

Article

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Synthesis of 5,6-Dihydrodibenzo[*b,h*][1,6]naphthyridines *via* Copper Bromide-Catalyzed
Intramolecular [4+2] Hetero-Diels-Alder Reactions[†]

Isravel Muthukrishnan,^a Perumal Vinoth,^a Thavaraj Vivekanand,^a Subbiah Nagarajan,^a C. Uma

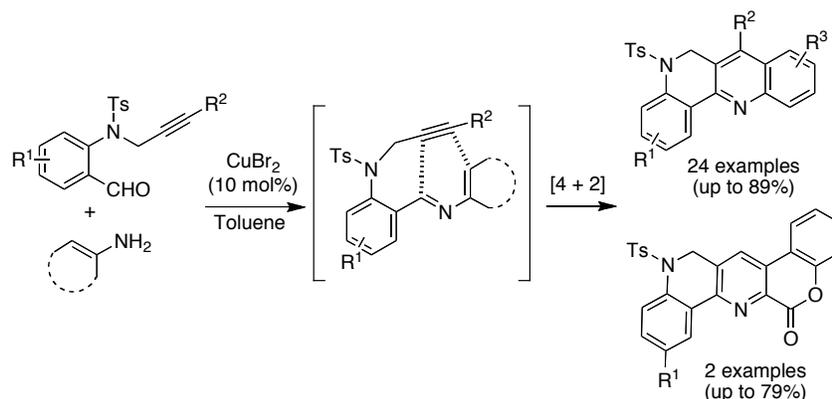
Maheswari,^a J. Carlos Menéndez^b and Vellaisamy Sridharan^{*a}

^aOrganic Synthesis Group, Department of Chemistry, School of Chemical and Biotechnology, SASTRA University,
Thanjavur 613401, Tamil Nadu, India. E-mail: vsridharan@scbt.sastra.edu, vesridharan@gmail.com

^bDepartamento de Química Orgánica y Farmacéutica, Facultad de Farmacia, Universidad Complutense, 28040
Madrid, Spain.

[†] Dedicated to Professor Shanmugam Muthusubramanian on the occasion of his retirement

GRAPHICAL ABSTRACT



ABSTRACT

A highly efficient synthesis of 5,6-dihydrodibenzo[*b,h*][1,6]naphthyridines was achieved by the reaction between 2-(*N*-propargylamino)benzaldehydes and arylamines in the presence of CuBr₂. The *in situ* generated electron-deficient heterodienenes bearing a tethered alkyne partner underwent

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3 intramolecular inverse electron-demand hetero Diels-Alder reaction (IEDDA) followed by air
4 oxidation to furnish the products in high yields. This reaction tolerated a large number of
5 substituents to afford diverse products under mild conditions. This strategy was also successfully
6 extended to the synthesis of 12,13-dihydro-6*H*-benzo[*h*]chromeno[3,4-*b*][1,6]naphthyridin-6-
7 ones starting from 3-amino-2*H*-chromen-2-one, again in high yields.
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18 INTRODUCTION

