One-Pot Tandem Synthesis of Furo[3,2-*h*]quinolines by a Sonogashira Cross-Coupling and Cyclization Reaction Supported by Basic Alumina Under Microwave Irradiation

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Abstract: Acetylenic 8-quinolinols generated in situ by the Sonogashira cross-coupling reaction are efficiently converted into furo[3,2-*h*]quinolines by microwave-assisted, copper-catalyzed, intramolecular cyclization in the presence of basic alumina.

Key words: heterocycles, furoquinoline, cross-coupling, cyclizations, solid-phase synthesis, microwave irradiation

New versatile and efficient methods for the syntheses of carbocyclic and heterocyclic[1–2] systems in a single operation are attracting increasing attention on the part of organic chemists. Heteroannulation of acetylenic compounds bearing tethered nucleophilic substituents is one such method that allows the assembly of several flexible building blocks, and this reaction is considered a cornerstone in the design of processes for the rapid generation of libraries of small drug-like molecules for high-throughput screening.[3] The required acetylenic substrates can be assembled by alkenylation of terminal alkynes[4] (the sp^2–sp coupling reaction) with aryl or alkenyl halides or triflates in a Sonogashira cross-coupling reaction, which is one of the most versatile and widely used reactions for the formation of acetylene derivatives. There are numerous reports on classical and modified Sonogashira reactions,[5–8] and recently many bioactive heterocyclic molecules, e.g. benzo[*b*]furans,[9] furo[3,2-*b*]pyridines, and furo[2,3-*b*]pyridines,[10] have been synthesized by various metal-catalyzed coupling/cyclization processes using several inorganic or organic bases, such as potassium *tert*-butoxide, cesium carbonate, or triethylamine, in organic solvents.

The furoquinoline moiety is present in many biologically active molecules,[11] including natural products.[12] Such compounds have previously been prepared by multistep synthetic operations.[13] The biological importance of furoquinolines, coupled with our recent success in establishing a basic alumina-supported reaction for forming C–C bonds by Suzuki–Miyaura cross-coupling under microwave irradiation,[14] prompted us to attempt to use the method for rapid and efficient synthesis of the furoquinoline moiety from α-acetylene derivatives of hydroxyquinolines prepared by the Sonogashira cross-coupling reaction.

Because microwave-assisted reactions have several advantages in comparison with conventional solution-phase reactions, we contemplated applying such a process for the synthesis of furo[3,2-*h*]quinolines. In this communication, we focus on the use of basic alumina in a one-pot synthesis of furo[3,2-*h*]quinolines under environmentally friendly conditions by microwave irradiation on a solid support in the presence of copper(I) iodide as a catalyst. To the best of our knowledge, this is the first report of the synthesis of furo[3,2-*h*]quinolines by a copper-catalyzed coupling in conjunction with a cyclization reaction using basic alumina.

We envisaged using 7-halogenated 8-hydroxyquinolines to prepare various aryl acetylenes that could subsequently be used in a one-pot, two-step synthesis of furo[3,2-*h*]quinolines. At the outset, we chose readily available 5-chloro-8-hydroxy-7-iodoquinoline (**1a**) and phenylethyne as model reaction partners and evaluated the outcomes of various conditions under microwave irradiation. Systematic studies of the reaction in the presence of various palladium catalysts with copper(I) iodide as the cocatalyst in organic solvents containing various bases showed that a moderate yield (45%) was obtainable by performing the reaction in *N*,*N*-dimethylformamide (DMF) with palladium(II) acetate/triphenylphosphine as the catalyst and copper(I) iodide as the cocatalyst in the presence of triethylamine as the base. A prototype reaction without DMF gave a low yield (20%) of the product, whereas a similar reaction in DMF in the presence of copper(I) iodide and triethylamine in the absence of the palladium catalyst gave an increased yield of 57%. The efficacy of copper(I) iodide as catalyst prompted us to extend the study to examine the effects of various solid supports.

