NJC

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/d1nj02643g

Silver-catalyzed tandem 5- and 6-*endo*-cyclizations *via* concomitant yne-ol-imine activation: selective entry to 2-aryldihydrofuroquinolines†

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Received 29th May 2021,
Accepted 13th July 2021

DOI: 10.1039/d1nj02643g

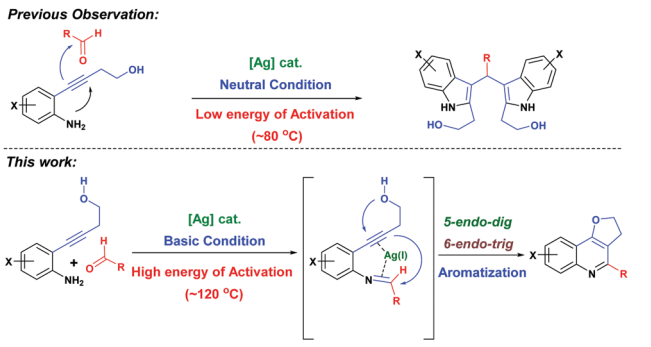
rsc.li/njc

A silver(I) catalyzed domino imination-intramolecular biheterocyclization-aromatization cascade has been developed to construct 2-aryl/-heteroaryl dihydrofuroquinolines in moderate to good yield using an aldehyde and unprotected 4-(2-aminophenyl)but-3-yn-1-ol as precursors. Sequential Ag-(I)-induced 5-*endo-dig* cyclization of the yne-ol part and 6-*endo-trig* cyclization of a proposed Ag-bound imine, followed by aromatization, furnish the furoquinoline derivatives.

Introduction

Indole and quinoline cores have been synthesized using numerous popular strategies as these ring-systems are part of the structure of a wide array of pharmaceuticals, agrochemicals and important natural products.[1] Cycloisomerizations involving 5- or 6-*endo*- or *-exo-dig* or *-trig* pathways are some of the most efficient and favourite cyclization processes for synthesizing these heterocyclic frameworks.[2] Though there are several examples of syntheses of heterocyclic cores employing metal catalyzed activation of alkenes, alkynes and carbon–heteroatom bonds *via* these cyclization processes,[2,3] construction of poly-hetero-cyclic scaffolds following the same strategy is somewhat less documented.[4] Such approaches towards poly-heterocyclic cores reduce chemical hazards of tedious multistep synthesis[4] and also enhance the efficacy of a chemical transformation. Notably, poly-hetero-cyclic compounds with indole or/and quinoline moieties have proven their potent medicinal activity against various fatal diseases.[1,4e] Moreover, in the past two decades, silver(I) has become an attractive catalyst for organic transformations due to its efficacy, easy availability and low-cost. To date, its alkynophilicity has influenced numerous elegant transformations.[5] Because of its σ- and/or π-Lewis acid character,[5] it can act as a potential activator of double/triple bonds. Thus, based on our experience on metal catalyzed cyclization[6] and our recent success in silver-catalyzed synthesis of bis-indolylarylmethane derivatives (BIAMs),[6d] we wondered whether a suitable silver-catalyzed methodology could be developed to achieve poly-heterocyclization putting a hydroxyl group on the alkyne chain of unprotected 2-alkynyl aniline along with *in situ* imination on it (Scheme 1). Importantly, Huang *et al.* isolated 2,3-fused indoles from their silver-catalyzed reaction[7] on N-protected 4-(2-aminophenyl)but-3-yn-1-ols and aldehydes, though their starting materials are similar to this investigation. They could not find any furoquinoline derivative during their transformation.

In this context, Ma's scandium(III)-catalyzed,[8a] Youn's dual-catalyzed (Pd(II)-acid)[8c] and Flynn's iodonium-catalyzed[8b,d] approaches are noteworthy. Dihydrofuro-1,2-dihydroquinoline derivatives were synthesized *via* $Sc(OTf)_3$ catalysis using N-protected *o*-alkynylanilines and aldehydes as precursors by Ma *et al.*[8a] Youn and co-workers reported the formation of furoquinoline **3a** (Table 1) in a $Pd(OAc)_2$-*p*-TsOH dual-catalysed process. They also showed that silver(I) did not catalyze the reaction to produce **3a** under their reaction conditions.[8c] Interestingly, Flynn's group was able to furnish **3a** in their metal-free iodonium-catalyzed approaches.[8b,d]



Scheme 1 Ag(I)-Catalyzed annulations under different reaction conditions.

