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Efficient synthesis of isoquinolines and pyridines *via* copper(I)-catalyzed multi-component reaction†

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A wide range of 3-substituted isoquinolines, steroidal pyridines, 5,6-dihydrobenzo[*f*]isoquinolines and 1,6-naphthyridine were synthesized in good yield *via* a ligand-free copper-catalyzed three-component reaction of β-halovinyl/aryl aldehyde, aromatic/aliphatic terminal alkyne and *tert*-butylamine/benzamidine in DMF under microwave irradiation. A catalyst-free reaction of *ortho*-alkynyl aryl/vinyl aldehydes with benzamidine under microwave irradiation also provided the 3-substituted isoquinoline and substituted pyridine derivatives in excellent yield.

Introduction

A reaction where one catalyst promotes more than one chemical transformation is always advantageous because this reaction eliminates the isolation of intermediates as well as forming several bonds from readily available starting materials.[1] On the other hand, multi-component reactions are recognized as powerful tools for the synthesis of organic compounds, since the products are formed in a single step and the diversity of the products is maintained by simply varying the starting materials.[2]

3-Aryl-substituted isoquinolines are of great pharmaceutical importance due to their wide range of biological activities.[3] They also constitute the building blocks of numerous biologically important natural products.[4] Some of the biologically active 3-arylisoquinoline derivatives are shown in Fig. 1. Synthesis of other pyridine annulated molecules such as steroidal pyridines,[5a–f] 5,6-dihydrobenzo[*f*]isoquinolines[5g] and 1,6-naphthyridine derivatives[5h] has received considerable attention in the literature as a result of their biological and pharmaceutical importance.

3-Arylisoquinolines are synthesized by Bischler–Napieralski and Pictet–Spengler reactions which require either harsh conditions or tedious reaction procedures.[6] Pd-catalyzed annulation processes are widely used to synthesize many nitrogen heterocycles such as isoquinolines[7] and 5,6-dihydrobenzo[*f*]isoquinolines.[5g] In addition to Pd, other transition metals such as Ni,[8a] Zr[8b] and Ag[8c] are also used to synthesize 3-substituted isoquinoline derivatives. Although these methods are useful for the synthesis of 3-arylisoquinolines and pyridine derivatives, they have some disadvantages such as the stepwise synthesis of *tert*-butylimines from β-halovinyl aldehydes, followed by coupling reaction of imine intermediates with alkynes and then cyclization of the resultant *ortho*-alkynyl aryl/vinyl aldehydes in presence of other catalysts (typically CuI),[7a–f] long reaction time, and low yield of the annulated products with terminal mono-substituted acetylenes.[7a] Moreover, transition metal complexes used as the catalytic systems are inadequate for large-scale reaction owing to the high cost of these metal complexes. From a synthetic point of view, it is essential for a chemist to develop an improved and facile procedure to synthesize these important heterocycles using a less expensive and more sustainable catalyst. Our interests in the synthesis of biologically important heterocycles have encouraged us to re-investigate a catalytic synthesis version of these important *N*-heterocycles.[9] Herein, we wish to report a microwave-assisted and CuI-catalyzed three-component reaction of β-halovinyl aldehydes, terminal alkynes and *tert*-butylamine/benzamidine under ligand-free conditions for the synthesis of nitrogen heterocycles. This efficient synthesis of nitrogen heterocycles

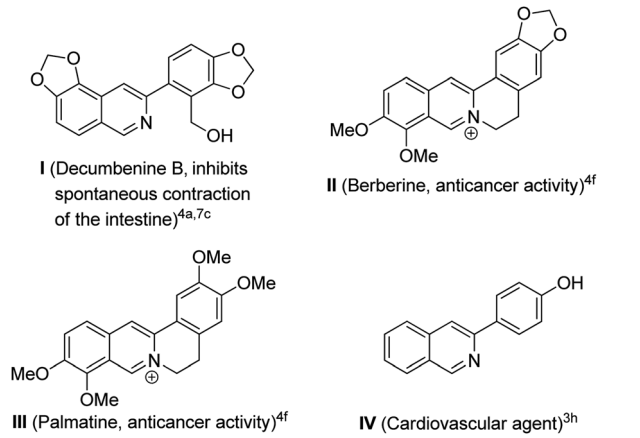

Fig. 1 Selected biologically active 3-arylisoquinoline derivatives.

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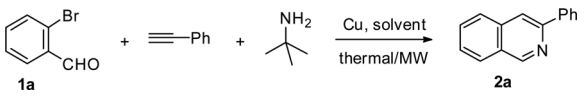
† Electronic supplementary information (ESI) available: Copies of ^{1}H NMR, ^{13}C NMR spectra of **2a–y** and MTT assay protocol. See DOI: 10.1039/c3ra46722h

Table 1 Effects of copper sources, solvents, amount of Cu(I) and source of energy on the reaction of 2-bromobenzaldehyde, phenylacetylene and *tert*-butylamine



Entry	Cu salt (mol%)	Solvent	Thermal/MW	Time	Yield[a] (%)
1	CuI (10)	DCE	120 °C	12 h	27
2	CuI (10)	DMF	120 °C	12 h	61
3	CuI (10)	Toluene	120 °C	12 h	25
4	CuI (10)	1,4-Dioxane	120 °C	12 h	40
5	CuBr (10)	DMF	120 °C	12 h	56
6	CuCl (10)	DMF	120 °C	12 h	44
7	$Cu(OAc)_2$ (10)	DMF	120 °C	12 h	<5
8	$Cu(OTf)_2$ (10)	DMF	120 °C	12 h	<5
9	—	DMF	120 °C	12 h	0
10	CuI (10)	DMF	720 W	4 min	92
11	CuI (5)	DMF	720 W	4 min	78
12	CuI (15)	DMF	720 W	4 min	91

[a] Isolated yield.

such as 3-substituted isoquinolines, steroidal pyridines, 5,6-dihydrobenzo[*f*]isoquinolines and 1,6-naphthyridine eliminates the above-mentioned problems with Pd catalysts.

Results and discussion

Initial studies were performed by using 2-bromobenzaldehyde **1a**, phenylacetylene and *tert*-butylamine as the model substrates, employing copper(I) iodide as the catalyst (Table 1) and 1,2-dichloroethane (DCE) as the solvent under thermal conditions at 120 °C. Gratifyingly, this reaction proceeded smoothly in DCE to afford regioselectively the annulated product **2a** in 27% yield in 12DCEh (entry 1, Table 1). Further investigation revealed that the solvent used played a significant role in this reaction. DMF was the most effective among the tested solvents and the yield of **2a** was increased to 61% (entry 2, Table 1), while there was sharp decrease in the yield to 25% (entry 3, Table 1) and 40% (entry 4, Table 1), when toluene and 1,4-dioxane were used respectively. Several other copper sources were also examined (entry 5–8, Table 1) and CuI turned out to be the best among others in view of the yield of the annulated product. The use of Cu(II) salts provided only trace amounts of the product **2a** (entry 7–8, Table 1) and no product was formed in the absence of Cu(I) (entry 9,Table 1).

