catalyzed oxidative carbonylative double cyclization of 4-(2-aminophenyl)-3-yn-1-ols **3**[a]



Entry	3	4	Yield of 4[b]/%
1[c]			70
2[d]	**3a**	**4a**	72
3	**3a**	**4a**	75
4[e]	**3a**	**4a**	55[f]
5[g]	**3a**	**4a**	54
6			72
7			73
8			60
9			64
10			72
11			80
12			82
13			73
14			88
15			80

Continued

Entry	3	4	Yield of 4[b]/%
16			89
17			82
18			75
19			72
20			76
21			73
22			71
23			73

[a] Unless otherwise noted, all reactions were carried out at 100 °C for 24 h in MeOH (0.10 mmol of **3** per mL of MeOH) under 60 atm of a 4 : 1 mixture of CO–air, in the presence of 0.33 mol% of PdI_2 and 3.3 mol% of KI. [b] Isolated yield based on starting **3**. [c] The reaction was carried out with 1 mol% of PdI_2 and 10 mol% of KI. [d] The reaction was carried out with 0.5 mol% of PdI_2 and 5 mol% of KI. [e] The reaction was carried out with 0.2 mol% of PdI_2 and 2 mol% of KI. [f] 5-Methyl-4,5-dihydropyrano[4,3-*b*]indol-1(3*H*)-one **5a** was also formed in 10% isolated yield. [g] The reaction was carried out with 0.2 mol% of PdI_2 and 2 mol% of KI and under 40 atm of a 1 : 7 mixture CO–air).

Conclusions

In conclusion, in this work we have studied the reactivity of 4-(2-aminophenyl)-3-yn-1-ols **3** under PdI_2/KI-catalyzed oxidative carbonylation conditions. In principle, these substrates could undergo divergent carbonylative double cyclization pathways (*O*-cyclization followed by *N*-cyclocarbonylation or vice versa), leading to isomeric polycyclic heterocycles, namely, 3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one derivatives **4** and 4,5-dihydropyrano[4,3-*b*]indol-1(3*H*)-ones **5**, respectively.

We have found that, while under unoptimized conditions (involving, in particular, the use of MeCN as the solvent) the reaction afforded a mixture of products **4** and **5**, only dihydrofuroquinolinone **4** could be obtained when performing the process in MeOH as the solvent. Under the final optimized conditions, these compounds have been synthesized in fair to high yields (60%—89%) and with excellent turnover numbers (180—267 mol of product per mol of Pd) over 19 examples.

Our method thus represents a new and convenient one-step approach for the synthesis of a particularly important class of fused heterocycles[12] starting from readily available starting materials (substrates **3**, carbon monoxide, and oxygen) under catalytic conditions, with the one-step selective and sequential formation of three new bonds and two cycles.

Experimental

General methods: Solvent and chemicals were reagent grade and were used without further purification. All reactions were analyzed by TLC on silica gel 60 F_{254} and by GLC using capillary columns with polymethylsilicone + 5% phenylsilicone as the stationary phase. Column chromatography was performed on silica gel 60 (70—230 mesh) or neutral alumina (90—170). Evaporation refers to the removal of solvent under reduced pressure. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C on a 300 or 500 spectrometer in $CDCl_3$ as the solvent with Me_4Si as internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively. IR spectra were taken with an FT-IR spectrometer. Mass spectra were obtained using a GC-MS apparatus at 70 eV ionization voltage (normal resolution) and by electrospray ionization mass spectrometry (ESI-MS) (high resolution). HRMS spectra were recorded with an IT-ToF spectrometer (Shimadzu, UK) using an ESI source working in positive mode, and were recorded in the 150—450 m/z range in infusion mode at 5 μL/min with an average of 2 min and 20 ms accumulation on the ion trap. The LC-MS experimental conditions were as follows: N_2 was employed as desolvation gas at 300 °C and a flow rate of 1.5 L/min, curved desorption line (CDL) and heat block temperature of 200 °C. The detector and interface voltage was set at 1.60 and 4.5 kV, respectively.