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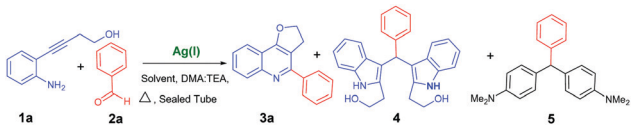
† Electronic supplementary information (ESI) available. CCDC 1952336. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1nj02643g

Table 1 Optimization of the bi-heterocyclization[a]



Entry	Catalyst (mol%)	Solvent	1a : 2a	Additives (DMA 20 mol% w.r.t **1a** in all cases)	t (h)	Yield[b,c] (%) **3a**	**4**	**5**
1	AgOTf (8)	Toluene	1 : 1	—	8	0	48	0[d]
2	AgOTf (3)	Toluene	2 : 3	—	8	0	30	0
3	AgOTf (3)	$PhNMe_2$ (DMA)	2 : 3	—	8	36	0	20
4	AgOTf (3)	Toluene	2 : 3	DMA	8	50	0	10
5	AgOTf (3)	Toluene	2 : 3	TEA	8	20	0	0
6	AgOTf (3)	Toluene	2 : 3	DMA : TEA (2 : 1)	6	76	0	5
7	CF_3CO_2Ag (3)	Toluene	2 : 3	DMA : TEA (2 : 1)	12	30	0	5
8	AgOTf (3)	DMSO	2 : 3	DMA : TEA (2 : 1)	12	20	0	5
9	AgOTf (3)	DMF	2 : 3	DMA : TEA (2 : 1)	12	60	0	5
10	Ag_2CO_3 (3)	EtOH + H_2O	2 : 3	DMA : TEA (2 : 1)	12	0	0	0
11	$AgNO_3$ (3)	EtOH + H_2O	2 : 3	DMA : TEA (2 : 1)	12	0	0	0
12	AgOAc (3)	EtOH + H_2O	2 : 3	DMA : TEA (2 : 1)	12	0	0	0
13	AgOTf (3) + $NaHCO_3$	Toluene	2 : 3	—	12	10	15	0
14	CF_3SO_3H	Toluene	2 : 3	—	12	0	0	0

[a] Reaction conditions: 1 (0.1 mmol), **2a** (0.1 or 0.15 mmol), catalyst (8 or 3 mol%), solvent (1 mL), at 120 °C. [b] Isolated yield w.r.t. 1. [c] Under argon. [d] 80 °C. DMA = *N*,*N*-dimethylaniline; TEA = triethylamine.

However, as our objective was to find an effective silver-catalyzed process for poly-heterocyclization, Belmont's work[9] motivated us to consider the role of nitrogenous additives to afford Prins type cyclic-etherification[8a] in a silver-catalyzed method. Thus, we decided to carry out an investigation by treating unprotected 4-(2-aminophenyl)but-3-yn-1-ol and benzaldehyde with silver(I) in the absence or presence of some nitrogenous bases/additives.

Results and discussion

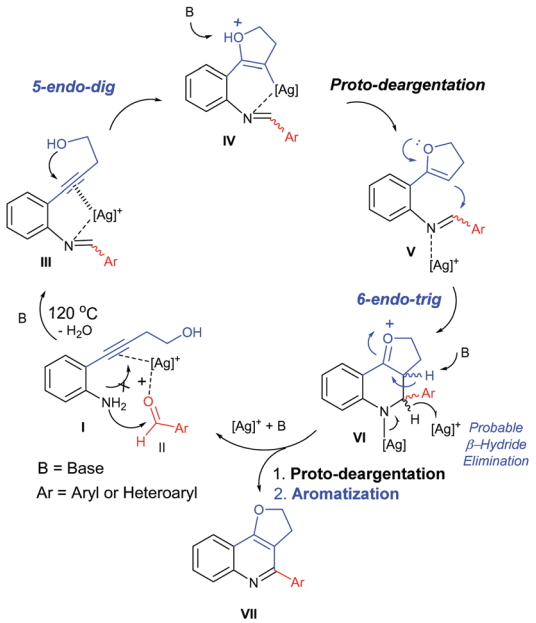
Initially, the reaction was conducted following our earlier conditions.[6d] AgOTf (8 mol%) was taken in toluene under argon and, subsequently, the substrates 4-(2-aminophenyl)but-3-yn-1-ol and benzaldehyde were added in a 1 : 1 ratio (this ratio is different from our previous report[6d]). The reaction mixture was stirred for 8 hours at 80 °C (Table 1, entry 1). Under these conditions, substituted bis-indolylbenzylmethane **4** was the only product isolated along with some unreacted starting materials. We then re-investigated the reaction at elevated temperature *i.e.* at 120 °C with low catalyst loading (3 mol%) by changing the mode of addition of the substrates and catalyst (Table 1, entry 2). Thus, the substrates 4-(2-aminophenyl)but-3-yn-1-ol and benzaldehyde (2 : 3) were stirred for 10 min in toluene at 120 °C in a sealed tube under argon.