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20 The inverse electron-demand hetero Diels-Alder reaction (IEDDA) between electron-deficient
21 heterodienes (benzylidene anilines) and electron-rich dienophiles, generally known as the
22 Povarov reaction, is a versatile transformation to access tetrahydroquinoline derivatives.^{1,2} These
23 reactions are normally catalyzed by metal Lewis acids by coordinating with the 1,3-heterodiene
24 nitrogen to further increase its electron-deficiency and thus minimize the LUMO energy of the
25 heterodiene to trigger the cycloaddition.³ During the past two decades, a large number of chiral
26 catalysts were also developed to obtain chiral tetrahydroquinolines, including natural products.⁴
27 This powerful reaction was further extended to obtain polyheterocyclic compounds by means of
28 intramolecular versions starting from heterodienes bearing a tethered alkene partner.⁵ Although
29 the majority of this kind of IEDDA reactions involved the use of olefins as the dienophiles and
30 thus afforded tetrahydroquinolines, a considerable effort has been devoted to the direct synthesis
31 of quinolines by using alkynes as dienophiles.⁶ The [4+2] cycloaddition between *in situ*
32 generated benzylidene anilines and alkynes for the direct access to quinolines can be catalyzed
33 by a number of acidic catalysts including triflic acid, SnCl₂, Fe(OTf)₃, Ga(OTf)₃, Sc(OTf)₃,
34 Cu(OTf)₂, molecular iodine, HClO₄-modified montmorillonite, K-10 under microwave
35 irradiation, potassium dodecatungstocobaltate trihydrate and CuI/La(OTf)₃ in ionic liquid,
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3 among others (Scheme 1a). Likewise, intramolecular [4+2] Povarov-type cycloaddition with
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5 tethered alkyne dienophiles have also been explored to access polycyclic heterocyclic
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7 compounds, normally restricted to the easily accessible salicylaldehyde-derived aryl aldehydes.⁷
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10 [1,6]-Naphthyridines and their benz-fused analogs dibenzo[*b,h*][1,6]naphthyridines are
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12 biologically significant molecules and exhibit numerous pharmacological activities. Thus,
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14 members of this class of polycyclic compounds act as potential inhibitors of telomere
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16 maintenance,⁸ topoisomerase I⁹ and FGF receptor-1 tyrosine kinase.¹⁰ Besides, 8-substituted-
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18 [1,6]naphthyridines exhibit HIV-1 integrase inhibitory activity and cytotoxicity against cancer
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20 cells.¹¹ Furthermore, dibenzo[*b,h*][1,6]naphthyridines are known for their fluorescence properties;
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22 for instance, the 2-acetylaminobenzaldehyde-derived dibenzo[*b,h*][1,6]naphthyridines have
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24 found application in fluorescent DNA labelling.¹² Despite the significance of
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26 dibenzo[*b,h*][1,6]naphthyridines in biology, only a limited number of reports deal with the direct
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28 synthesis of these compounds. The main methodologies developed with this purpose include the
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30 silica-gel catalyzed, three-component reaction between 2-hydroxyacetophenone, aryl aldehydes
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32 and malononitrile,¹³ the neat reaction between 4-chloro-2-methylquinoline and aminoketones¹⁴
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34 and a few others.¹⁵ Recently, Wang and co-workers reported the synthesis of
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36 dibenzo[*b,h*][1,6]naphthyridines involving the Sc(OTf)₃-catalyzed cascade reaction between *o*-
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38 aminoacetophenone with methanamine in moderate to good yields (Scheme 1b).¹⁶ A one-pot
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40 synthesis of these compounds starting from 2-acetylaminobenzaldehydes was also reported
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42 (Scheme 1c).¹² Notwithstanding these few reports, no efficient, general methods are available to
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44 access these significant compounds.
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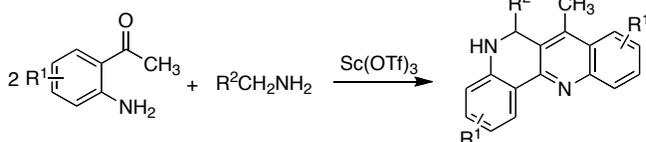
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In view of the unique biological and fluorescence properties of dibenzo[*b,h*][1,6]naphthyridines and the scarcity available procedures, development of simple and efficient protocols for their synthesis from readily available starting materials is highly desirable. In this context, we envisaged an intramolecular [4+2] cycloaddition between the *in situ* generated benzyldiene anilines derived from 2-aminoarylaldehydes bearing a tethered alkyne partner and arylamines to afford the title compounds (Scheme 1d). The proposed route involves initial cycloaddition followed by spontaneous dehydrogenation. To the best of our knowledge, the envisioned intramolecular Povarov-type [4+2] cycloaddition-oxidation strategy has not been reported for the synthesis of dibenzo[*b,h*][1,6]naphthyridines. Furthermore, owing to the lack of access to 2-(*N*-propargylamino)benzaldehydes, the synthetic utility of these compounds has not been well explored.¹⁷