General procedure for the synthesis of dihydrofuroquinolinones from 4-(2-aminophenyl)-3-yn-1-ols 3 (Table 2): A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (1.5 mg, 4.16×10^{-3} mmol), KI (6.9 mg, 4.16×10^{-2} mmol) and a solution of **1** (1.25 mmol; **3a**, 219.5 mg; **3b**, 237.0 mg; **3c**, 313.5 mg; **3d**, 236.0 mg; **3e**, 262.0 mg; **3f**, 236.8 mg; **3g**, 261.7 mg; **3h**, 236.5 mg; **3i**, 254.3 mg; **3j**, 253.9 mg; **3k**, 279.3 mg; **3l**, 253.4 mg; **3m**, 279.0 mg; **3n**, 314.2 mg; **3o**, 366.2 mg; **3p** (crude product, see the Supporting Information for details), 345.8 mg; **3q**, 304.5 mg; **3r**, 332.0 mg; **3s**, 286.4 mg) in MeOH (12.5 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (48 atm) and air (12 atm). After being stirred at 100 °C for 24 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and products **4a–s** were purified by column chromatography on silica gel using as eluent 80 : 20 hexane-AcOEt (**4q** and **4s**); 70 : 30 hexane-AcOEt (**4r**); hexane-AcOEt from 70 : 30 to 0 : 100 (**4c**); hexane-AcOEt from 60 : 40 to 0 : 100 (**4h–o**) and hexane-AcOEt from 50 : 50 to 0 : 100 (**4a–b**, **4d–g** and **4p**).

5-Methyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4a). Yield: 189.4 mg, starting from 219.5 mg 4-(2-(methylamino)phenyl)but-3-yn-1-ol **3a** (75%; Table 2, entry 3). Pale yellow solid, mp = 117—118 °C. IR (KBr): ν = 1659 (s), 1620 (m), 1512 (m), 1420 (m), 1358 (w), 1250 (m), 1103 (m), 1003 (m), 910 (m), 779 (m), 748 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.68 (d, J = 7.8, 1H, H-9), 7.56—7.50 (m, 1H, H-7), 7.30 (dist d, J = 8.6, 1H, H-6), 7.22—7.16 (m, 1H, H-8), 4.77 (t, J = 9.3, 2H, OCH_2), 3.65 (s, 3H, NMe), 3.20 (t, J = 9.3, 3H, OCH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.9, 161.4, 140.5, 130.8, 122.9, 121.5, 114.5, 112.5, 108.3, 73.3, 29.0, 28.0; GC-MS: m/z = 201 (M^+, 100), 200 (93), 172 (12), 144 (20), 104 (12), 77 (13); HRMS-ESI (m/z): [$(M+H)^+$] calcd for $(C_{12}H_{12}NO_2)^+$: 202.0863; found, 202.0876. The spectroscopic data agreed with those reported.[16]

5-Ethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4b). Yield: 195.3 mg, starting from 237.0 mg of 4-(2-(ethylamino)phenyl)but-3-yn-1-ol **3b** (72%; Table 2, entry 6). Pale yellow solid, mp = 73—75 °C. IR (KBr): ν = 1651 (s), 1636 (m), 1620 (m), 1504 (w), 1420 (m), 1358 (w), 1265 (m), 1196 (w), 1150 (w), 1111 (m), 910 (m), 756 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.75 (d, J = 7.8, 1H, H-9), 7.60—7.53 (m, 1H, H-7), 7.39 (dist d, J = 8.7, 1H, H-6), 7.24—7.18 (m, 1H, H-8), 4.81 (t, J = 9.3, 2H, OCH_2), 3.36 (q, J = 7.1, 3H, NCH_2), 3.25 (t, J = 9.3, 3H, OCH_2CH_2), 1.34 (t, J = 7.1, 3H, NCH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.0, 161.0, 139.5, 130.9, 123.2, 121.4, 114.4, 112.9, 108.4, 73.4, 36.8, 28.0, 13.1; GC-MS: m/z = 215 (M^+, 100), 214 (83), 187 (81), 186 (85), 170 (30), 130 (26); HRMS-ESI (m/z): [$(M+H)^+$] calcd for $(C_{13}H_{15}NO_2)^+$: 216.1019; found, 216.1012.

5-Benzyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4c). Yield: 252.0 mg, starting from 313.5 mg of 4-(2-(benzylamino)phenyl)but-3-yn-1-ol **3c** (73%; Table 2, entry 7). Pale yellow solid, mp = 155—156 °C. IR (KBr): ν = 1657 (s), 1597 (w), 1504 (m), 1418 (w), 1256 (w), 1136 (m), 1084 (w), 1001 (w), 756 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, J = 7.8, 1H, H-9), 7.43—7.36 (m, 1H, H-7), 7.31—7.17 (m, 6H, aromatic), 7.17—7.11 (m, 1H, aromatic), 5.53 (s, br, NCH_2), 4.81 (t, J = 9.3, 2H, OCH_2), 3.29 (t, J = 9.3, 3H, OCH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.0, 161.0, 139.5, 136.5, 130.4, 128.2, 126.6, 126.1, 122.6, 121.2, 114.9, 112.4, 107.7, 73.0, 44.9, 27.5; GC-MS: m/z = 277 (M^+, 100), 276 (98), 200 (16), 171 (40), 130 (0), 115 (8), 91 (80); HRMS-ESI (m/z): [$(M+H)^+$] calcd for $(C_{18}H_{16}NO_2)^+$: 278.1176; found, 278.1205.