After that, AgOTf was added to the stirred solution and it was allowed to run for 8 hours with TLC monitoring. But remarkable change was not found except formation of a complex mixture. Moreover, formation of a small amount of bis-indolylbenzylmethane **4** was observed. Despite our unsuccessful efforts under neutral conditions, we turned our attention to run this investigation under basic conditions. Inspired by Belmont's obervation,[9] we envisioned that a polyheterocyclization cascade might occur *via* Ag(I)-catalyzed domino activation of the yne-ol-imine unit, which could possibly be developed *in situ*, in the presence of nitrogenous additives. Thus, the reaction was conducted using *N*,*N*-dimethylaniline (DMA) as a solvent (Table 1, entry 3). To our astonishment, bis-indolylbenzylmethane **4** was not formed and the desired tandem bi-cyclization was observed under these conditions. Relatively low polar 2-phenyl 2′, 3′-dihydrofuroquiniline **3a** was obtained in 36% yield, albeit an unwanted adduct **5** was formed *via* condensation between DMA and the aldehyde (20%). It reveals that Ag(I) shows different activity in the presence of nitrogenous solvent/additives. To increase the yield of **3a**, we thought that DMA could be used as an additive instead of using it as a solvent. Thus, the domino process was run with 20 mol% of *N*,*N*-dimethylaniline (DMA) in toluene at 120 °C using AgOTf as a catalyst (3 mol%) (Table 1, entry 4). The yield of tricyclic scaffold **3a** increased dramatically (50%) along with a small amount of adduct **5** (10%). The use of a non-nucleophilic base triethylamine (TEA) instead of DMA did not produce better results (Table 1, entry 5). **3a** was formed only in 20% yield. To reduce the formation of **5**, it was decided to use TEA in conjunction with DMA. Surprisingly, when the reaction was carried out with a combination of nitrogeneous bases *N*,*N*-dimethylaniline–triethylamine (DMA–TEA; 20 mol% : 10 mol%) keeping the catalyst loading and other parameters the same, **3a** was obtained in satisfactory yield (76%) and formation of adduct **5** was observed only in a trace amount (≈5%) (Table 1, entry 6). However, silver trifluoroacetate did not show better catalytic activity under these conditions (Table 1; entry 7). Notably, polar aprotic solvent DMF was found to be another effective workable medium compared to DMSO for this transformation (Table 1; entries 9 and 8). Other silver catalysts (Ag_2CO_3, $AgNO_3$, and AgOAc) did not catalyze the reaction in polar protic solvents

(Table 1; entries 10–12). Furthermore, **3a** was formed in a small amount with some bis-indolylbenzylmethane **4** when $NaHCO_3$ was used as a base instead of DMA–TEA (Table 1; entry 13). Trifluoromethane-sulfonic acid itself did not show any catalytic activity for this transformation (Table 1; entry 14). Thus, AgOTf proved to be an effective catalyst among others (Table 1, entry 4). Finally, this optimization process led to the conclusion that sequential 5-*endo-dig* and 6-*endo-trig* biheterocyclization could be achieved to furnish 2-phenyl-2′,3′-dihydrofuroquiniline **3a** under basic conditions with low catalyst loading (3 mol%) and high energy of activation (120 °C) (Table 1; entry 6), while bis-indolylbenzylmethane **4** could be formed under neutral conditions with relatively high catalyst loading (8 mol%) and low energy of activation (80 °C) (Table 1; entry 1) from the same substrate combination.

Herein, to understand this silver-catalyzed domino biheterocyclization, a plausible mechanistic manifold has been proposed (Scheme 2) where Ag(I) is supposed to catalyze the intermolecular *in situ* imination selectively *via* condensation between the aldehyde (**II**) and amine (**I**) under basic conditions to furnish a probable intermediate **III**, instead of promoting usually found intramolecular 5-*endo-dig* cyclization between the amine group ($-NH_2$) and alkyne unit leading to a pyrrole core. Loosely bound Ag(I) of intermediate **III** may then induce Prins-type 5-*endo-dig* cyclization *via* activation of the alkyne unit to afford a proposed Ag-bound intermediate **IV**.

It is noteworthy that silver-catalyzed *in situ* imination and Prins-type cyclization may occur simultaneously to produce intermediate **IV**. At this stage, proto-deargentation may occur to produce the dihydrofuran core. Ag(I) then coordinates to the imine nitrogen (**V**) and thus induces 6-*endo-trig* cyclization of the enol-substructure to the electrophilic imine carbon of V to furnish Ag-bound bi-heterocyclic core **VI**, which on proto-deargentation followed by aromatization transformed into 2-aryl/heteroaryl dihydrofuroquinolines **VII**. A plausible explanation of this silver-catalyzed aromatization could be given based on the usual captodative effect of silver. Ag(I)-induced probable β-hydride elimination from **VI** followed by regeneration of Ag(I) from N-bound-silver might develop aromatization in the presence of a nitrogenous base to furnish **VII** under an argon atmosphere (Scheme 2).[10]