The results, which are summarized in Table 1, showed that whereas the use of magnesium oxide, titanium dioxide, or montmorillonite K10 as a solid support was unsatisfactory, activated carbon as solid support effected cycloisomerization after the Sonogashira cross-coupling reaction to yield 63% of the product within 6 min in the presence of copper(I) iodide as the catalyst (1 mol%) and triethylamine as the base (entry 10). Changing of template

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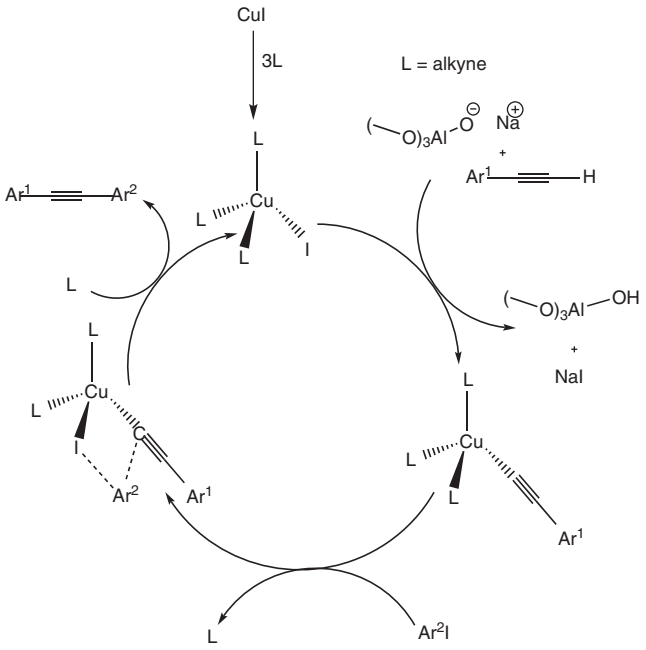
to silica gel increased the yield to 75% (entry 12), whereas acidic alumina gave a 78% yield (entry 14), neutral alumina gave an 84% yield (entry 16), and basic alumina gave a 90% yield (entry 18), even in the absence of triethylamine as a base (entries 20, 21, and 22). Note that reactions with triethylamine as a base in the absence of basic alumina gave very low yields, even with enhanced loadings of the catalyst (entries 24 and 25).

The good performance of basic alumina may be attributable to its role as a base that leads to the formation of copper acetylides through deprotonation of the alkyne by the oxide ions of the solid framework[14] as shown in Scheme 1. It is likely that Cu(I) coordinates with the alkynyl moiety of substrate, which then undergoes intramolecular nucleophilic attack by the oxygen atom of the 8-hydroxyquinoline moiety through 5-*endo*-dig cyclization in preference to the 4-*exo*-dig mode of cyclization that would be expected according to Baldwin's rules.[15] Finally, protodemetalation by hydroxy groups on the surface of the alumina affords the cycloisomerized product.



Scheme 1 Plausible pathway for the basic alumina-mediated Sonogashira cross-coupling reaction of **1a** and an aralkyne

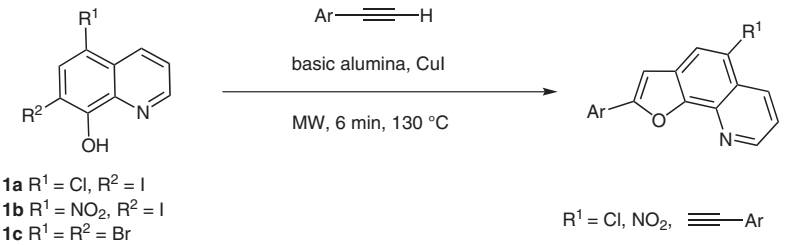
To examine the applicability of this method in the synthesis of other furo[3,2-*h*]quinolines, we examined the reactions of 5-nitro-7-iodo-8-hydroxyquinoline (**1b**), 5,7-dibromo-8-hydroxyquinoline (**1c**), or 5,7-diiodo-8-hydroxyquinoline (**1d**) with various aryl and heteroaryl alkynes. Excellent yields were obtained in all cases (Table 2). The electronic effects of substituents on the coupling efficiencies were negligible for both the aryl halide and the acetylenic reactant. As a result, excellent yields were obtained from the reaction of the various haloquinolines, regardless of the electronic properties of the electrophilic substituents (entries 1, 6, 10, and 14), although the presence of substituents at the *ortho* or *para* positions in phenylethyne reactants reduced the yield slightly (entries 3, 4, 7, 9, and 12). Heteroaromatic 2-pyridylethynes gave somewhat higher yields (entries 5 and 13).