5,7-Dimethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4d). Yield: 162.0 mg, starting from 236.0 mg of 4-(4-methyl-2-(methylamino)phenyl)but-3-yn-1-ol **3d** (60%; Table 2, entry 8). Pale yellow solid, mp = 170—172 °C. IR (KBr): ν = 1659 (s), 1628 (s), 1605 (s), 1420 (w), 1150 (w), 1058 (m), 895 (m), 756 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 (d, J = 8.0, 1H, H-9), 7.13 (s, 1H, H-6), 7.03 (dist d, J = 8.0, 1H, H-8), 4.78 (t, J = 9.2, 2H, OCH_2), 3.66 (s, 3H, NMe), 3.21 (t, J = 9.2, 3H, OCH_2CH_2) 2.49 (s, 3H, Me at C-7); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.1, 161.5, 141.5, 140.7, 123.0, 122.8, 114.7, 110.3, 107.3, 73.3, 29.0, 27.9, 22.4; GC-MS: m/z = 215 (M^+, 100), 214 (82), 186 (12), 158 (20), 118 (12); HRMS-ESI (m/z): [$(M+H)^+$] calcd for $(C_{13}H_{15}NO_2)^+$: 216.1019; found, 216.1010.

7-Chloro-5-methyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4e). Yield: 188.0 mg, starting from 262.0 mg of 4-(4-chloro-2-(methylamino)phenyl)but-3-yn-1-ol **3e** (64%; Table 2, entry 9). Pale yellow solid, mp = 187—189 °C. IR (KBr): ν = 1659 (s), 1589 (m), 1420 (w), 1381 (m), 1096 (m), 1003 (w), 880 (m), 772 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (d, J = 8.3, 1H, H-9), 7.37 (s, 1H, H-6), 7.20 (dist d, J = 8.3, 1H, H-8), 4.82 (t, J = 9.2, 2H, OCH_2), 3.67 (s, 3H, NMe), 3.24 (t, J = 9.2, 3H, OCH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.7, 161.3, 141.3, 137.1, 124.2, 122.0, 114.6, 111.1, 108.6, 73.5, 29.2, 28.0; GC-MS: m/z = 237 [$(M+2)^+$, 34], 236 (44), 235 (M^+, 100), 234 (94), 206 (12), 178 (20), 138 (19), 115 (17); HRMS-ESI (m/z): [$(M+H)^+$] calcd for $(C_{12}H_{12}ClNO_2)^+$: 236.0473; found, 236.0452.

5,8-Dimethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4f). Yield: 194.5 mg, starting from 236.8 mg of 4-(5-methyl-2-(methylamino)phenyl)but-3-yn-1-ol **3f** (72%; Table 2, entry 10). Pale yellow solid, mp = 110—112 °C. IR (KBr): ν = 1659 (s), 1636 (s), 1574 (m), 1512 (w), 1435 (w), 1358 (w), 1250 (w), 802 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 (s, br, 1H, H-9), 7.36 (dist dd, J = 8.7, 2.0, 1H, H-7), 7.23 (dist d, J = 8.7, 1H, H-6), 4.78 (t, J = 9.3, 2H, OCH_2), 3.66 (s, 3H, NMe), 3.22 (t, J = 9.3, 3H, OCH_2CH_2) 2.41 (s, 3H, Me at C-8); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.8, 161.3, 138.6, 132.1, 131.2, 122.6, 114.4, 112.5, 108.3, 73.3, 29.0, 28.0, 20.6;

GC-MS: *m*/*z* = 215 (M^+, 100), 214 (94), 200 (10), 186 (13), 172 (9), 158 (20), 144 (10), 118 (14), 91 (18); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{13}H_{15}NO_2$)$^+$: 216.1019; found, 216.1019.