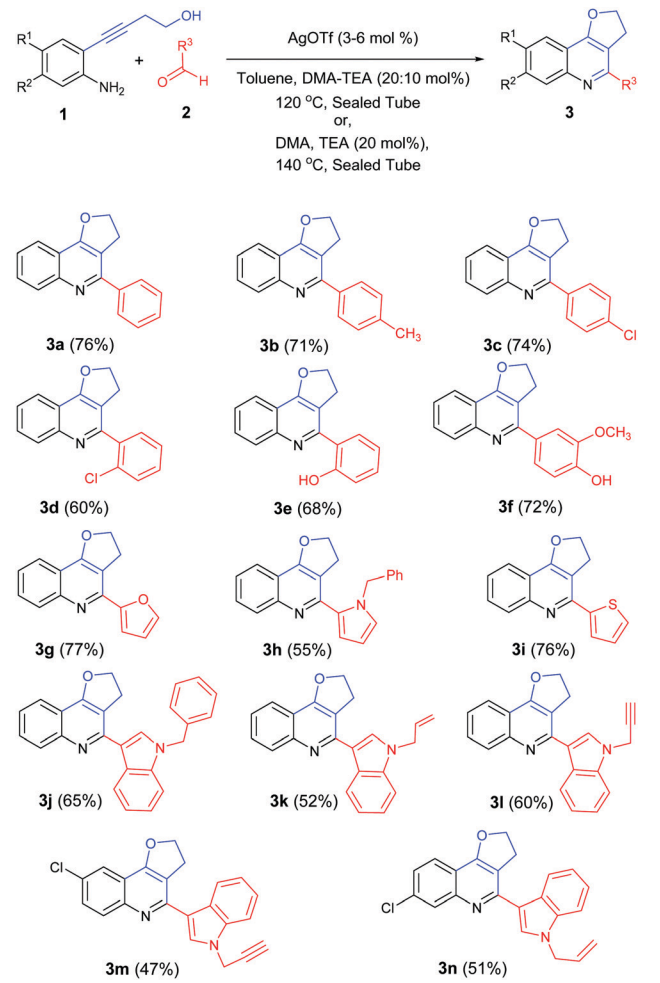


Scheme 2 Proposed mechanism for bihererocyclization.

In this transformation, sequential σ- and π-electronic rearrangements occur in a tandem bond-making-bond-breaking cascade under the influence of domino silver catalysis. In view of the wide applicability of quinoline derivatives in pharmacology,[1] the scope of the synthesis of 2-aryl dihydrofuroquinoline derivatives was explored based on the optimized condition **4** (Table 1, entry 6). Thus, a set of 2-aryl/heteroaryl dihydrofuroquinolines (**3a–n**) were synthesized in moderate to good yield (47–78%) from unprotected 4-(2-aminoaryl)but-3-yn-1-ols **1** and various aldehydes **2** (Table 2). Benzaldehyde and its *p*-Me and *p*-Cl analogues responded well to afford the corresponding products in good yield (71–76%; **3a–c**; Table 2). Whereas, the product yields from *o*-substituted benzaldehydes were comparatively low presumably due to steric hindrance which may arise during 6-*endo-trig* cyclization (60–68%; **3d and e**; Table 2). But this bicyclization worked well for *o*-hydroxy benzaldehyde (**3e**, 68%) compared to *o*-chloro benzaldehyde (**3d**, 60%). This difference in yield could be explained by reduced steric hindrance in the transition state arising due to probable H-bonding between the hydroxyl group and the imine nitrogen. When the reaction was carried out with vanillin, the corresponding product was formed in 72% yield (**3f**). It is noteworthy that *m*- and *p*-substituents on the benzene nucleus did not influence the product yield. Moreover, as various heterocyclic cores like furan/thiophene or pyrrole in a molecule usually make it medicinally significant,[1] an attempt was made to tether these heterocycles to the dihydrofuroquinoline scaffold. To our delight, the domino reaction proceeded smoothly with furfural and thiophene-2-carbaldehyde to produce corresponding products **3g** (77%) and **3i** (76%) in good yield.

But, unprotected pyrrole-2-aldehyde failed to produce the expected product except a complex mixture. However, **3h** was isolated in moderate yield (55%) on executing the reaction with benzyl protected pyrrole 2-aldehyde. We then tried to incorporate an indole core into this scaffold. Optimized condition **6** (Table 1, entry 6) did not work well for this transformation with the substrate N-protected-indole-3-carbaldehydes. Following these conditions, when the reaction was conducted at 120 °C in toluene with additives DMA–TEA (2 : 1) and AgOTf (3 mol%), 2-indolyl dihydrofuroquinoline **3j** was obtained only in 30% yield. To modify the reaction conditions, it was allowed to run in DMA using it as a solvent instead of toluene in conjunction with 20 mol% of TEA at 140 °C. Surprisingly, the product yield was improved and **3j** was obtained in 65% yield along with some aldehyde–DMA adduct (15% w.r.t aldehyde). Similarly, **3k** and **3l** were obtained in moderate yields (52 and 60% respectively) under these conditions. In view of the medicinal importance of the chloro-substituted quinoline core embodied in chloroquine, hydroxychloroquine *etc.*, **3m** and **3n** were synthesized in moderate

Table 2 Scope of 2-aryl 2′,3′-dihydrofuroquinoline **3**



yield (47% and 51% respectively) from corresponding chloro-substituted alkyne-amines **1b** and **1c**. Notably, 2-indolyl dihydrofuroquinoline cannot be synthesized using unprotected 1*H*-indole-3-carbaldehyde as a starting material. However, the thus obtained N-protected-2-indolyl dihydrofuroquinolines have the scope of further functionalization on their protecting groups. On the contrary, when the reaction was run using aliphatic aliphatic aldehydes as starting materials such as propionaldehyde and acrolein, an inseparable complex mixture was obtained.

The structure of **3j** was confirmed by X-ray crystallographic analysis (Fig. 1). Detailed spectral analysis determined the structures of all products.

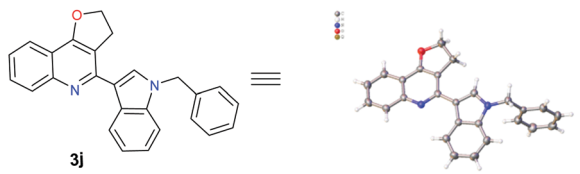


Fig. 1 Molecular structure of **3j** by X-ray single crystal analysis.