At this stage of the investigation, we attempted first to find an efficient system for annulation of the β-bromophenyl aldehyde and terminal alkyne under thermal conditions. Following this we were interested in looking for more attractive reaction conditions in terms of time and reaction yield. Therefore, we examined the influence of microwave (MW) irradiation on the reaction of **1a**, phenylacetylene and *tert*-butylamine in the presence of 10 mol% CuI using the best solvent DMF. A substantial increase in the yield of **2a** (92%) along with a significant reduction in the reaction time from 12 h to 4 min was observed (entry 10, Table 1). We also explored the effect of catalyst loading on the yield of the reaction. When the quantity of CuI was reduced to 5 mol%, the yield decreased to 78% (entry 11, Table 1) under microwave irradiation. Increase of catalyst loading to 15 mol% did not affect the yield of the reaction (entry 12, Table 1).

With the optimized reaction conditions in hand (entry 10, Table 1), a series of terminal aliphatic and aromatic alkynes were tested under this condition with 2-bromobenzaldehyde to afford 3-substituted isoquinolines **2b–e** in 75–84% yields (entry 2–5, Table 2). In addition to 2-bromobenzaldehyde **1a**, we were pleased to observe that 2-chloroaryl aldehydes such as 6-chlorobenzo[1,3]dioxole-5-carbaldehyde (**1b**) also worked well for this reaction with the same catalyst loading to afford isoquinolines **2f–h** in 71–84% yields (entry 6–8, Table 2). It was interesting to note that these optimized reaction conditions were also effective for annulations of β-bromovinyl aldehydes to pyridine derivatives. For example, the annulations of steroidal β-bromovinyl aldehyde **1c**[9b] with different aryl and alkyl group-substituted terminal alkynes under optimized reaction conditions afforded the steroidal pyridines **2i–n** in 70–82% yields (entry 9–14, Table 2).

Similarly, β-bromovinyl aldehydes such as 1-bromo-3,4-dihydronaphthalene-2-carbaldehyde (**1d**)[9b] and 1-bromo-6-methoxy-3,4-dihydronaphthalene-2-carbaldehyde (**1e**)[9b] reacted with a range of aliphatic/aromatic terminal alkynes to afford 9,10-dihydrobenzo[*f*]isoquinolines **2o–s** in 72–83% yields (entry 15–19, Table 2). In order to find out the feasibility of the present methodology for the preparation of the 1,6-naphthyridine derivative, 2-chloro-5-(*p*-tolyl)pyridine-3-carbaldehyde (**1f**)[9c] was treated with phenylacetylene under similar reaction conditions to afford the expected product **2t** in 70% yield (entry 20, Table 2). It was observed that aliphatic terminal alkynes afforded relatively low yields of the annulated products in comparison with that of aromatic terminal alkynes. In all these cases, no dimerized by-product of the terminal alkyne was observed. Moreover, good functional-group compatibility was demonstrated with aromatic alkynes substituted with methyl, methoxy and fluoro groups and all proved to be effective annulation partners.

Recently, when we were trying to perform the synthesis of the eight-membered heterocycle **4** (Scheme 1) by the reaction of equimolar amounts of 2-(phenylethynyl)benzaldehyde (**3a**), benzamidine hydrochloride and triethylamine under microwave irradiation (720 W, 140 °C, 14 bar), we obtained only the isoquinoline derivative **2a** (89%) and benzonitrile from the reaction mixture after 5 min of reaction time. A literature search on similar cyclization reactions revealed various methods for the regioselective cyclization reaction of *ortho*-arylalkynyl aldehyde derivatives to isoquinolines. For example, (i) Gao and Zhang developed an efficient Ag(I)-catalyzed regioselective cyclization reaction of *ortho*-alkynylaryl aldehyde oxime derivatives to isoquinolines where benzaldehyde was formed as the side product (reaction (1), Scheme 2);[10] (ii) Larock *et al.* reported the synthesis of isoquinolines from *N*-*tert*-butyl-2-(1-alkynyl) arylaldimines in the presence of Lewis acid catalyst (Pd, Cu) where isobutene was eliminated (reaction (2), Scheme 2);[7a,b] (iii)

Table 2 CuI-catalyzed synthesis of pyridine-fused compounds[a]

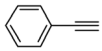
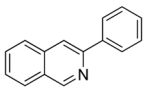
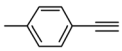
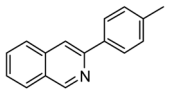
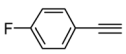
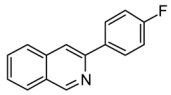
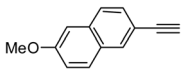
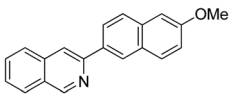
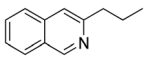
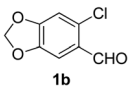
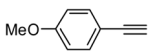
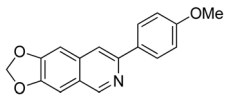
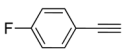
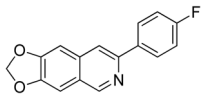
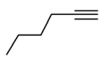
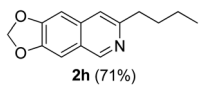
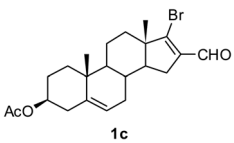
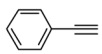
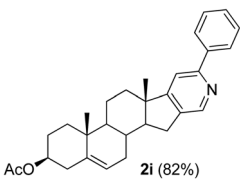
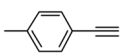
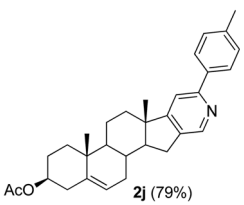
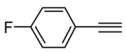
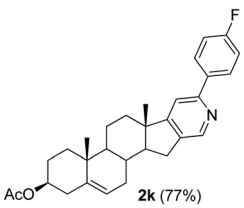
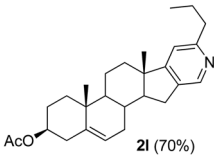
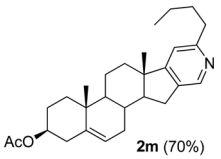
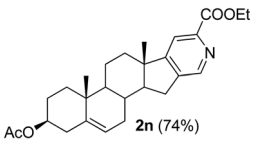
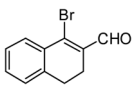
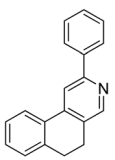
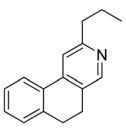
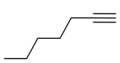
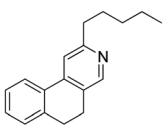
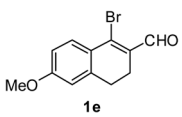
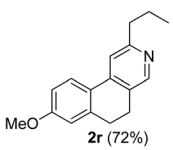
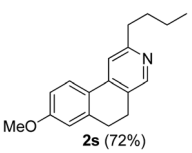
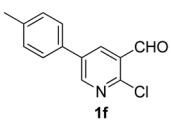
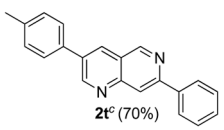
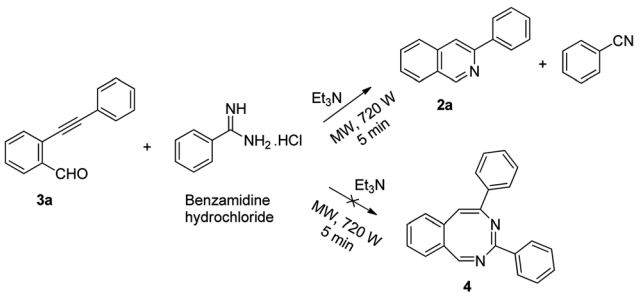
Entry	β-Halovinyl aldehyde	Alkyne	Product[b] (% Yield)
1	 **1a**		 **2a** (92%)
2	**1a**		 **2b** (84%)
3	**1a**		 **2c** (76%)
4	**1a**		 **2d** (79%)
5	**1a**		 **2e** (75%)
6	 **1b**		 **2f** (84%)
7	**1b**		 **2g** (78%)
8	**1b**		 **2h** (71%)
9	 **1c**		 **2i** (82%)
10	**1c**		 **2j** (79%)
11	**1c**		 **2k** (77%)