8-Chloro-5-methyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4g). Yield: 234.9 mg, starting from 261.7 mg of 4-(5-chloro-2-(methylamino)phenyl)but-3-yn-1-ol **3g** (80%; Table 2, entry 11). Pale yellow solid, mp = 174—175 °C. IR (KBr): *v* = 1659 (s), 1636 (s), 1504 (w), 1435 (w), 1250 (m), 1103 (m), 918 (w), 810 (w), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 7.65 (dist d, *J* = 2.3, 1H, H-9), 7.48 (dist dd, *J* = 9.0, 2.4, 1H, H-7), 7.26 (dist d, *J* = 9.1, 1H, H-6), 4.80 (t, *J* = 9.3, 2H, OCH_2), 3.65 (s, 3H, NMe), 3.22 (t, *J* = 9.3, 3H, OCH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 161.9, 161.0, 139.2, 131.1, 127.2, 122.3, 115.9, 113.5, 109.5, 73.5, 29.2, 28.0; GC-MS: *m*/*z* = 237 [(M+2)$^+$, 33], 236 (41), 235 (M^+, 100), 234 (83), 206 (11), 178 (14), 138 (14), 115 (11); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{12}H_{12}ClNO_2$)$^+$: 236.0473; found, 236.0450.

2,5-Dimethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4h). Yield: 221.0 mg, starting from 236.5 mg of 5-(2-(methylamino)-phenyl)pent-4-yn-2-ol **3h** (82%; Table 2, entry 12). Pale yellow solid, mp = 84—86 °C. IR (KBr): *v* = 1651 (s), 1620 (s), 1589 (m), 1504 (w), 1458 (w) 1420 (m), 1358 (m), 1250 (m), 1157 (w), 1103 (m), 1034 (m), 756 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 74 (dd, *J* = 7.8, 1.1, 1H, H-9), 7.58—7.52 (m, 1H, H-7), 7.35 (d, *J* = 8.6, 1H, H-6), 7.25—7.17 (m, 1H, H-8), 5.24—5.13 (m, 1H, O*CH*CH_3), 3.69 (s, 3H, NMe), 3.36 (dist dd, *J* = 15.2, 9.6, 1H, C*H*HCHCH_3), 2.83 (dd, *J* = 15.2, 7.1, 1H, CH*H*CHCH_3), 1.54 (d, *J* = 6.3, 3H, CHCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 162.2, 161.6, 140.6, 138.8, 123.1, 121.5, 114.5, 112.8, 107.9, 82.6, 35.1, 29.1, 22.1; GC-MS: *m*/*z* = 215 (M^+, 75), 200 (100), 186 (5), 144 (7), 104 (6), 77 (10); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{13}H_{15}NO_2$)$^+$: 216.1019; found, 216.1015.

2-Ethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4i). Yield: 210.2 mg, starting from 254.3 mg of 6-(2-(methylamino)phenyl)hex-5-yn-3-ol **3i** (73%; Table 2, entry 13). Pale yellow solid, mp = 78—80 °C. IR (KBr): *v* = 1659 (s), 1597 (m), 1512 (w9, 1458 (m), 1420 (m), 1357 (m), 1296 (w), 1250 (m), 1103 (m), 903 (w), 756 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 7.75 (d, *J* = 7.8, 1H, H-9), 7.57—7.52 (m, 1H, H-7), 7.34 (dist d, *J* = 8.6, 1H, H-6), 7.24—7.17 (m, 1H, H-8), 5.04—4.95 (m, 1H, O*CH*CH_2CH_3), 3.68 (s, 3H, NMe), 3.30 (dist dd, *J* = 15.3, 9.8, 1H, C*H*HCHCH_2CH_3), 2.88 (dd, *J* = 15.3, 7.4, 1H, CH*H*CHCH_2CH_3), 1.95—1.85 (m, 1H, CHC*H*HCH_3), 1.85—1.74 (m, 1H, CHCH*H*CH_3), 1.06 (t, *J* = 7.4, 3H, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 161.2, 161.1, 139.0, 130.8, 127.2, 122.4, 115.9, 113.7, 109.0, 82.8, 35.1, 29.2, 22.1; GC-MS: *m*/*z* = 229 (M^+, 61), 200 (100), 188 (16) 144 (9), 104 (8), 77 (13); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{14}H_{17}NO_2$)$^+$: 230.1176; found, 230.1157.