Conclusions

In conclusion, we have observed a unique behavior of a silver catalyst to induce a domino biheterocyclization *via* tandem 5-*endo-dig* and 6-*endo-trig* cyclizations of the yne-ol-imine unit followed by aromatization in the presence of nitrogenous additives which may act as ligands[11] for silver(I) under basic conditions. We have also synthesized 2-indolyl, -pyrrolyl, -thiophenyl, -furanyl and -aryl substituted dihydrofuroquinoline derivatives following this optimized domino process in moderate to good yields. As all these heterocycles are part of the structure of various medicinally significant molecules, these newly derived 2-aryl/heteroaryl dihydrofuroquinolines may find their use in the pharmaceutical industry. In a wider sense, the domino process described herein might get decent entry to a silver-mediated oxidative rearrangement of yne-ol-imine systems. The scope of this reaction and structural modifications of some of the compounds are currently under investigation in our laboratory.

Experimental section

General methods

Solvents were dried and distilled following standard procedures. TLC analyses were carried out on aluminium sheets coated with silica gel 60 F254. All chemical reactions were run under an argon atmosphere in flame-dried glassware. Flash chromatography was done using Merck silica gel 60 (partial size 0.04–0.063 mm). ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz Bruker NMR spectrometer at 25 °C (100 MHz for ^{13}C). All ^{13}C NMR spectra were proton decoupled. Chemical shifts were quoted in parts per million (ppm) referenced to 0.00 ppm for tetramethylsilane. Data for ^{1}H NMR spectra are provided as follows: chemical shift (δ shift), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, brs = broad singlet), integration, coupling constant (J in Hz). A PerkinElmer FT-IR spectrometer was used for recording infrared (IR) spectra.

General procedure for the synthesis of alkyne-amines 1a–c

Alkyne-amines (**1a–c**) were synthesized on a gram-scale from 2-iodoaniline and 3-butyn-1-ol employing a palladium-copper catalyzed Sonogashira coupling reaction.

Synthesis of 4-(2-aminophenyl)but-3-yn-1-ol (1a)

$PdCl_2(PPh_3)_2$ (0.064 g, 0.09 mmol), CuI (0.036 g, 0.19 mmol) and 2-iodoaniline (2 gm, 9.13 mmol) were taken in a round bottom flask previously flushed with argon, and triethylamine (15 mL) was added to it at room temperature. After that, 3-butyn-1-ol (0.645 gm, 9.2 mmol) was added dropwise. The reaction mixture was stirred for 12 hours at room temperature. After completion, Et_2O and water were added and the product was extracted with Et_2O. The organic layer was washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography on silica

gel (hexane–ethylacetate; 6 : 1) to afford 1.24 gm (7.7 mmol) of 4-(2-aminophenyl)but-3-yn-1-ol in 84% yield.

General procedure for the synthesis of the dihydrofuroquinoline derivatives 3a–i: synthesis of 4-phenyl-2, 3-dihydrofuro[3,2-*c*]quinoline (3a)

A combination of DMA (15 mg, 0.12 mmol)–TEA (6 mg, 0.06 mmol) (20 mol% : 10 mol% w. r. t. alkyne) was taken in a sealed tube at 25 °C. A mixture of 4-(2-aminophenyl)but-3-yn-1-ol **1a** (100 mg, 0.62 mmol) and benzalaldehyde **2a** (99 mg, 0.93 mmol) in toluene (0.5 mL) was then added dropwise *via* a cannula into the sealed tube and the reaction mixture was placed in a pre-heated oil bath at 120 °C and was stirred for 10 minutes. After that, AgOTf (6 mg, 0.02 mmol, 3 mol% with respect to alkyne **1**) was taken in anhydrous toluene (0.5 mL) and was added dropwise into the reaction mixture by a syringe under an argon atmosphere. It was monitored by TLC. Upon completion, the solvent was removed under a vacuum and the crude product was subjected to flash column chromatography (5% EA/hexane) to afford the pure product **3a** (116 mg, 0.47 mmol) in 76% yield. The following products (**3a–i**) are obtained from this study and their spectral data are included.

General procedure for syntheses of the dihydrofuroquinoline derivatives 3j–n: synthesis of 4-(1-benzyl-1*H*-indol-3-yl)-2, 3-dihydrofuro[3,2-*c*]quinoline (3j)

4-(2-Aminophenyl)but-3-yn-1-ol **1a** (1 g, 6.2 mmol) and *N*-benzyl-indole-3-carbaldehyde **2j** (2.18 g, 9.3 mmol) were added into a mixture of DMA (10 mL) and TEA (0.12 g, 1.2 mmol, 20 mol% with respect to alkyne) in a sealed tube. The reaction mixture was placed in a pre-heated oil bath at 140 °C and was stirred for 10 minutes. After that, AgOTf (60 mg, 0.2 mmol, 3 mol% with respect to alkyne **1**) was added into the reaction mixture. It was monitored by TLC. Upon completion, the solvent was removed under a vacuum and the crude product was subjected to flash column chromatography (10% EA/hexane) to afford the pure product **3j** (1.5 g, 4 mmol) in 65% yield. The following products **3k–n** are obtained from this study and their spectral data are included. Some aldehyde–DMA adduct (15–20% with respect to aldehyde) was formed during each transformation.