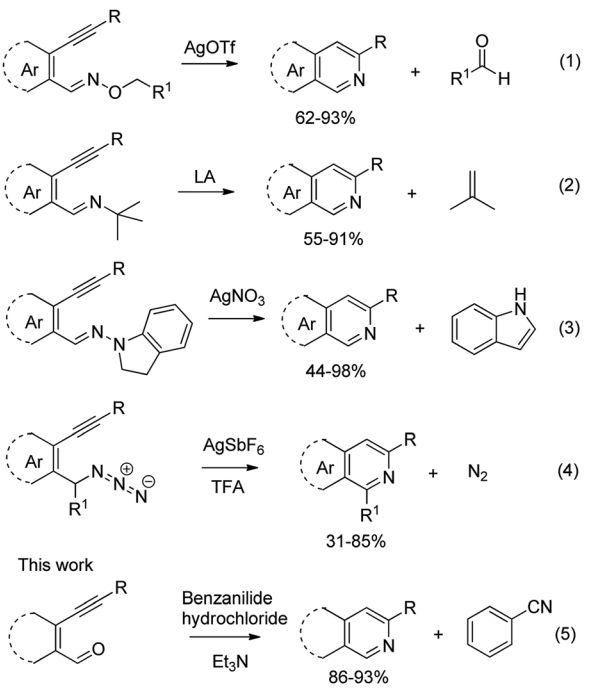
Table 2 (*Contd.*)

Entry	β-Halovinyl aldehyde	Alkyne	Product[b] (% Yield)
12	**1c**		 **2l** (70%)
13	**1c**		 **2m** (70%)
14	**1c**		 **2n** (74%)
15	 **1d**		 **2o** (83%)
16	**1d**		 **2p** (75%)
17	**1d**		 **2q** (73%)
18	 **1e**		 **2r** (72%)
19	**1e**		 **2s** (72%)
20	 **1f**		 **2t**[c] (70%)

[a] Conditions: 10 mol% CuI, β-halovinyl aldehyde (1 mmol), alkyne (1.1 mmol) and *tert*-butylamine (2 mmol) in DMF (1 mL) was irradiated in a closed vessel in a Synthos 3000 microwave reactor at 720 W (140 °C and 14 bar) for 4 min. [b] Refers to the amount of product isolated by chromatography. [c] The reaction was performed for 8 min.



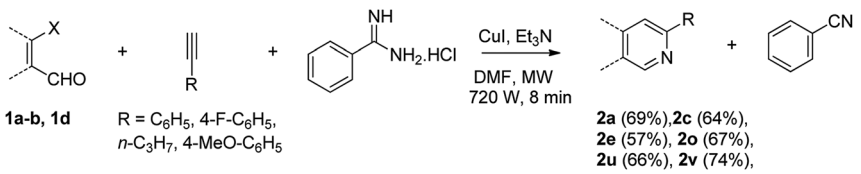
Scheme 1 Catalyst-free synthesis of isoquinolines.



Scheme 2 Synthesis of isoquinolines.

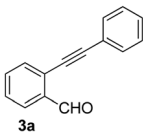
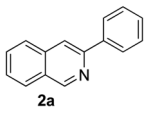
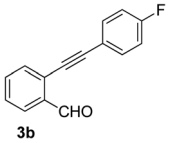
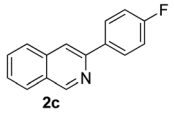
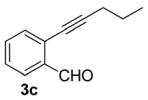
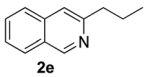
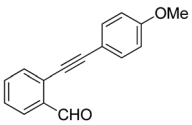
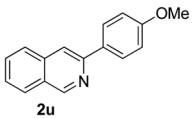
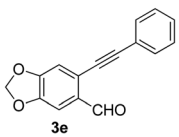
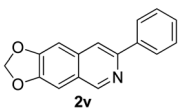
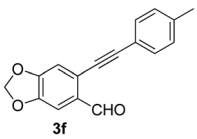
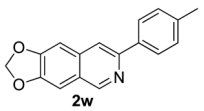
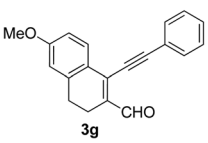
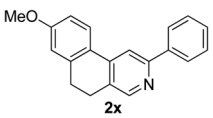
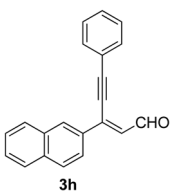
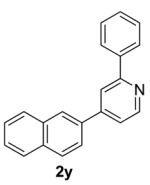
Ghavtadze *et al.* explored the silver nitrate-assisted cyclization of *N*-{2-[alkynyl(hetero)aryl]methylene}indolin-1-amines to give the pyridine derivatives where indole was liberated as a leaving group (reaction (3), Scheme 2);[11] (iv) Liang *et al.* studied the synthesis of substituted isoquinolines using 2-alkynylbenzyl azides as the starting material and Ag complex as the catalyst (reaction (4), Scheme 2).[8c] Our catalyst-free, simple method of cyclization of *ortho*-arylalkynyl aldehyde (**3a**) to the isoquinoline derivative **2a** using benzamidine (reaction (5), Scheme 2) prompted us to study the cyclization reaction with some more of the known *ortho*-arylalkynyl aldehydes (**3b–h**) which were prepared using a known procedure.[12] As shown in Table 3, various substituted *ortho*-alkynyl aryl/vinyl aldehydes (**3b–h**) were reacted with benzamidine hydrochloride in the presence of triethylamine under microwave irradiation to afford substituted isoquinolines **2a**, **2c**, **2e**, **2u–w** in 86–93% yield (entry 1–6, Table 3) and pyridine derivatives **2x,y** in 86–93% yield (entry 7–8, Table 3). Encouraged by these results we were interested to see the feasibility of the above copper-catalyzed three-component reaction using benzamidine hydrochloride in place of *tert*-butylamine as the source of nitrogen under microwave energy. We were delighted to see that this three-component reaction also worked well in the presence of benzamidine hydrochloride even though the yields of the products were less as compared to the above *tert*-butylamine reaction. Thus, the three-component reaction of β-haloaryl aldehydes **1a**, **1b**, **1d** with phenylacetylene and benzamidine hydrochloride provided isoquinoline derivatives **2a** (69%), **2v** (74%) and **2o** (67%) respectively under microwave irradiation (720 W, 140 °C, 14 bar, 8 min) in the presence of triethylamine (Scheme 3). We also performed the multi-component reactions of **1a** and benzamidine hydrochloride with 4-fluorophenylacetylene, *n*-propylacetylene and 4-methoxyphenylacetylene under the above reaction conditions to afford compounds **2c** (64%), **2e** (57%) and **2u** (66%) respectively (Scheme 3).