Table 1 Optimization of Catalyst (CuI) Loadings on Various Solid Supports

Entry	Solid support[a]	Catalyst (mol%)	Temp (°C)	Time (min)	Yield[b] (%)
(A)	With Et_3N as base				
1	MgO	1.0	130	15	NR[c]
2	MgO	2.0	130	15	NR
3	TiO_2	1.0	130	6	30
4	TiO_2	2.0	130	6	30
5	montmorillonite K10	1.0	130	6	38
6	montmorillonite K10	2.0	130	15	38
7	activated carbon	1.0	90	8	50
8	activated carbon	1.0	130	8	52
9	activated carbon	1.0	110	8	63
10	activated carbon	1.0	130	6	63
11	activated carbon	2.0	130	6	63
12	silica gel	1.0	130	6	75
13	silica gel	2.0	130	6	75
14	acidic alumina	1.0	130	6	78
15	acidic alumina	2.0	130	6	78
16	neutral alumina	1.0	130	6	84
17	neutral alumina	2.0	130	6	84
18	basic alumina	1.0	130	6	90
19	basic alumina	2.0	130	6	90
(B)	Without Et_3N:				
20	basic alumina	1.0	130	6	90
21	basic alumina	2.0	130	6	90
22	basic alumina	0.5	130	6	90
23	basic alumina	0.1	130	6	72
(C)	With Et_3N only:				
24	–	1.0	130	6	20
25	–	2.0	130	6	20

[a] All the reactions were performed by using **1a** (10 mmol) and phenylacetylene (10–30 mmol), with CuI as catalyst under microwave irradiation at 250 W.
[b] Isolated yield.
[c] NR = No reaction.

Table 2 Sonogashira Cross-Coupling Reaction and Subsequent Intramolecular Cyclization of 8-Hydroxyquinolines with Various Alkynes Under Microwave Irradiation



1a R^1 = Cl, R^2 = I
1b R^1 = NO_2, R^2 = I
1c R^1 = R^2 = Br
1d R^1 = R^2 = I

R^1 = Cl, NO_2, ≡—Ar

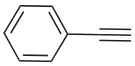
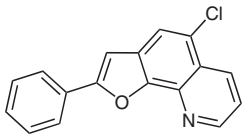
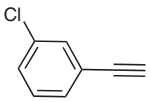
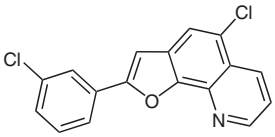
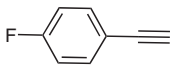
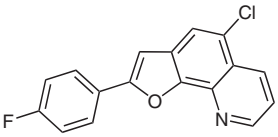
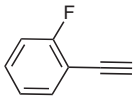
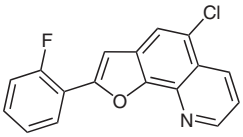
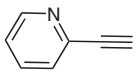
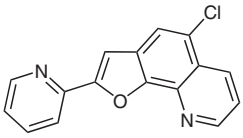
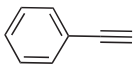
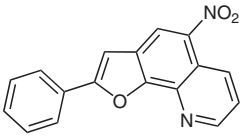
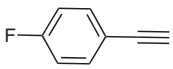
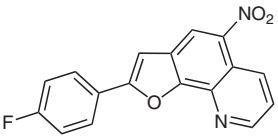
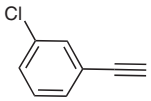
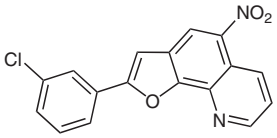
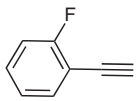
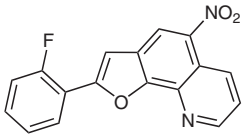
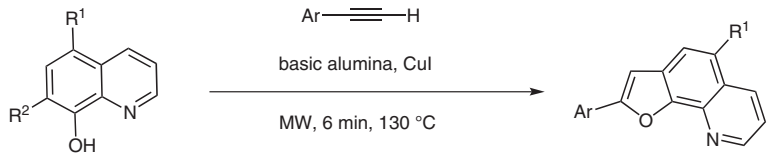
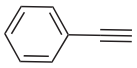
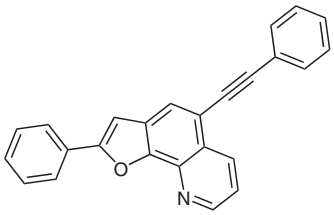
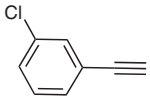
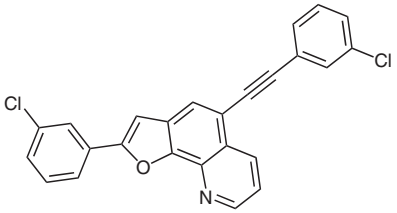
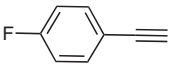
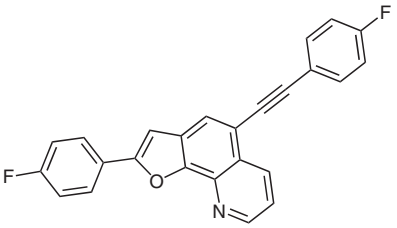
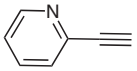
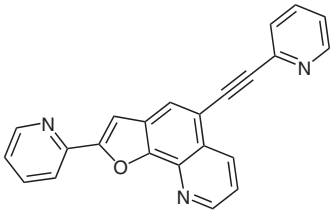
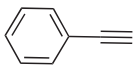
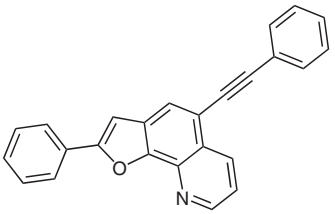
Entry	Quinoline[a]	Acetylene	Product[a]	Yield[b] (%)
1	**1a**		**2a** 	90
2	**1a**		**2b** 	92
3	**1a**		**2c** 	85
4	**1a**		**2d** 	88
5	**1a**		**2e** 	94
6	**1b**		**3a** 	92
7	**1b**		**3b** 	87
8	**1b**		**3c** 	93
9	**1b**		**3d** 	90