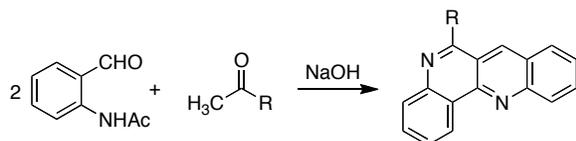
(a) [4 + 2] Cycloaddition of benzylidene anilines and alkynes



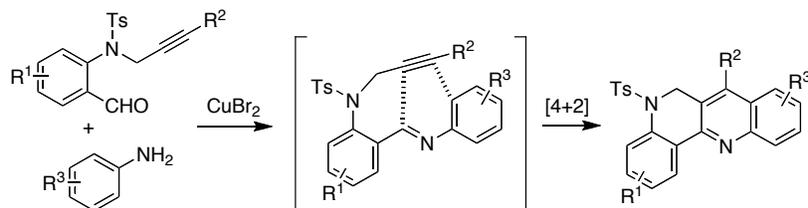
(b) Wang and co-workers (Ref. 16)



(c) Okuma and co-workers (Ref. 12)



(d) This work: Synthesis of 5,6-dihydrodibenzo[*b,h*][1,6]naphthyridines via intramolecular [4+2] cycloaddition



Scheme 1. One-pot access to quinolines and dibenzo[*b,h*][1,6]naphthyridines

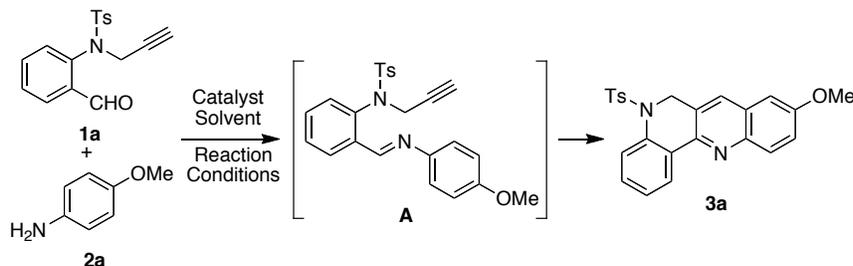
RESULTS AND DISCUSSION

To explore the possibility of our planned synthesis, our initial efforts were directed to the identification of a suitable catalytic system and reaction conditions. The required precursor 2-(*N*-tosyl-*N*-propargylamino)benzaldehyde **1a** was synthesized in a few straightforward steps starting from 2-aminobenzyl alcohol. With a properly tethered alkyne dienophile partner, we studied the intramolecular [4+2] cycloaddition, combining **1a** with *p*-anisidine **2a** in the presence of a variety of catalysts under diverse reaction conditions (Table 1). At the outset, we investigated the role of Lewis acids including CAN, InCl₃, BiCl₃ and Sc(OTf)₃ to trigger the cycloaddition in acetonitrile at 25 °C. Use of 10 mol % of these catalysts did not afford the product **3a**; instead,