Based on our findings and literature information,[13] a plausible mechanism for the tandem reaction is proposed as shown in Scheme 4. The formation of a π-complex between the Cu(I) ion and the triple bond in the presence of the base *tert*-buylamine activates the triple bond towards deprotonation to form copper(I) acetylide **5a**. Subsequently, oxidative addition of this copper(I) acetylide **5a** with β-halovinyl aldehyde in the presence of *tert*-butylamine generates probably copper(III) imine species **5b**,[13a(Scheme 29),d] which on reductive elimination produces copper-coordinated intermediate **5c**. The intermediate **5c** undergoes 6-*endo*-dig cyclization to provide regioselectively the iminium intermediate **5d**. Fragmentation of the *tert*-butyl group of **5d** to relieve the strain resulting from interaction of the *tert*-butyl group with the substituent present in the *ortho*-position, followed by protonation, leads to the formation of compound **2** with the liberation of Cu(I) catalyst.[14] Furthermore, a possible mechanism of cyclization of compound **3** in the presence of benzamidine hydrochloride is shown in Scheme 5. Benzamidine hydrochloride forms imine **5e** with aldehyde **3** in presence of base triethylamine. The 6-*endo*-dig-cyclization of **5e** and subsequent C–N bond cleavage lead to the formation of compound **2** and benzonitrile. The formation of benzonitrile was proved by taking thin layer chromatography of the crude



Scheme 3 Multicomponent synthesis of 3-substituted isoquinolines and substituted pyridines.

Table 3 Catalyst-free synthesis of 3-substituted isoquinolines and substituted pyridines[a]

Entry	*ortho*-Alkynyl aryl/vinyl aldehydes	Product	Yield[b] (%)
1	 3a	 2a	89
2	 3b	 2c	87
3	 3c	 2e	86
4	 3d	 2u	93
5	 3e	 2v	90
6	 3f	 2w	89
7	 3g	 2x	86
8	 3h	 2y	93

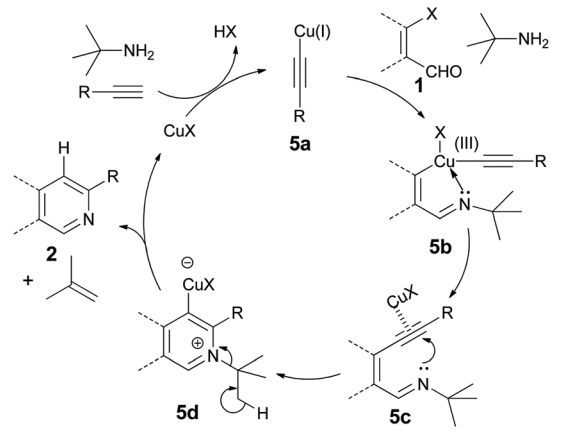
[a] Conditions: *ortho*-alkynyl aryl/vinyl aldehydes (1 mmol), benzamidine hydrochloride (1.1 mmol) and triethylamine (1.1 mmol) was irradiated in a closed vessel in a Synthos 3000 microwave reactor at 720 W (140 °C and 14 bar) for 5 min. [b] Refers to the amount of product isolated by chromatography.

reaction mixture and confirmed by the presence of the molecular ion peak $[M^+]$ at m/z 103 in GC-MS.

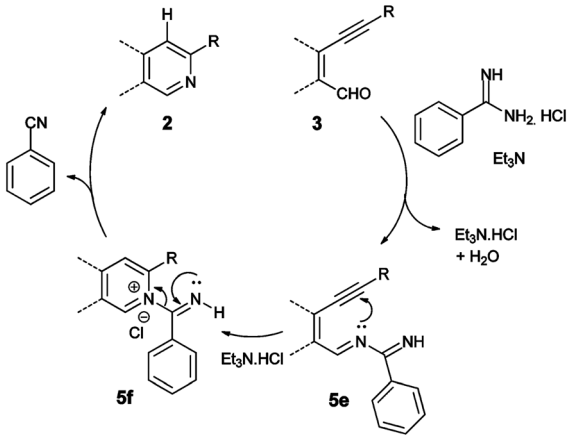
Because of the anticancer activity shown by different isoquinoline derivatives and heterosteroids, all the compounds were screened *in vitro* for cytotoxic activities against the cervical HeLa cancer cell line and prostate DU 205 cancer cell line using the MTT-microcultured tetrazolium assay[15] and drug doxorubicin as a positive control. Unfortunately, none of the tested compounds could show promising cytotoxic activity against the cervical HeLa cancer cell line (compounds **2a–y**, $IC_{50} \geqslant 100$ μM, doxorubicin $IC_{50} = 9.76 \pm 0.1141$ μM) and prostate DU 205 cancer cell line (compounds **2a–y**, $IC_{50} \geqslant 100$ μM, doxorubicin $IC_{50} = 9.00 \pm 0.721$ μM).

Conclusions

In conclusion, we have demonstrated very efficient multicomponent reactions for the synthesis of biologically important 3-substituted isoquinolines, steroid-fused pyridines, 5,6-dihydrobenzo[*f*]isoquinolines and 1,6-naphthyridine. These copper-catalyzed microwave-assisted annulation reactions are much more efficient than the known transition metal-catalyzed



Scheme 4 Plausible mechanism of Cu(I)-mediated formation of 2.



Scheme 5 Plausible mechanism of catalyst-free formation of 2.

reactions in terms of the rate of reaction, cost of catalyst and steps of the reactions. A wide range of terminal alkynes undergo this reaction with β-halovinyl/aryl aldehydes and *tert*-butylamine/benzamidine to provide good to excellent yield of products. Moreover, a catalyst-free synthesis of biologically important 3-substituted isoquinoline and substituted pyridine derivatives was developed using *ortho*-alkynyl aryl/vinyl aldehydes, benzamidine hydrochloride and triethylamine as the starting materials under microwave irradiation.