2,5,7-Trimethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4j). Yield: 252.0 mg, starting from 253.9 mg of 5-(4-methyl-2-(methylamino)phenyl)pent-4-yn-2-ol **3j** (88%; Table 2, entry 14). Pale yellow solid, mp = 79—80 °C. IR (KBr): *v* = 1651 (s), 1605 (m), 1558 (w), 1520 (w), 1420 (m), 1358 (w), 1250 (w), 1157 (w), 1103 (m), 1034 (w), 880 (w), 810 (m), 756 (m), cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 7.59 (dist d, *J* = 8.0, 1H, H-9), 7.12 (s, 1H, H-6), 7.01 (d, *J* = 7.9, 1H, H-8), 5.22—5.07 (m, 1H, O*CH*CH_3), 3.65 (s, 3H, NMe), 3.33 (dist dd, *J* = 15.1, 9.6, 1H, C*H*HCHCH_3), 2.80 (dist dd, *J* = 15.1, 7.2, 1H, CH*H*CHCH_3), 2.48 (s, 3H, Me at C-7), 1.52 (d, *J* = 6.3, 3H, CHCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 162.3, 161.7, 141.4, 140.8, 122.9, 114.7, 110.5, 106.9, 82.5, 35.1, 29.0, 22.3, 22.1; GC-MS: *m*/*z* = 229 (M^+, 59), 214 (100), 186 (4), 158 (6), 115 (5), 91 (8); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{14}H_{16}NO_2$)$^+$: 230.1176; found, 230.1164.

7-Chloro-2,5-dimethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4k). Yield: 251.2 mg, starting from 279.3 mg of 5-(4-chloro-2-(methylamino)phenyl)pent-4-yn-2-ol **3k** (80%; Table 2, entry 15). Pale yellow solid, mp = 159—160 °C. IR (KBr): *v* = 1651 (s), 1558 (m), 1505 (m), 1420 (w), 1381 (m), 1288 (m), 1250 (w), 1211 (w), 1103 (m), 1034 (w), 995 (w), 756 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 7.61 (dist dd, *J* = 8.3, 2.8, 1H, H-9), 7.31 (s, br, 1H, H-6), 7.19—7.13 (m, 1H, H-8), 5.24—5.14 (m, 1H, C*H*CH_3), 3.63 (s, 3H, NMe), 3.34 (dist dd, *J* = 15.3, 9.7, 1H, C*H*HCHCH_3), 2.80 (dd, *J* = 15.3, 7.2, 1H, CH*H*CHCH_3), 1.54 (d, *J* = 6.3, 3H, CHCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 161.7, 161.3, 141.3, 136.9, 124.2, 121.9, 114.5, 111.1, 108.0, 82.8, 35.1, 29.1, 22.1; GC-MS: *m*/*z* = 251 [(M+2)$^+$, 22], 249 (M^+, 64), 236 (31), 234 (100), 178 (4); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{13}H_{13}ClNO_2$)$^+$: 250.0629; found, 250.0655.

2,5,8-Trimethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4l). Yield: 255.0 mg, starting from 253.4 mg of 5-(5-methyl-2-(methylamino)phenyl)pent-4-yn-2-ol **3l** (89%; Table 2, entry 16). Pale yellow solid, mp = 78—80 °C. IR (KBr): *v* = 1659 (s), 1574 (w), 1443 (m), 1358 (w), 1211 (m), 1111 (m), 1034 (w), 810 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 7.53 (s, br, 1H, H-9), 7.37 (dist d, *J* = 8.6, 1H, H-7), 7.27—7.22 (m, 1H, H-6), 5.24—5.13 (m, 1H, C*H*CH_3), 3.67 (s, 3H, NMe), 3.36 (dist dd, *J* = 15.2, 9.6, 1H, C*H*HCHCH_3), 2.82 (dist dd, *J* = 15.2, 7.1, 1H, CH*H*CHCH_3), 2.41 (s, 3H, Me at C-8), 1.54 (d, *J* = 6.3, 3H, CHCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 162.0, 161.5, 138.7, 132.1, 131.2, 122.7, 114.4, 112.6, 107.9, 82.5, 35.2, 29.1, 22.1, 20.6; GC-MS: *m*/*z* = 229 (M^+, 62), 214 (100), 158 (6), 118 (6), 115 (6), 91 (12); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{14}H_{16}NO_2$)$^+$: 230.1176; found, 230.1155.