Table 2 Sonogashira Cross-Coupling Reaction and Subsequent Intramolecular Cyclization of 8-Hydroxyquinolines with Various Alkynes Under Microwave Irradiation (continued)



1a R^1 = Cl, R^2 = I
1b R^1 = NO_2, R^2 = I
1c R^1 = R^2 = Br
1d R^1 = R^2 = I

R^1 = Cl, NO_2, ≡—Ar

Entry	Quinoline[a]	Acetylene	Product[a]	Yield[b] (%)
10	**1c**		**4a** 	89
11	**1d**		**5a** 	91
12	**1d**		**5b** 	86
13	**1d**		**5c** 	93
14	**1d**		**4a** 	90

[a] Reaction conditions: basic alumina (500 mg), quinoline (10 mmol), aralkyne (10–30 mmol), CuI (0.5 mol%), microwave irradiation (MW), 130 °C, 6 min.
[b] Isolated yields. The products were characterized by mass spectrometry and by ^{1}H and ^{13}C NMR spectroscopy.

We also investigated the reusability of basic alumina for the reaction of **1a** with phenylethyne. When the alumina was washed with acetone and water and then calcined at 150 °C for five hours, the recovered basic alumina could be recycled three or four times with an insignificant change in its activity. To examine the advantages of using microwave irradiation, we also performed the reaction with **1a** and phenylethyne in an oil bath at 130 °C under otherwise identical reaction conditions. It is noteworthy that only a 30% yield of **2a** was obtained after 20 hours of

reaction, whereas a 90% yield was obtained after microwave irradiation for six minutes.

In summary, we have developed a concise and convergent protocol for preparing various substituted furo[3,2-*h*]quinolines by a one-pot process that involves sequential coupling and cyclization of halogenated 8-hydroxyquinolines with alkynes (both of which are readily available) in the presence of basic alumina under microwave irradiation. The operational simplicity, energy efficiency, and general applicability of the procedure, as well as reusability of the basic alumina, are expected to ensure that of this chemistry will be extended to the synthesis of other heterocyclic compounds of interest.