4-phenyl-2, 3-dihydrofuro[3,2-*c*]quinoline (3a)

White crystalline solid, mp. 58–60 °C. IR (neat, cm^{-1}): 3056, 2960, 2916, 1630, 1588, 1551, 1506, 1493, 1411, 1342, 1267, 1086, 918, 906, 760, 701. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.8 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.83–7.79 (m, 2H), 7.60–7.56 (m, 1H), 7.44–7.33 (m, 4H), 4.78 (t, J = 9 Hz, 2H), 3.47 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 155.6, 149.2, 139.9, 129.7, 129.3, 128.8, 128.6, 128.3, 125.4, 121.4, 116.0, 115.1, 73.1, 30.1; elemental analysis observed: C, 82.38; H, 5.19; N, 5.51; calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30; N, 5.66.

4-p-tolyl-2, 3-dihydrofuro[3,2-*c*]quinoline (3b)

White crystalline solid, mp. 85–87 °C. IR (neat, cm^{-1}): 3085, 2994, 2905, 1631, 1588, 1549, 1498, 1425, 1340, 1272, 1085, 926, 818, 749; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 8 Hz, 2H), 7.61–7.57 (m, 1H), 7.38 (t, J = 7.4 Hz, 1H), 7.24 (d, J = 8 Hz, 2H), 4.81 (t, J = 8.8 Hz, 2H), 3.51 (t, J = 8.8 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 155.5, 149.0, 138.9, 137, 129.7, 129.3, 129.1, 128.3, 125.3, 121.4, 115.9, 115.0, 73.1, 30.2, 21.4; elemental analysis observed: C, 82.55; H, 5.62; N, 5.23; calcd for $C_{18}H_{15}NO$:C, 82.73; H, 5.79; N, 5.36.

4-(4-chlorophenyl)-2, 3-dihydrofuro[3,2-*c*]quinoline (3c)

White crystalline solid, mp. 121–123 °C. IR (neat, cm^{-1}): 2961, 2920, 2854, 1629, 1589, 1572, 1548, 1488, 1410, 1390, 1337, 1261, 1086, 1012, 845, 812, 763; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.8 Hz, 2H), 7.61–7.57 (m, 1H), 7.41–7.37 (m, 3H), 4.80 (t, J = 9 Hz, 2H), 3.47 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 154.2, 149.1, 138.3, 134.9, 129.9, 129.7, 129.2, 128.7, 125.6, 121.4, 116.0, 114.9, 73.1, 30.1; elemental analysis observed: C, 72.29; H, 4.20; N, 4.85; calcd for $C_{17}H_{12}ClNO$: C, 72.47; H, 4.29; N, 4.97.

4-(2-chlorophenyl)-2,3-dihydrofuro[3,2-*c*]quinoline (3d)

White crystalline solid, mp. 117–119 °C. IR (neat, cm^{-1}): 3060, 2973, 2923, 2863, 1632, 1598, 1552, 1508, 1477, 1405, 1277, 1260, 1088, 1059, 913, 760, 643; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.62–7.57 (m, 1H), 7.44–7.38 (m, 3H), 7.32–7.27 (m, 2H), 4.79 (t, J = 9 Hz, 2H), 3.21 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 155.1, 148.9, 139.1, 132.3, 130.7, 129.8, 129.7, 129.3, 127.1, 125.8, 121.4, 117.2, 116.2, 73.4, 28.7; elemental analysis observed: C, 72.32; H, 4.18; N, 4.83; calcd for $C_{17}H_{12}ClNO$:C, 72.47; H, 4.29; N, 4.97.

2-(2,3-dihydrofuro[3,2-*c*]quinolin-4-yl)phenol (3e)

Yellow crystalline solid, mp. 142–144 °C. IR (neat, cm^{-1}): 3424, 2923, 1635, 1609, 1584, 1500, 1418, 1251, 1090, 755, 737; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91–7.85 (m, 2H), 7.69 (d, J = 8 Hz, 1H), 7.63–7.59 (m, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz, 2H), 7.02 (d, J = 8.4 Hz, 1H), 6.82 (t, J = 7.6 Hz, 1H), 4.85 (t, J = 9 Hz, 2H), 3.69 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 161.3, 155.4, 145.4, 131.4, 130.6, 128.1, 126.7, 125.7, 121.5, 119.9, 118.6, 118, 115.6, 113.6, 73, 31.6; elemental analysis observed: C, 77.29; H, 4.90; N, 5.16; calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32.