Experimental

General methods

Melting points were measured with a Buchi B-540 melting point apparatus and are uncorrected. IR spectra were recorded using an Elmer FT-IR-2000 spectrometer using KBr pellets or as a thin film using chloroform. NMR spectra were recorded using an Avance DPX 300 MHz FT-NMR spectrometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on a Trace DSQ GCMS instrument. All the commercially available regents were used as received. All experiments were monitored by thin layer chromatography (TLC). TLC was performed on pre-coated silica gel plates (Merck). Column chromatography was performed on silica gel (100–200 mesh, Merck). All MW reactions were carried out in a Synthos 3000 (Anton Paar) microwave reactor.

General procedure for the multi-component synthesis of compounds 2a–t using *tert*-butylamine. A mixture of halo aldehyde (1 mmol), 10 mol% CuI, terminal alkyne (1.1 mmol) and *tert*-butylamine (2 mmol) in DMF (1 mL) was irradiated in a closed vessel in a Synthos 3000 microwave reactor at 720 W (140 °C and 14 bar) for 4–8 min. After completion of the reaction, as indicated by TLC, the reaction mixture was treated with water (40 mL) and then extracted with ethyl acetate (50 mL). The organic portion was washed with water, dried over anhydrous sodium sulfate and the solvent was removed to obtain a crude product which on silica gel column chromatographic purification using EtOAc/hexane (1 : 4) as eluent afforded compounds **2a–t**.

3-Phenylisoquinoline.[7c] ***(2a)*** Yellow gum, yield: 92% (188 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 7.2 Hz, 2H), 7.60 (t, J = 7.9 Hz, 1H), 7.69 (t, J = 7.1 Hz, 1H), 7.89 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 8.08 (s, 1H), 8.12 (d, J = 7.3 Hz, 2H), 9.35 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 116.6, 126.9, 127.0, 127.1, 127.6, 127.8, 128.5, 128.7, 128.8, 130.2, 130.5, 136.7, 139.6, 151.3, 152.4. IR ($CHCl_3$, cm^{-1}): 3058, 2971, 1790, 1626, 1592, 1492, 1448, 1205, 977, 764. MS (EI, *m*/*z*): 205 [M$^+$]. Anal. calcd for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82. Found: C, 87.59; H, 5.49; N, 6.67%.

*3-(p-Tolyl)isoquinoline (**2b**).* Brown solid, yield: 84% (184 mg). M.p. 71–72 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.44 (s, 3H), 7.33 (d, J = 8.1 Hz, 2H), 7.52 (t, J = 7.8 Hz, 1H), 7.63 (t, J = 7.8 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 8.00 (s, 1H), 8.07 (d, J = 7.8 Hz, 2H), 9.33 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 116.0, 126.9, 127.6, 127.63, 129.6, 130.5, 136.7, 136.8, 138.5, 151.2, 152.3. IR ($CHCl_3$, cm^{-1}): 1626, 1589, 1516, 1447, 823, 751. MS (EI, *m*/*z*): 219.1 [M$^+$]. Anal. calcd for $C_{16}H_{13}N$: C, 87.64; H, 5.98; N, 6.39. Found: C, 87.69; H, 5.99; N, 6.57%.

*3-(4-Fluorophenyl)isoquinoline (**2c**).* Yellow solid, yield: 76% (170 mg). M.p. 124–125 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13–7.22 (m, 2H), 7.53 (t, J = 6.9 Hz, 1H), 7.65 (t, J = 6.9 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 6.6 Hz, 1H), 7.93 (s, 1H), 8.12–8.02 (m, 2H), 9.28 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 115.5, 115.8, 116.2, 126.8, 127.1, 127.5, 128.7, 128.8, 130.6, 135.7, 136.6, 150.2, 152.4, 164.0 (d, J_{C-F} = 246 Hz). IR ($CHCl_3$, cm^{-1}): 1625, 1600, 1581, 1512, 836. MS (EI, *m*/*z*): 223 [M$^+$]. Anal. calcd for $C_{15}H_{10}FN$: C, 80.70; H, 4.51; N, 6.27. Found: C, 80.82; H, 4.60; N, 6.42%.

*3-(6-Methoxynaphthalen-2-yl)isoquinoline (**2d**).* Light yellow solid, yield: 79% (225 mg). M.p. 171–172 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.95 (s, 3H), 7.17–7.26 (m, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.70 (t, J = 6.9 Hz, 1H), 7.83–7.91 (m, 3H), 8.00 (d, J = 8.1 Hz, 1H), 8.18–8.23 (m, 2H), 8.59 (s, 1H), 9.37 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.4, 105.6, 116.4, 119.2, 125.2, 126.1, 126.9, 127.0, 127.3, 127.6, 129.2, 130.3, 130.6, 134.7, 136.8, 151.2, 152.5, 158.1. IR ($CHCl_3$, cm^{-1}): 1621, 1260, 1024, 853, 773, 743. MS (EI, *m*/*z*): 285.1 [M$^+$]. Anal. calcd for $C_{20}H_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 84.27; H, 5.36; N 4.76%.

*3-Propylisoquinoline (**2e**).* Yellow gum, yield: 75% (128 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.00 (t, J = 7.2 Hz, 3H), 1.80 (hextet, J = 7.2 Hz, 2H), 2.91 (t, J = 7.7 Hz, 2H), 7.44 (s, 1H), 7.50 (t, J = 7.7 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.73 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 9.19 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 23.2, 40.1, 118.1, 126.1, 126.3, 127.1, 127.5, 130.2, 136.5, 152.0, 155.5. IR ($CHCl_3$, cm^{-1}): 2960, 2932, 2871, 1630, 1592, 1456, 751. MS (EI, *m*/*z*): 171 [M$^+$]. Anal. calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.03; H, 7.55; N, 8.29%.

*7-(p-Methoxyphenyl)-[1,3]-dioxolo[4,5-g]isoquinoline (**2f**).* Red solid, yield: 84% (234 mg). M.p. 159–160 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.86 (s, 3H), 6.07 (s, 2H), 7.01 (d, J = 7.8 Hz, 2H), 7.06 (s, 1H), 7.16 (s, 1H), 7.79 (s, 1H), 7.99 (d, J = 7.8 Hz, 2H), 9.02 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.4, 101.6, 102.6, 103.1, 114.1, 115.5, 124.6, 128.0, 132.2, 135.2, 148.1, 149.9, 150.2, 151.1, 159.9. IR ($CHCl_3$, cm^{-1}): 1598, 1455, 1225, 1026. MS (EI, *m*/*z*): 279 [M$^+$]. Anal. calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.24; H, 4.80; N, 5.25%.