8-Chloro-2,5-dimethyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4m). Yield: 255.8 mg, starting from 279.0 mg of 5-(5-chloro-2-(methylamino)phenyl)pent-4-yn-2-ol **3m** (82%; Table 2, entry 17). Pale yellow solid, mp = 139—141 °C. IR (KBr): *v* = 1659 (s), 1566 (w), 1504 (w), 1435 (m), 1358 (m), 1258 (w), 1103 (m), 1034 (w), 887 (w), 772 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 7.69 (s, br, 1H, H-9), 7.49 (dist d, *J* = 8.7, 1H, H-7), 7.27 (dist d, *J* = 9.4, 1H, H-6), 5.25—5.15 (m, 1H, C*H*CH_3), 3.66 (s, 3H, NMe), 3.36 (dist dd, *J* = 15.4, 9.7, 1H, C*H*HCHCH_3), 2.82 (dist dd, *J* = 15.4, 7.2, 1H, CH*H*CHCH_3), 1.54 (d, *J* = 6.3, 3H, CHCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 161.2, 161.1, 139.0, 130.8, 127.2, 122.4, 115.9, 113.7, 109.0, 82.8, 35.1, 29.2, 22.1; GC-MS: *m*/*z* = 251 [(M+2)$^+$, 20], 249 (M^+, 64), 236 (33), 234 (100), 219 (5), 138 (7), 115 (6); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{13}H_{13}ClNO_2$)$^+$: 250.0629; found, 250.0621.

5-Methyl-2-phenyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4n). Yield: 260.6 mg, starting from 314.2 mg of 4-(2-(methylamino)phenyl)-1-phenylbut-3-yn-1-ol **3n** (75%; Table 2, entry 18). Pale yellow solid, mp = 95—96 °C. IR (KBr): *v* = 1659 (s), 1597 (m), 1504 (w), 1458 (w), 1420 (m), 1358 (m), 1288 (w), 1250 (m), 1157 (w), 1103 (m), 756 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 7.81 (d, *J* = 7.7, 1H, H-9), 7.62-7.55 (m, 1H, H-7), 7.45—7.30 (m, 6H, H-6 + Ph), 7.27—7.20 (m, 1H, H-8), 6.00 (dd, *J* = 10.1, 7.9, 1H C*H*Ph), 3.71 (s, 3H, NMe), 3.70 (dist dd, *J* = 15.5, 10.1, 1H, C*H*HCHPh), 3.26 (dd, *J* = 15.5, 7.9, 1H, CH*H*CHPh), ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 162.3, 161.2, 141.0, 140.7, 131.0, 128.8, 128.5, 125.9, 123.2, 121.7, 114.5, 112.4, 107.8, 86.5, 36.3, 29.1; GC-MS: *m*/*z* = 277 (M^+, 100), 260 (82), 246 (10), 260 (4), 115 (25), 77 (32); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{18}H_{16}NO_2$)$^+$: 278.1176; found, 278.1165. The spectroscopic data agreed with those reported.[17]

2-Mesityl-5-methyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4o). Yield: 287.8 mg, starting from 366.2 mg of 1-mesityl-4-(2-(methylamino)phenyl)but-3-yn-1-ol **3o** (72%; Table 2, entry 19). Pale yellow solid, mp = 194—195 °C. IR (KBr): *v* = 1651 (s), 1597 (m), 1504 (w), 1458 (w), 1419 (m), 1350 (w), 1288 (w), 1242 (m), 1157 (w), 1103 (m), 895 (m), 756 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 7.81—7.70 (m, 1H, H-9), 7.65—7.54 (m, 1H, H-7), 7.45—7.35 (m, 1H, H-6), 7.30—7.16 (m, 1H, H-8), 6.89 (s, 2H, mesityl ring), 6.45—6.31 (m, 1H, O*CH*CH_2), 3.74 (s, 3H, NMe), 3.64—3.51 (m, 1H, OCHC*H*H), 3.28—3.14 (m, 1H, OCHCH*H*), 2.31 (s, 6H, 2 Me on mesityl ring), 2.29 (s, 3H, Me on mesityl ring); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 162.3, 161.2, 140.8, 138.0, 136.8, 132.6, 131.0, 130.2, 123.1, 121.7, 114.6, 112.6, 108.8, 84.4, 34.3, 29.1, 20.8, 20.1; GC-MS: *m*/*z* = 319 (M^+, 100), 318 (44), 304 (39), 290 (8), 200 (29), 176 (14); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{21}H_{22}NO_2$)$^+$: 320.1645; found, 320.1630.