IR spectra were recorded on a Jasco FTIR model 410 spectrophotometer. ^{1}H spectra were recorded in $CDCl_3$ with TMS as internal standard on a Bruker 300MHz and 600MHz DPX spectrometers operating at 300 and 600 Hz, respectively; the ^{13}C NMR were similarly recorded at 74.99 and 150 MHz, respectively. ESI (positive-ion) mass spectra were recorded an using LC-ESI-Q-TOF Micromass mass spectrometer. Microwave irradiation was performed by using a mono-mode Discover microwave reactor (CEM Corp., Matthews, NC, USA), which was used in the Sonogashira cross-coupling reaction and the subsequent intramolecular cyclization. All the chemicals (aralkynes, halogenated 8-hydroxyquinolines, basic alumina, and catalysts) were purchased from Sigma-Aldrich Co. (Milwaukee, WI, USA). Organic solvents for chromatographic purification were purchased from E. Merck (India) Ltd. (Mumbai, India), and were of analytical grade. All chromatographic purifications were performed with silica gel (100–200 mesh) obtained from SRL (New Delhi, India).

Products 2–5; General Procedure

$CHCl_3$ (10 mL) was added to a mixture of the halogenated 8-hydroxyquinoline (10 mmol) and basic alumina (500 mg) in a round-bottomed flask. The organic layer was evaporated to dryness under reduced pressure, and the solid mixture was stirred at r.t. for an additional 10–15 min to ensure efficient mixing. The aralkyne (10–30 mmol) and CuI (0.5 mol%) were added, the flask was fitted with a septum, and the mixture irradiated in the microwave reactor at 130 °C (250 W) for 6 min while the reaction was monitored by TLC. The mixture was then cooled and EtOAc (25 mL) was added, and the slurry was stirred at r.t. for 10 min. The mixture was vacuum filtered through a sintered glass funnel and the product was isolated by flash chromatography.

In the recycling experiment, the residue was washed successively with acetone (3 × 25 mL) and water (3 × 25 mL) and then calcined at 150 °C. The calcined material could be reused in further coupling reactions.

5-Chloro-2-phenylfuro[3,2-*h*]quinoline (2a)

Brown solid; yield: 90%; mp 125–126 °C; R_f = 0.50 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 2922, 2850, 1610, 1572, 1352 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.16 (s, 1 H), 7.39 (m, 1 H), 7.50 (m, 3 H), 7.85 (s, 1 H), 8.03 (d, J = 7.5 Hz, 2 H), 8.65 (dd, J_1 = 1.5 Hz, J_2 = 8.7 Hz, 1 H), 9.05 (dd, J_1 = 1.5 Hz, J_2 = 4.2 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 101.8 (CH), 120.2 (CH), 120.7 (CH), 123.7 (C), 125.2 (CH), 126.1 (C), 128.3 (C), 128.8 (CH), 128.9 (CH), 129.7 (C), 133.8 (CH), 136.8 (C), 148.2 (C), 150.7 (CH), 157.7 (C).

ESI-MS: *m/z* 280 [M + H]$^+$, 282 [M + 2 + H]$^+$, 302 [M + Na]$^+$, 304 [M + 2 + Na]$^+$.

HRMS (EI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_{10}ClNNaO$: 302.0349; found: 302.0290.

5-Chloro-2-(3-chlorophenyl)furo[3,2-*h*]quinoline (2b)

White solid; yield: 92%; mp 179–180 °C; R_f = 0.45 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 1732, 1579, 1509, 1467, 1437, 1404 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.10 (s, 1 H), 7.36 (m, 2 H), 7.52 (m, 1 H), 7.76 (s, 1 H), 7.82 (d, J = 6.9 Hz, 1 H), 7.96 (s, 1 H), 8.61 (d, J = 8.4 Hz, 1 H), 9.03 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 102.8 (CH), 120.3 (CH), 120.9 (CH), 123.2 (CH), 124.0 (C), 125.1 (CH), 126.4 (C), 128.2 (C), 128.9 (CH), 130.0 (CH), 131.2 (C), 134.0 (CH), 135.0 (C), 136.4 (C), 148.1 (C), 150.6 (CH), 156.2 (C).

ESI-MS: *m/z* 314 [M + H]$^+$, 316 [M + 2 + H]$^+$, 336 [M + Na]$^+$, 336 [M + 2 + Na]$^+$.

HRMS (EI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_9Cl_2NNaO$: 335.9959; found: 335.9980.