*7-(p-Fluorophenyl)-[1,3]-dioxolo[4,5-g]isoquinoline (**2g**).* Brown solid, yield: 78% (208 mg). M.p. 161–162 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.11 (s, 2H), 7.09–7.21 (m, 4H), 7.84 (s, 1H), 8.00–8.07 (m, 2H), 9.05 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 101.7, 102.7, 103.1, 115.5, 115.8, 116.1, 124.9, 128.4, 135.1, 135.8, 148.4, 149.6, 150.1, 151.2, 163.1 (d, J_{C-F} = 246 Hz). IR ($CHCl_3$, cm^{-1}): 1602, 1463, 1233, 956, 843. MS (EI, *m*/*z*): 267.0 [M$^+$]. Anal. calcd for $C_{16}H_{10}FNO_2$: C, 71.91; H, 3.77; N, 5.24. Found: C, 71.98; H, 3.83; N, 5.45%.

*7-Butyl-[1,3]-dioxolo[4,5-g]isoquinoline (**2h**).* Brown solid, yield: 71% (163 mg). M.p. 68–69 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (t, J = 7.2 Hz, 3H), 1.25–1.41 (m, 2H), 1.72 (pentate, J = 7.8 Hz, 2H), 2.83 (t, J = 6.6 Hz, 2H), 6.03 (s, 2H), 6.95 (s, 1H), 7.11 (s, 1H), 7.27 (s, 1H), 8.88 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 22.5, 32.2, 37.5, 101.4, 102.0, 103.0, 117.9, 124.1, 135.0, 147.8, 149.6, 151.0, 154.7. IR ($CHCl_3$, cm^{-1}): 1605, 1483, 1457, 1237, 1037, 940. MS (EI, *m*/*z*): 229.1 [M$^+$]. Anal. calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.37; H, 6.71; N, 6.39%.

*3β-Acetoxy-6′-phenyl-5,16-androstadieno[16,17-c]pyridine (**2i**).* Yellow solid, yield: 82% (362 mg). M.p. 185–186 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 3H), 1.04 (s, 3H), 0.79–2.4 (m, 14H), 1.97 (s, 3H), 2.40–2.58 (m, 1H), 2.64–2.82 (m, 1H), 4.47–4.64 (m, 1H), 5.36 (d, J = 4.6 Hz, 1H), 7.22 (s, 1H), 7.25–7.50 (m, 4H), 7.88 (d, J = 7.3 Hz, 2H), 8.46 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.7, 19.4, 20.6, 21.5, 27.7, 29.8, 30.8, 31.6, 34.2, 36.9, 38.1, 45.7, 50.4, 57.2, 73.8, 113.8, 122.1, 127.0, 128.7, 137.4, 139.6, 140.0, 145.2, 155.8, 164.5, 170.6. IR ($CHCl_3$, cm^{-1}) 2926, 2854, 1731, 1657, 1243, 1031. MS (EI, *m*/*z*): 381.2 [M$^+$ − 60]. Anal. calcd for $C_{30}H_{35}NO_2$: C, 81.59; H, 7.99; N, 3.17. Found: C, 81.49; H, 7.96; N, 3.24%.

*3β-Acetoxy-6′-(p-tolyl)-5,16-androstadieno[16,17-c]pyridine (**2j**).* Black solid, yield: 79% (360 mg). M.p. 206–208 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.97 (s, 3H), 1.09 (s, 3H), 2.05 (s, 3H), 0.90–2.42 (m, 15H), 2.40 (s, 3H), 2.55 (t, J = 11.4 Hz, 1H), 2.80 (dd, J = 14.7 Hz and 5.1 Hz, 1H), 4.49–4.78 (m, 1H), 5.42 (d, J = 4.6 Hz, 1H), 7.26 (d, J = 7.8 Hz, 2H), 7.45 (s, 1H), 7.86 (d, J = 8.4 Hz, 2H), 8.50 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.4, 20.6, 21.3, 21.5, 22.7, 27.7, 29.7, 30.8, 31.6, 34.1, 36.85, 36.9, 38.1, 45.5, 50.4, 57.2, 73.8, 113.4, 122.1, 126.8, 129.4, 137.0, 137.2, 138.4, 140.0, 145.4, 155.9, 164.0, 170.6. IR ($CHCl_3$, cm^{-1}): 1729, 1374, 1254, 1034, 823, 753. MS (EI, *m*/*z*): 395.2 [M$^+$ − 60]. Anal. calcd for $C_{31}H_{37}NO_2$: C, 81.72; H, 8.19; N, 3.07. Found: C, 81.75; H, 8.28; N, 3.27%.

*3β-Acetoxy-6′-[p-fluorophenyl]-5,16-androstadieno[16,17-c]pyridine (**2k**).* Red solid, yield: 77% (354 mg). M.p. 176–177 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.0 (s, 3H), 1.11 (s, 3H), 2.05 (s, 3H), 0.89–2.36 (m, 15H), 2.59 (t, J = 11.2 Hz, 1H), 2.78 (dd, J = 14.6 Hz and 5.0 Hz, 1H), 4.49–4.77 (m, 1H), 5.44 (d, J = 7.5 Hz, 1H), 7.14 (t, J = 8.4 Hz, 2H), 7.43 (s, 1H), 7.93 (t, J = 6.0 Hz, 2H), 8.50 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.6, 19.4, 20.6, 21.5, 27.7, 29.6, 29.7, 29.8, 30.8, 31.6, 34.1, 36.85, 36.9, 38.1, 45.7, 50.3, 57.2, 73.8, 115.5, 115.7, 122.1, 128.8, 128.9, 140.0, 163.1 (d, J_{C-F} = 223 Hz), 170.6. IR ($CHCl_3$, cm^{-1}): 2927, 1722, 1245, 1033. MS (EI, *m*/*z*): 399.2 [M$^+$ − 60]. Anal. calcd for $C_{30}H_{34}FNO_2$: C, 78.40; H, 7.46; N, 3.05. Found: C, 78.51; H, 7.29; N, 3.13%.

*3β-Acetoxy-6′-propyl-5,16-androstadieno[16,17-c]pyridine (**2l**).* Yellow solid, yield: 70% (285 mg). M.p. 161–162 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.95 (s, 3H), 1.10 (s, 3H), 2.04 (s, 3H), 0.90–2.60 (m, 20H), 2.71–2.80 (m, 4H) 4.55–4.68 (m, 1H), 5.42 (d, J = 5.3 Hz, 1H), 6.93 (s, 1H), 8.35 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 18.6, 19.3, 20.6, 21.4, 23.4, 27.7, 29.7, 30.8, 31.6, 34.1, 36.8, 36.9, 38.1, 39.9, 45.5, 50.4, 57.1, 73.7, 115.8, 122.0, 136.1, 140.0, 143.9, 159.8, 164.6, 170.5. IR ($CHCl_3$, cm^{-1}) 2928, 2853, 1733, 1244, 1033. MS (EI, *m*/*z*): 347.3 [M$^+$ − 60]. Anal. calcd for $C_{27}H_{37}NO_2$: C, 79.56; H, 9.15; N, 3.44. Found: C, 79.58; H, 9.20; N, 3.30%.