4-(2,3-dihydrofuro[3,2-*c*]quinolin-4-yl)-2-methoxyphenol (3f)

Greyish white crystalline solid, mp. 175–177 °C. IR (neat, cm^{-1}): 3444, 2921, 2853, 1626, 1587, 1538, 1495, 1387, 1368, 1291, 1181, 1057, 971, 845, 733, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.61–7.56 (m, 2H), 7.38 (t, J = 7.4 Hz, 1H), 7.27 (dd, J = 2, J = 8 Hz, 1H), 6.93 (d, J = 8 Hz, 1H), 4.82 (t, J = 9 Hz, 2H), 3.94 (s, 3H), 3.52 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 164, 154.8, 148.6, 148.3, 147.9, 130.9, 130.2, 129.1, 125.6, 121.9, 121.6, 115.7, 115.6, 112.7, 73.6, 56.1, 30.3; elemental analysis observed: C, 73.57; H, 5.08; N, 4.66; calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78.

4-(furan-2-yl)-2,3-dihydrofuro[3,2-*c*]quinoline (3g)

Greyish white crystalline solid, mp. 77–79 °C. IR (neat, cm^{-1}): 2961, 2924, 1632, 1590, 1504, 1424, 1345, 1248, 1088, 1034, 885, 808, 748, 657; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.8 Hz, 1H), 7.81 (d, J = 8 Hz, 1H), 7.58–7.54 (m, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.06 (d, J = 3.2 Hz, 1H), 6.51 (t, J = 1.6 Hz, 1H), 4.82 (t, J = 9 Hz, 2H), 3.57 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 153.6, 149.0, 145.9, 143.9, 129.8, 128.9, 125.2, 121.3, 115.9, 113.3, 111.9, 111.1, 73.2, 29.9; elemental analysis observed: C, 75.86; H, 4.59; N, 5.79; calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90.

4-(1-benzyl-1*H*-pyrrol-2-yl)-2, 3-dihydrofuro[3,2-*c*]quino-line (3h)

Pale yellow crystalline solid, mp. 68–70 °C. IR (neat, cm^{-1}): 3060, 2921, 2850, 1630, 1591, 1501, 1476, 1438, 1420, 1327, 1262, 1087, 1043, 906, 764, 720; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 4.8 Hz, 1H), 7.79 (d, J = 8 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.14–7.05 (m, 3H), 6.96 (d, J = 7.2 Hz, 2H), 6.82 (s, 1H), 6.58–6.56 (m, 1H), 6.22 (t, J = 3.2 Hz, 1H), 5.82 (s, 2H), 4.77 (t, J = 9 Hz, 2H), 3.41 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 149.2, 148.5, 139.8, 130.7, 129.4, 128.7, 128.4, 126.9, 126.8, 126.2, 124.8, 121.3, 115.5, 114.8, 112.8, 108.1, 72.9, 52.4, 30.6; elemental analysis observed: C, 80.73; H, 5.47; N, 8.44; calcd for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58.

4-(thiophen-2-yl)-2, 3-dihydrofuro[3,2-*c*]quinoline (3i)

Greyish white crystalline solid, mp. 114–116 °C. IR (neat, cm^{-1}): 2961, 2922, 2855, 1628, 1587, 1552, 1503, 1370, 1344, 1261, 1080, 1024, 804, 761, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.8 Hz, 1H), 7.78 (d, J = 8 Hz, 1H), 7.57–7.53 (m, 1H),7.47 (brs, 1H), 7.38 (dd, J = 2, J = 4.8 Hz, 1H), 7.34–7.30 (m, 1H), 7.08–7.05 (m, 1H), 4.84–4.78 (m, 2H), 3.54–3.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 149.3, 148.9, 144.8, 129.8, 128.8, 128.3, 127.9, 126.7, 125.1, 121.3, 115.9, 113.1, 72.9, 30.3; elemental analysis observed: C, 70.95; H, 4.30; N, 5.41; calcd for $C_{15}H_{11}NOS$: C, 71.12; H, 4.38; N, 5.53.

4-(1-benzyl-1*H*-indol-3-yl)-2, 3-dihydrofuro[3,2-*c*]quino-line (3j)

White crystalline solid, mp. 180–182 °C. IR (neat, cm^{-1}): 3137, 2964, 2920, 1629, 1593, 1540, 1504, 1393, 1366, 1297, 1058, 921, 894, 772, 731; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 5.6 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.60–7.56 (m, 1H) 7.49 (s, 1H), 7.36–7.32 (m, 1H), 7.26–7.19 (m, 6H), 7.08 (d, J = 2 Hz, 1H), 7.07 (s, 1H), 5.32 (s, 2H), 4.81 (t, J = 9 Hz, 2H), 3.43 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 152.4, 149.4, 137.1, 129.4, 129.3, 129, 128.9, 127.9, 127.6, 126.8, 124.5, 123.7, 123.1, 121.3, 116.2, 115.6, 113.9, 109.7, 72.8, 50.4, 30.7; elemental analysis observed: C, 82.76; H, 5.27; N, 7.29; calcd for $C_{26}H_{20}N_2O$: C, 82.95; H, 5.35; N, 7.44.