5-Chloro-2-(4-fluorophenyl)furo[3,2-*h*]quinoline (2c)

White solid; yield: 85%; mp 178–179 °C; R_f = 0.45 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 1603, 1495, 1444, 1354, 1233, 1158 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.04 (s, 1 H), 7.15 (t, J = 8.4 Hz, 2 H), 7.52 (dd, J_1 = 4.2 Hz, J_2 = 8.4 Hz, 1 H), 7.79 (s, 1 H), 7.97 (m, 2 H), 8.62 (d, J = 8.4 Hz, 1 H), 9.03 (br d, J = 3.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 101.4 (CH), 115.7 (CH), 116.0 (CH), 120.1 (CH), 120.7 (CH), 123.6 (C), 126.0 (C), 127.0 (CH), 127.1 (CH), 128.2 (C), 133.7 (CH), 136.6 (C), 148.0 (C), 150.6 (CH), 156.6 (C), 161.4 (C), 164.7 (C).

ESI-MS: *m/z* 298 [M + H]$^+$, 300 [M + 2 + H]$^+$, 320 [M + Na]$^+$, 322 [M + 2 + Na]$^+$.

HRMS (EI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_9ClFNNaO$: 320.0254; found: 320.0330.

5-Chloro-2-(2-fluorophenyl)furo[3,2-*h*]quinoline (2d)

Gray solid; yield: 88%; mp 159–160 °C; R_f = 0.45 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 2922, 2851,1618, 1581, 1487 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.21 (m, 5 H), 7.49 (m, 1 H), 7.65 (m, 1 H), 7.87 (s, 1 H), 8.33 (t, J = 7.5 Hz, 1 H), 8.66 (d, J = 8.1 Hz, 1 H), 9.05 (d, J = 3 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 106.9 (C), 107.1 (C), 115.9 (CH), 116.2 (C), 120.5 (C), 121.0 (CH), 124.1 (C), 124.4 (C), 124.5 (CH), 126.2 (C), 127.6 (CH), 128.6 (CH), 130.0 (CH), 130.2 (CH), 133.9 (CH), 136.8 (C), 150.7 (CH).

ESI-MS: *m/z* 298 [M + H]$^+$, 300 [M + 2 + H]$^+$, 320 [M + Na]$^+$, 322 [M + 2 + Na]$^+$.

HRMS (EI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_9ClFNNaO$: 320.0254; found: 320.0330.

5-Chloro-2-(pyridin-2-yl)furo[3,2-*h*]quinoline (2e)

Gray solid; yield: 94%; mp 191–192 °C; R_f = 0.55 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 2924, 2852, 1610, 1573, 1356 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.29 (m, 1 H), 7.57 (dd, J_1 = 4.2 Hz, J_2 = 8.4 Hz, 1 H), 7.62 (s, 1 H), 7.83 (td, J_1 = 1.8 Hz, J_2 = 7.8

Hz, 1 H), 7.92 (s, 1 H), 8.24 (d, J = 7.8 Hz, 1 H), 8.69 (m, 2 H), 9.07 (dd, J_1 = 4.2 Hz, J_2 = 1.2 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 105.2 (CH), 120.2 (CH), 120.8 (CH), 121.2 (CH), 123.4 (CH), 124.4 (C), 126.5 (C), 128.2 (C), 134.0 (CH), 136.9 (C), 137.0 (CH), 148.7 (C), 148.8 (C), 149.9 (CH), 150.8 (CH), 157.0 (C).

ESI-MS: *m/z* 281 $[M + H]^+$, 283 $[M + 2 + H]^+$, 303 $[M + Na]^+$, 305 $[M + 2 + Na]^+$.

HRMS (EI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{10}ClN_2O$: 281.0482; found: 281.0436.

5-Nitro-2-phenylfuro[3,2-*h*]quinoline (3a)
Yellow solid; yield: 92%; mp 189–190 °C; R_f = 0.50 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 1565, 1525, 1504, 1407, 1316 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47 (m, 4 H), 7.65 (m, 1 H), 8.03 (d, *J* = 6.9 Hz, 2 H), 8.69 (s, 1 H), 9.12 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 102.3 (CH), 119.2 (C), 120.1 (CH), 122.5 (CH) 125.3 (CH), 126.0 (C), 128.8 (CH), 129.6 (CH), 133.0 (CH), 135.4 (C), 141.7 (C), 151.1 (CH), 151.8 (C), 159.2 (C).