*3β-Acetoxy-6′-butyl-5,16-androstadieno[16,17-c]pyridine (**2m**).* Yellow solid, yield: 69% (291 mg). M.p. 168 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 3H), 1.10 (s, 3H), 2.04 (s, 3H), 0.90–2.62 (m, 22H), 2.71–2.80 (m, 4H) 4.55–4.68 (m, 1H), 5.43 (d, J = 4.5 Hz, 1H), 6.91 (s, 1H), 8.34 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 18.6, 19.3, 20.6, 21.4, 22.7, 28.8, 29.7, 30.8, 31.6, 32.4, 34.1, 36.8, 38.1, 45.4, 50.4, 57.2, 73.8, 115.5, 122.1, 135.8, 140.0, 144.8, 160.5, 163.7, 170.5. IR ($CHCl_3$, cm^{-1}): 2955, 2934, 2855, 1733, 1245, 1033, 755. MS (EI, *m*/*z*): 361.2 [M$^+$ − 60]. Anal. calcd for $C_{28}H_{39}NO_2$: C, 79.76; H, 9.32; N, 3.32. Found: C, 79.78; H, 9.37; N, 3.42%.

*3β-Acetoxy-6′-ethoxycarbonyl-5,16-androstadieno[16,17-c]pyridine (**2n**).* Yellow solid, yield: 74% (324 mg). M.p. 129 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.98 (s, 3H), 1.10 (s, 3H), 1.45 (t, J = 7.4 Hz, 3H), 2.05 (s, 3H), 1.11–3.00 (m, 17H), 4.48 (q, J = 7.1 Hz, 2H), 4.50–4.65 (m, 1H), 5.43 (d, J = 4.6 Hz, 1H), 7.90 (s, 1H), 8.59 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 18.5, 19.3, 20.5, 21.4, 27.7, 30.2, 30.8, 31.5, 34.0, 36.9, 38.1, 45.7, 50.3, 57.1, 61.9, 73.7, 118.2, 121.9, 140.0, 142.8, 145.9, 146.9, 164.4, 170.6. IR ($CHCl_3$, cm^{-1}) 2850, 1728, 1374, 1246, 1031. MS (EI, *m*/*z*): 377.2 [M$^+$ − 60]. Anal. calcd for $C_{27}H_{35}NO_4$: C, 74.11; H, 8.06; N, 3.20. Found: C, 74.25; H, 8.14; N, 3.39%.

*3-Phenyl-9,10-dihydrobenzo[f]isoquinoline (**2o**).* Yellow gum, yield: 83% (213 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.86–3.05 (m, 4H), 7.02–7.52 (m, 6H), 7.82–8.04 (m, 4H), 8.56 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 28.5, 114.8, 124.3, 126.9, 127.3, 128.7, 128.8, 129.6, 130.5, 132.1, 138.3, 139.7, 142.7, 148.8, 156.6. IR ($CHCl_3$, cm^{-1}): 2926, 2850, 1599, 1475, 1448, 771, 743. MS (EI,

m/*z*): 257.1 [M^+]. Anal. calcd for $C_{19}H_{15}N$: C, 88.68; H, 5.88; N, 5.44. Found: C, 88.76; H, 5.64; N, 5.59%.

*3-Propyl-9,10-dihydrobenzo[f]isoquinoline (**2p**).* Yellow gum, yield: 75% (167 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.93 (t, J = 7.4 Hz, 3H), 1.74 (hextet, J = 7.3 Hz, 2H), 2.71–2.90 (m, 6H), 7.10–7.32 (m, 3H), 7.40 (s, 1H), 7.72 (t, J = 3.6 Hz, 1H), 8.32 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 23.3, 25.1, 28.5, 40.0, 116.7, 124.3, 127.2, 128.6, 129.2, 129.5, 132.0, 138.4, 142.6, 147.7, 160.6. IR ($CHCl_3$, cm^{-1}): 2959, 2933, 2871, 1603, 1544, 1483, 772. MS (EI, *m*/*z*): 223 [M^+]. Anal. calcd for $C_{16}H_{17}N$: C, 86.05; H, 7.67; N, 6.27. Found: C, 85.94; H, 7.60; N, 6.19%.

*3-Pentyl-9,10-dihydrobenzo[f]isoquinoline (**2q**).* Yellow gum, yield: 73% (183 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (t, J = 6.9 Hz, 3H), 1.25–1.52 (m, 4H), 1.71–1.81 (m, 2H), 2.79–2.94 (m, 6H), 7.15–7.39 (m, 3H), 7.47 (s, 1H), 7.77–7.83 (m, 1H), 8.39 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 22.6, 25.1, 28.5, 29.8, 31.6, 38.0, 116.7, 124.3, 127.2, 128.6, 129.2, 129.5, 132.0, 138.4, 142.6, 147.6, 160.9. IR ($CHCl_3$, cm^{-1}): 2955, 2930, 2857, 1603, 1545, 1451, 754. MS (EI, *m*/*z*): 251.1 [M^+]. Anal. calcd for $C_{18}H_{21}N$: C, 86.01; H, 8.42; N, 5.57. Found: C, 86.29; H, 8.53; N, 5.78%.

*7-Methoxy-3-propyl-9,10-dihydrobenzo[f]isoquinoline (**2r**).* Yellow gum, yield: 72% (182 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.01 (t, J = 7.4 Hz, 3H), 1.72–1.89 (m, 2H), 2.72–2.97 (m, 6H), 3.87 (s, 3H), 6.82 (d, J = 2.1 Hz, 1H), 6.89 (dd, J = 8.5 Hz and 2.3 Hz, 1H), 7.43 (s, 1H), 7.75 (d, J = 8.6 Hz, 1H), 8.36 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 23.2, 25.1, 28.8, 39.3, 55.4, 113.0, 113.8, 116.4, 124.5, 126.1, 128.3, 140.5, 161.0. IR ($CHCl_3$, cm^{-1}): 2960, 2932, 1602, 1464, 1259, 1045. MS (EI, *m*/*z*): 253 [M^+]. Anal. calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.69; H, 7.55; N, 5.75%.

*3-Butyl-7-methoxy-9,10-dihydrobenzo[f]isoquinoline (**2s**).* Yellow gum, yield: 72% (192 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 7.3 Hz, 3H), 1.29–1.40 (m, 2H), 1.62–1.72 (m, 2H), 2.72–2.81 (m, 6H), 3.81 (s, 3H), 6.82 (dd, J = 8.3 Hz and 2.6 Hz, 1H), 7.25 (d, J = 2.7 Hz, 1H), 7.13 (d, J = 8.3 Hz, 1H), 7.35 (s, 1H), 8.32 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 22.6, 25.4, 27.7, 32.3, 37.9, 55.5, 109.9, 114.8, 116.6, 119.2, 129.3, 129.4, 130.6, 133.1, 142.3, 148.1, 158.8, 161.0. IR ($CHCl_3$, cm^{-1}) 2962, 2930, 1601, 1463, 1257, 1042. MS (EI, *m*/*z*): 267 [M^+]. Anal. calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.96; H, 7.87; N, 5.56%.