4-(5-Methyl-4-oxo-2,3,4,5-tetrahydrofuro[3,2-*c*]quinolin-2-

yl)benzonitrile (4p). Yield: 288.1 mg, starting from 345.8 mg of crude 4-(1-hydroxy-4-(2-(methylamino)phenyl)but-3-yn-1-yl)benzonitrile **3p** (76%; Table 2, entry 20). Pale yellow solid, mp = 212—213 °C. IR (KBr): ν = 2230 (m), 1659 (s), 1636 (m), 1597 (w), 1504 (w), 1420 (m), 1350 (w), 1288 (w), 1211 (w), 1157 (m), 926 (w), 841 (w), 756 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.82 (d, J = 7.8, 1H, H-9), 7.69 (dist d, J = 8.2, 2H, aromatic), 7.56—7.59 (m, 1H, H-7), 7.52 (dist d, J = 8.2, 2H, aromatic), 7.41 (dist d, J = 8.6, 1H, H-6), 7.30—7.24 (m, 1H, H-8), 6.06 (dd, J = 10.4, 7.5, 1H, OC*H*CH_2), 3.77 (dist dd, J = 15.5, 10.4, 1H, OCHC*H*H), 3.71 (s, 3H, NMe), 3.19 (dist dd, J = 15.5, 7.5, 1H, OCHCH*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.5, 160.5, 145.8, 140.3, 132.2, 130.8, 125.8, 122.5, 121.3, 117.9, 114.2, 111.8, 111.7, 106.9, 84.5, 36.0, 28.6; GC-MS: m/z = 302 (M^+, 100), 285 (47), 273 (18), 257 (6), 200 (95), 134 (16), 104 (19), 77 (29); HRMS-ESI (m/z): [(M+H)$^+$] calcd for $(C_{19}H_{15}N_2O_2)^+$: 303.1128; found, 303.1113.

5'-Methyl-3',5'-dihydro-4'*H*-spiro[cyclohexane-1,2'-furo[3,2-*c*]quinolin]-4'-one (4q). Yield 246.8 mg, starting from 304.5 mg of 1-(3-(2-(methylamino)phenyl)prop-2-yn-1-yl)cyclohexan-1-ol **3q** (73%; Table 2, entry 21). Pale yellow solid, mp = 115—116 °C. IR (KBr): ν = 2932 (s), 2855 (m), 1667 (s), 1651 (s), 1635 (s), 1597 (m), 1504 (w), 1420 (m), 1358 (m), 1288 (w), 1242 (w), 1103 (m), 1034 (w), 903 (w), 756 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.77 (d, J = 7.8, 1H, H-9), 7.58—7.51 (m, 1H, H-7), 7.35 (dist d, J = 8.5, 1H, H-6), 7.24—7.17 (m, 1H, H-8), 3.69 (s, 3H, NMe), 2.98 [s, 2H, O(C)CH_2], 1.96—1.87 (m, 2H, aliphatic), 1.87—1.77 (m, 2H, aliphatic), 1.77—1.68 (m, 2H, aliphatic), 1.60—1.45 (m, 4H, aliphatic); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.8, 161.4, 140.6, 130.7, 123.2, 121.2, 114.4, 113.1, 107.4, 92.8, 39.1, 37.3, 29.8, 25.0, 22.9; GC-MS: m/z = 269 (M^+, 88), 252 (30), 226 (88), 213 (12), 188 (100), 134 (21), 104 (10), 77 (19); HRMS-ESI (m/z): [(M+H)$^+$] calcd for $(C_{17}H_{20}NO_2)^+$: 270.1489; found, 270.1518.

2,5-Dimethyl-2-phenyl-3,5-dihydrofuro[3,2-*c*]quinolin-4(2*H*)-one (4r). Yield: 259.2 mg, starting from 332.0 mg of 5-(2-(methylamino)phenyl)-2-phenylpent-4-yn-2-ol **3r** (71%; Table 2, entry 22). Pale yellow solid, mp = 146—147 °C. IR (KBr): ν = 1659 (s), 1636 (s), 1597 (m), 1574 (w), 1504 (w), 1420 (m), 1404 (m), 1358 (m), 1288 (m), 1250 (m), 1188 (w), 1088 (m), 1057 (m), 1003 (w), 756 (m), 702 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.90 (dd, J = 7.8, 1.4, 1H, H-9), 7.60—7.55 (m, 1H, H-7), 7.50—7.45 (m, 2H, aromatic), 7.39—7.33 (m, 3H, aromatic), 7.30—7.23 (m, 2H, aromatic) 3.69 (s, 3H, NMe), 3.48 (dist d, J = 15.3, 1H, [O(C)C*H*H], 3.41 (dist d, J = 15.3, 1H, [O(C)CH*H*], 1.86 [s, 3H, CH_3(C)Ph]; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.3, 161.2, 145.7, 140.7, 130.9, 128.5, 127.4, 124.3, 123.1, 114.5, 112.7, 107.5, 92.8, 42.8, 29.5, 29.0; GC-MS: m/z = 291 (M^+, 44), 276 (100), 274 (64), 248 (10), 214 (23), 134 (11), 105 (12), 77 (26); HRMS-ESI (m/z): [(M+H)$^+$] calcd for $(C_{19}H_{18}NO_2)^+$: 292.1332; found, 292.1353. The spectroscopic data agreed with those reported.[17]