ESI-MS: *m/z* 291$[M + H]^+$, 313 $[M + Na]^+$.

HRMS (EI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{10}N_2NaO_3$: 313.0589; found: 313.0547.

2-(4-Fluorophenyl)-5-nitrofuro[3,2-*h*]quinoline (3b)
Yellow solid; yield: 87%; mp 202–203 °C; R_f = 0.50 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 1606, 1527, 1499, 1409, 1314 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.23 (m, 3 H), 7.67 (dd, J_1 = 4.2 Hz, J_2 = 8.4 Hz, 1 H), 8.03 (td, J_1 = 2.4 Hz, J_2 = 5.4 Hz, 2 H), 8.70 (s, 1 H), 9.13 (m, 2 H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 102.2 (C), 116.2 (CH), 119.4 (C), 121.4 (CH), 125.4 (CH), 126.2 (C), 127.5 (CH), 133.2 (CH), 135.6 (CH), 142.0 (C), 151.4 (CH), 152.0 (C), 158.6 (C), 162.7 (C), 164.4 (C).

ESI-MS: *m/z* 331 $[M + Na]^+$.

HRMS (EI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_9FN_2NaO_3$: 331.0495; found: 331.0452.

2-(3-Chlorophenyl)-5-nitrofuro[3,2-*h*]quinoline (3c)
Yellow solid; yield: 93%; mp 200–201 °C. R_f = 0.45 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 2919, 2847, 1557, 1523, 1473 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30 (s, 1 H), 7.43 (m, 2 H), 7.67 (dd, J_1 = 3.9 Hz, J_2 = 7.2 Hz, 1 H), 7.88 (d, *J* = 6.6 Hz, 1 H), 8.02 (s, 1 H), 8.68 (s, 1 H), 9.12 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 103.5 (CH), 119.6 (C), 120.1 (CH), 122.8 (CH), 123.5 (CH), 125.3 (CH), 125.8 (C), 129.6 (CH), 130.2 (CH), 130.6 (C), 133.2 (CH), 135.2 (C), 135.6 (C), 142.1 (C), 151.4 (CH), 152.1 (C), 157.8 (C).

ESI- MS: *m/z* 325 $[M + H]^+$, 327 $[M + 2 + H]^+$, 347 $[M + Na]^+$, 349 $[M + 2 + Na]^+$.

HRMS (EI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_9ClN_2NaO_3$: 347.0199; found: 347.0222 $[M + Na]^+$.

2-Phenyl-5-(phenylethynyl)furo[3,2-*h*]quinoline (4a)
Brown solid; yield: 89% (from **1c**) or 90% (from **1d**); mp 165–166 °C; R_f = 0.48 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 2850, 1606, 1481, 1178, 1074 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.20 (s, 1 H), 7.41 (m, 4 H), 7.49 (t, *J* = 7.8 Hz, 2 H), 7.55 (dd, J_1 = 4.2 Hz, J_2 = 8.4 Hz, 1 H), 7.66 (dd, J_1 = 1.8 Hz, J_2 = 8.4 Hz, 2 H), 8.06 (m, 3 H), 8.83 (dd, J_1 = 1.8 Hz, J_2 = 8.4 Hz, 1 H), 9.06 (dd, J_1 = 1.8 Hz, J_2 = 4.8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 86.5 (C), 93.6 (C), 102.1 (C), 116.6 (C), 120.8 (CH), 123.1 (C), 124.8 (CH), 125.3 (CH), 126.6 (C), 128.4 (CH), 128.5 (CH), 128.6 (CH), 128.8 (CH), 129.0 (CH), 129.8 (C), 131.6 (CH), 135.4 (CH), 136.6 (C), 149.5 (CH), 150.6 (C), 157.7 (C).

ESI-MS: *m/z* 346 $[M + H]^+$, 368 $[M + Na]^+$.

HRMS (EI): *m/z* $[M + Na]^+$ calcd for $C_{25}H_{15}NNaO$: 368.1051 $[M + Na]^+$; found: 368.1046.