4-(1-allyl-1*H*-indol-2-yl)-2,3-dihydrofuro[3,2-*c*]quinoline (3k)

Greyish white crystalline solid, mp. 159–161 °C. IR (neat, cm^{-1}): 3285, 2923, 2851, 1610, 1519, 1461, 1344, 1185, 1162, 1121, 1058, 943, 812, 744, 658; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (brs, 1H), 8.08 (d, J = 8.8 Hz, 1H), 7.82 (d, J = 8 Hz, 1H), 7.61–7.55 (m, 1H) 7.39 (s, 1H), 7.28–7.21 (m, 3H), 5.97–5.88 (m, 1H), 5.15 (d, J = 10.4 Hz, 1H), 5.04 (dd, J = 8 Hz, J = 1 Hz, 1H), 4.77 (t, J = 9 Hz, 2H), 4.68–4.66 (m, 2H), 3.41 (t, J = 9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 152.3, 149.2, 136.7, 132.9, 129.3, 128.8, 128.7, 127.3, 124.3, 123.4, 122.7, 121.2, 121.1, 117.7, 115.7, 115.4, 113.8, 109.5, 72.6, 49, 30.6; elemental analysis observed: C, 80.79; H, 5.48; N, 8.41; calcd for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58.

4-(1-(prop-2-ynyl)-1*H*-indol-2-yl)-2,3-dihydrofuro[3,2-*c*]-quinoline (3l)

Pale yellow crystalline solid, mp. 148–150 °C. IR (neat, cm^{-1}): 3271, 2962, 2909, 2123, 1628, 1587, 1542, 1504, 1390, 1296, 1191, 1059, 895, 735, 655; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, J = 7.2 Hz, 1H), 8.10 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8 Hz, 1H), 7.59 (d, J = 7.2 Hz, 1H), 7.56 (s, 1H), 7.36–7.32 (m, 2H), 7.30–7.23 (m, 2H), 4.84 (d, J = 2.4, 2H), 4.81 (t, J = 9 Hz, 2H), 3.46 (t, J = 9 Hz, 2H), 2.39 (t, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 151.9, 149.1, 136.2, 129.3, 128.8, 128.1, 127.5, 124.4, 123.7, 122.9, 121.3, 121.2, 116.1, 115.4, 113.8, 109.1, 74.1, 72.6, 35.9, 30.4; elemental analysis observed: C, 81.22; H, 4.88; N, 8.48; calcd for $C_{22}H_{16}N_2O$: C, 81.46; H, 4.97; N, 8.64.

8-chloro-4-(1-(prop-2-ynyl)-1*H*-indol-3-yl)-2, 3-dihydro-furo[3,2-*c*]quinoline (3m)

Yellow crystalline solid, mp. 163–165 °C. IR (neat, cm^{-1}): 3096, 2922, 2817, 1652, 1526, 1468, 1401, 1386, 1175, 1136, 1038, 990, 928, 747; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 6.8 Hz, 1H), 7.99 (d, J = 8.8 Hz, 1H), 7.79 (d, J = 2.4 Hz, 1H), 7.54 (s, 1H), 7.49 (dd, J = 2 Hz, J = 8.8 Hz, 1H), 7.35 (d, J = 6.8 Hz, 1H), 7.30–7.24 (m, 2H), 4.85 (d, J = 2.4 Hz, 2H), 4.81 (t, J = 9 Hz, 2H), 3.45 (t, J = 9 Hz, 2H), 2.39 (t, J = 2.4 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 152.4, 146.3, 132.3, 136.5, 130.5, 130.4, 130.1, 128.4, 127.6, 123.8, 123.3, 121.7, 120.5, 116.1, 114.7, 109.4, 74.5, 72.9, 36.3, 30.7; elemental analysis observed: C, 73.31; H, 4.12; N, 7.65; calcd for $C_{22}H_{15}ClN_2O$: C, 73.64; H, 4.21; N, 7.81.

4-(1-allyl-1*H*-indol-3-yl)-7-chloro-2,3-dihydrofuro[3,2-*c*]-quinoline (3n)

Greyish white crystalline solid, mp. 160–162 °C IR (neat, cm^{-1}): 2941, 1624, 1585, 1537, 1494, 1417, 1306, 1286, 1213, 1054, 909, 748; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (brs, 1H), 8.07 (brs, 1H), 7.76–7.72 (m, 1H), 7.39 (s, 1H), 7.26–7.19 (m, 4H), 5.99–5.89 (m, 1H), 5.17 (d, J = 10.4 Hz, 1H), 5.06 (d, J = 16.8 Hz, 1H), 4.81–4.76 (m, 2H), 4.69 (d, J = 1.2 Hz, 2H), 3.43–3.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 153.5, 149.7, 136.9, 135.3, 132.9, 129.3, 127.8, 127.4, 125.3, 123.8, 123, 122.8, 121.4, 117.9, 114.1, 113.9, 109.7, 72.9, 49.2, 30.8; elemental analysis observed: C, 73.11; H, 4.66; N, 7.81; calcd for $C_{22}H_{17}ClN_2O$: C, 73.23; H, 4.75; N, 7.76.

Author contributions

The project was conceived and supervised by S. Karmakar. All experiments were conducted by S. Karmakar and P. Das. The

manuscript and ESI were prepared by S. Karmakar, and S. Kundu carried out X-ray single crystal structure analysis. All authors have given approval to the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We gratefully acknowledge the ''Science and Engineering Research Board (SERB), Department of Science and Technology (DST), Government of India'' (Grant No. SERB/F/4912/2013-14) for the financial support of this research.

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