(6b*RS*,10a*SR*)-5-Methyl-6b,7,8,9,10,10a-hexahydrobenzofuro[3,2-*c*]quinolin-6(5*H*)-one (4s). Yield: 232.5 mg, starting from 286.4 mg of (1*RS*,2*SR*)-2-((2-(methylamino)phenyl)ethynyl)cyclohexan-1-ol **3s** (73%; Table 2, entry 23). Pale yellow solid, mp = 162—163 °C. IR (KBr): ν = 1643 (s), 1589 (w), 1450 (w), 1419 (w), 1381 (m), 1219 (w), 1150 (w), 1096 (m), 1026 (w), 934 (w), 756 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.77 (d, J = 6.5, 1H, H-9), 7.62—7.47 (m, 1H, H-7), 7.35 (dist d, J = 8.2, 1H, H-6), 7.25—7.15 (m, 1H, H-8), 4.14—4.0 (m, 1H, OCH), 3.68 (s, 3H, NMe), 3.01—2.85 (m, 1H, cyclohexyl ring), 2.85—2.71 (m, 1H, cyclohexyl ring), 2.50—2.35 (m, 1H, cyclohexyl ring), 2.07—1.95 (m, 1H, cyclohexyl ring), 1.95—1.79 (m, 2H, cyclohexyl ring), 1.58—1.30 (m, 3H, cyclohexyl ring); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.8, 161.6, 140.6, 130.8, 122.9, 121.5, 114.5, 113.1, 112.8, 92.7, 48.2, 30.5, 28.8, 28.5, 25.5, 24.6; GC-MS: m/z = 255 (M^+, 100), 226 (72), 212 (28), 188 (39), 147 (22), 122 (15), 77 (21); HRMS-ESI (m/z): [(M+H)$^+$] calcd for $(C_{16}H_{18}NO_2)^+$: 256.1332; found, 256.1308.

Oxidative carbonylation of 4-(2-(methylamino)phenyl)but-3-yn-1-ol 3a under unoptimized conditions leading to a mixture of 4a and 5a (Table 1, entry 1). A 50 mL stainless steel autoclave was charged in the presence of air with PdI_2 (8.0 mg, 2.2×10^{-2} mmol), KI (36.5 mg, 2.2×10^{-1} mmol) and a solution of **3a** (78.2 mg, 0.45 mmol) in CH_3CN (4.5 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (5 atm) and air (35 atm). After being stirred at 100 °C for 15 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and products **4a** and **5a** were purified by column chromatography on silica gel using as eluent hexane-AcOEt from 80 : 20 to 0 : 100 [order of elution: **5a** (40.5 mg, 45%), **4a** (19.1 mg, 21%)].

5-Methyl-4,5-dihydropyrano[4,3-*b*]indol-1(3*H*)-one (5a). Yellow solid, mp 59—61 °C. IR (KBr): ν = 1713 (s), 1697 (s), 1551 (w), 1489 (m), 1412 (w), 1319 (w), 1265 (m), 1204 (m), 1134 (s), 1088 (m), 972 (m), 910 (w), 779 (m), 748 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.07—7.95 (m, 1H, aromatic), 7.30—7.15 (m, 3H, aromatic), 4.46 (t, J = 6.1, 2H, OCH_2), 3.56 (s, 3H, NMe), 2.87 (t, J = 6.1, 2H, OCH_2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.6, 146.6, 137.4, 125.3, 123.0, 122.3, 120.4, 109.5, 101.4, 66.0, 30.0, 21.7; GC-MS: m/z = 201 (M^+, 100), 171 (69), 143 (72), 115 (23), 85 (19); HRMS-ESI (m/z): [(M+H)$^+$] calcd for $(C_{12}H_{12}NO_2)^+$: 202.0863; found, 202.0882.

Supporting Information

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