*7-Phenyl-3-(p-tolyl)-1,6-naphthyridine (**2t**).* Yellow solid, yield: 70% (207 mg). M.p. 190–191 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.38 (s, 3H), 7.02–7.60 (m, 7H), 8.12 (d, J = 7.3 Hz, 2H), 8.18–8.34 (m, 2H), 9.28 (s, 1H), 9.33 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 117.6, 122.6, 127.2, 129.0, 129.2, 130.1, 131.9, 134.1, 135.0, 138.7, 138.9, 150.2, 152.8, 154.6, 154.9. IR (KBr, cm^{-1}) 2923, 2850, 1352, 810, 767. MS (EI, *m*/*z*): 296 [M^+]. Anal. calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 85.13; H, 5.44; N, 9.58%.

General procedure for the catalyst-free synthesis of compounds 2a, 2c, 2e, 2u–y. A mixture of *ortho*-alkynyl aryl/vinyl aldehyde (1 mmol), benzamidine hydrochloride (1.1 mmol) and triethylamine (2.1 mmol) was irradiated in a closed vessel in a Synthos 3000 microwave reactor at 720 W (140 °C and 14 bar) for 5 min. After completion of the reaction, as indicated by TLC, the reaction mixture was treated with water (40 mL) and then extracted with ethyl acetate (40 mL). The organic portion was washed with water, dried over anhydrous sodium sulfate and the solvent was removed to obtain a crude product which on silica gel column chromatographic purification using EtOAc/hexane (1 : 4) as eluent afforded compounds **2a**, **2c**, **2e**, **2u–y**. The spectral data of compounds **2a** (89%, 182 mg), **2c** (87%, 194 mg) and **2e** (86%, 147 mg) are similar to those mentioned above.

*3-(4-Methoxyphenyl)isoquinoline (**2u**).* Red solid, yield: 93% (219 mg). M.p. 85–87 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.87 (s, 3H). 7.04 (d, J = 8.7 Hz, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.65 (t, J = 6.9 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.96 (d, J = 11.7 Hz, 1H), 7.98 (s, 1H), 8.09 (d, J = 9.3 Hz, 2H), 9.30 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.4, 114.2, 115.4, 126.7, 126.8, 127.4, 127.6, 128.2, 130.5, 132.2, 136.8, 151.0, 152.3, 160.1. IR ($CHCl_3$, cm^{-1}): 1608, 1515, 1249, 834. MS (EI, *m*/*z*): 235 [M^+]. Anal. calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.78; H, 5.63; N, 5.79%.

*7-Phenyl-[1,3]-dioxolo[4,5-g]isoquinoline (**2v**).* Brown solid, yield: 90% (224 mg). M.p. 111–112 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.96 (s, 2H), 6.97 (d, J = 3.3 Hz, 1H), 7.08 (d, J = 2.4 Hz, 1H), 7.35–7.51 (m, 3H), 7.79 (s, 1H), 8.05 (d, J = 6.9 Hz, 2H), 9.00 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 101.6, 102.7, 103.0, 116.3, 124.9, 126.8, 127.2, 128.3, 128.8, 129.2, 135.0, 139.6, 148.3, 150.0, 150.3, 151.0. IR ($CHCl_3$, cm^{-1}): 1600, 1481, 1459, 1232, 1038. MS (EI, *m*/*z*): 249 [M^+]. Anal. calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 77.31; H, 4.37; N, 5.68%.

*7-(p-Tolyl)-[1,3]-dioxolo[4,5-g]isoquinoline (**2w**).* Brown solid, yield: 89% (234 mg). M.p. 152–153 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.41 (s, 3H), 6.01 (s, 2H), 7.01 (s, 1H), 7.13 (s, 1H), 7.29 (d, J = 8.1 Hz, 2H), 7.80 (s, 1H), 7.95 (d, J = 8.1 Hz, 2H), 9.01 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 101.6, 102.7, 103.0, 116.0, 124.8, 126.6, 129.5, 135.1, 136.6, 138.2, 148.2, 149.9, 150.3, 151.1. IR ($CHCl_3$, cm^{-1}): 1598, 1480, 1456, 1224, 1035. MS (EI, *m*/*z*): 263 [M^+]. Anal. calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.49; H, 4.78; N, 5.53%.

*7-Methoxy-3-phenyl-9,10-dihydrobenzo[f]isoquinoline (**2x**).* Yellow gum, yield: 86% (247 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.86–2.96 (m, 4H), 3.90 (s, 3H), 6.93 (dd, J = 8.3 Hz and 2.5 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 7.30–7.57 (m, 5H), 7.98 (s, 1H), 8.02 (d, J = 7.3 Hz, 1H), 8.59 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.5, 27.6, 55.6, 110.0, 114.9, 127.0, 128.5, 128.8, 129.0, 129.5, 130.6, 130.8, 132.9, 139.2, 143.0, 148.4, 158.9. IR ($CHCl_3$, cm^{-1}): 2926, 2851, 1601, 1542, 1481, 1220, 771. MS (EI, *m*/*z*): 287.1 [M^+]. Anal. calcd for $C_{20}H_{17}NO$: C, 83.59; H, 5.96; N, 4.87. Found: C, 83.57; H, 6.09; N, 4.78%.

*4-(Naphthalen-2-yl)-2-phenylpyridine (**2y**).* Yellow gum, yield: 93% (261 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35–7.54 (m, 6H), 7.74 (dd, J = 8.5 Hz and 1.6 Hz, 1H), 7.82–7.93 (m, 1H), 7.91 (t, J = 8.3 Hz, 2H), 8.00 (d, J = 0.5 Hz, 1H), 8.05–8.13 (m, 3H), 8.74 (d, J = 5.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 119.0, 120.5, 124.5, 126.5, 126.8, 126.9, 127.2, 127.8, 128.5, 128.9, 129.0, 129.2, 133.5, 133.51, 135.7, 139.4, 149.3, 150.1, 158.1. IR ($CHCl_3$, cm^{-1}): 2924, 1621, 1222, 776. MS (EI, *m*/*z*): 281.1 [M^+]. Anal. calcd for $C_{21}H_{15}N$: C, 89.65; H, 5.37; N, 4.98. Found: C, 89.49; H, 5.21; N, 4.76%.

General procedure for the multi-component synthesis of compounds 2a, 2c, 2e, 2o, 2u,v using benzamidine hydrochloride. A mixture of halo aldehyde (1 mmol), 10 mol% CuI, terminal alkyne (1.1 mmol), benzamidine hydrochloride (1.1 mmol) and triethylamine (2.1 mmol) in DMF (1 mL) was irradiated in a closed vessel in a Synthos 3000 microwave reactor at 720 W (140 °C and 14 bar) for 8 min. After completion of the reaction, as indicated by TLC, the reaction mixture was treated with water (40 mL) and then extracted with ethyl acetate (40 mL). The organic portion was washed with water, dried over anhydrous sodium sulfate and the solvent was removed to obtain a crude product which on silica gel column chromatographic purification using EtOAc/hexane (1 : 4) as eluent afforded compounds **2a**, **2c**, **2e**, **2o**, **2u,v** whose spectral data are similar to those mentioned above.

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