2-(3-Chlorophenyl)-5-[(3-chlorophenyl)ethynyl]furo[3,2-*h*]quinoline (5a)
Gray solid; yield: 91%; mp 209–210 °C; R_f = 0.52 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 2206, 1597, 1506, 1472, 1403 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.21 (s, 1 H), 7.38 (m, 4 H), 7.53 (d, *J* = 7.2 Hz, 1 H), 7.57 (dd, J_1 = 4.2 Hz, J_2 = 8.4 Hz, 1 H), 7.64 (s, 1 H), 7.89 (d, *J* = 7.2 Hz, 1 H), 8.03 (s, 1 H), 8.05 (s, 1 H), 8.77 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1 H) 9.07 (dd, J_1 = 1.2 Hz, J_2 = 4.2 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 87.5 (C), 92.2 (C), 103.1 (CH), 116.3 (C), 121.1 (CH), 123.3 (CH), 124.7 (C), 125.1 (2 × CH), 125.2 (CH), 126.8 (C), 128.1 (C), 128.8 (CH), 128.9 (CH), 129.7 (C), 129.8 (CH), 130.1 (CH), 131.4 (CH), 134.4 (C), 135.0 (C), 135.2 (CH), 136.5 (C), 149.8 (C), 150.8 (CH), 156.2 (C).

ESI-MS: *m/z* 414 $[M + H]^+$, 416 $[M + 2 + H]^+$, 436 $[M + Na]^+$, 438 $[M + 2 + Na]^+$.

HRMS (EI): *m/z* $[M + Na]^+$ calcd for $C_{25}H_{13}Cl_2NNaO$: 436.0272; found: 436.0267.

2-(4-Fluorophenyl)-5-[(4-fluorophenyl)ethynyl]furo[3,2-*h*]quinoline (5b)
White solid; yield: 86%; mp 239–240 °C; R_f = 0.45 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 1602, 1502, 1405, 1339, 1299 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.11 (m, 3 H), 7.18 (t, *J* = 8.4 Hz, 2 H), 7.55 (dd, J_1 = 4.2 Hz, J_2 = 8.4 Hz, 1 H), 7.60–7.65 (m, 2 H), 8.23 (d, *J* = 9.6 Hz, 3 H), 8.75 (d, *J* = 8.4 Hz, 1 H), 9.06 (d, *J* = 3 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 86.1 (C), 92.5 (C), 101.8 (CH), 115.9 (CH), 116.1 (CH), 116.6 (C), 119.1 (C), 120.8 (CH), 124.8 (CH), 126.4 (C), 127.3 (CH), 128.4 (C), 133.6 (CH), 135.3 (CH), 136.6 (C), 149.5 (C), 150.7 (CH), 156.9 (C), 161.9 (C), 162.3 (C) 163.5 (C).

ESI-MS: *m/z* 382 $[M + H]^+$, 404 $[M + Na]^+$.

HRMS (EI): *m/z* $[M + Na]^+$ calcd for $C_{25}H_{13}F_2NNaO$: 404.0863; found: 404.0789.

2-(Pyridin-2-yl)-5-[(pyridin-2-yl)ethynyl]furo[3,2-*h*]quinoline (5c)
Gray solid; yield: 93%; mp 181–182 °C; R_f = 0.45 (20% PE–EtOAc).

IR (KBr, ν_{max}) = 2208, 1581, 1506, 1467, 1425, 1341 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (m, 2 H), 7.56 (m, 3 H), 7.74 (m, 2 H), 8.09 (s, 1 H), 8.17 (m, 1 H), 8.65 (br s, 2 H), 8.80 (d, *J* = 7.8 Hz, 1 H), 9.02 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 86.0 (C), 92.8 (C), 105.3 (CH), 115.6 (C), 120.0 (CH), 121.1 (CH), 122.8 (CH), 123.1 (CH), 126.0

(CH), 126.9 (C), 127.1 (CH), 127.8 (C), 135.2 (CH), 136.1 (CH), 136.2 (C), 136.6 (CH), 143.0 (C), 148.3 (C), 149.6 (CH), 149.9 (CH), 150.0 (C), 150.5 (CH), 156.7 (C).

ESI-MS: *m/z* 348 $[M + H]^+$, 370 $[M + Na]^+$.

HRMS (EI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{14}N_3O$: 348.1137 $[M + H]^+$; found: 348.1119: *m/z* $[M + Na]^+$ calcd for $C_{23}H_{13}NaN_3O$: 370.0956; found: 370.0952.

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