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3 formation of the intermediate imine **A** was observed from the crude $^1\text{H-NMR}$ spectra in all cases.
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5 To our delight, elevation of temperature to $80\text{ }^\circ\text{C}$ triggered the [4+2] cycloaddition-oxidation
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7 sequence furnishing the product dibenzo[*b,h*][1,6]naphthyridine **3a** in moderate yields (entries 1
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9 to 8). However, in all the tested Lewis acids, the reactions were fairly slow and, even after 24 h,
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11 some unreacted intermediate imine was observed. InCl_3 and $\text{Sc}(\text{OTf})_3$ were superior, yielding
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13 75% and 67% of the product, respectively (entries 4 and 8). On the other hand, change of
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15 solvents did not significantly improve the yield (entries 9 to 12). Encouraged by these
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17 preliminary results, we subsequently moved to copper salts as catalysts. Gratifyingly, switching
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19 the catalyst to CuCl (10 mol%) increased the rate of the reaction remarkably affording 80% of
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21 the product in just one-hour reaction time at $25\text{ }^\circ\text{C}$. Indeed, 5 mol% of the catalyst was sufficient
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23 to allow complete conversion and to yield 81% of the product in toluene (entries 13 and 14). In
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25 order to improve the isolated yield and to avoid the byproducts of decomposition, we carried out
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27 the reaction at $5\text{ }^\circ\text{C}$, but only imine formation was noticed with traces of the product **3a** (entry
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29 15). A subsequent solvent screening revealed that acetonitrile, dioxane, DCM, DCE, ethanol and
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31 THF were inefficient to improve the yield (entries 16-23). Among the other tested cuprous
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33 halides, CuI failed to afford the product and CuBr yielded 56% of **3a** in 1h (entries 24 and 25).
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35 On the other hand, the last copper halide to be tested CuBr_2 (10 mol%) was the most efficient one
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37 in terms of yield providing 88% of the isolated product. Although the reaction time was 20
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39 hours, the reaction was clean and no side products or decomposition was observed (entry 26).
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41 The reaction time was reduced to 12 hours with 30 mol% of the catalyst, and $\text{Cu}(\text{OAc})_2$ was
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43 inefficient (entries 27 and 28). The reaction was also carried out in the presence 10 mol% of
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45 CuCl_2 and a comparable yield with CuCl was obtained albeit in longer reaction time (entry 29).
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Finally, we settled on CuBr₂ (10 mol%) as the catalyst and toluene as the solvent for subsequent studies due to the high yield and neatness of the reaction.

Table 1. Optimization of reaction conditions^a



Entry	Catalyst	mol%	Solvent	Temp. (°C)	Reaction time (h)	Yield of 3a (%) ^b
1	CAN	10	MeCN	25	24	- ^c
2	CAN	10	MeCN	80	24	58 ^d
3	InCl ₃	10	MeCN	25	24	- ^c
4	InCl ₃	10	MeCN	80	24	75 ^d
5	BiCl ₃	10	MeCN	25	24	- ^c
6	BiCl ₃	10	MeCN	80	24	61 ^d
7	Sc(OTf) ₃	10	MeCN	25	24	- ^c
8	Sc(OTf) ₃	10	MeCN	80	24	67 ^d
9	InCl ₃	10	Toluene	80	24	70 ^d
10	InCl ₃	10	DCE	80	24	61 ^d
11	Sc(OTf) ₃	10	Toluene	80	24	71 ^d
12	Sc(OTf) ₃	10	DCE	80	24	65 ^d
13	CuCl	10	Toluene	25	1	80
14	CuCl	5	Toluene	25	1	81
15	CuCl	5	Toluene	5	6	trace ^d
16	CuCl	5	MeCN	25	24	trace ^d
17	CuCl	20	MeCN	25	6	65
18	CuCl	5	Dioxane	25	24	23 ^d
19	CuCl	20	Dioxane	25	1	52
20	CuCl	20	EtOH	25	24	- ^c
21	CuCl	5	DCM	25	1	63
22	CuCl	5	DCE	25	1	68
23	CuCl	5	THF	25	24	trace ^d
24	CuI	10	Toluene	25	24	- ^c
25	CuBr	10	Toluene	25	1	56 ^c
26 ^f	CuBr₂	10	Toluene	25	20	88
27	CuBr ₂	30	Toluene	25	12	89
28	Cu(OAc) ₂	10	Toluene	25	12	22 ^c
29	CuCl ₂	10	Toluene	25	8	82

^aAll reactions were carried out with **1a** (0.5 mmol) and **2a** (0.5 mmol) with catalyst in 3 mL toluene. ^b Isolated yield. ^c Only imine **A** formation was observed. ^d Unreacted imine **A** was noticed in the crude ¹H NMR spectra. ^e No imine or unreacted aldehyde was present. ^f Optimized reaction conditions.

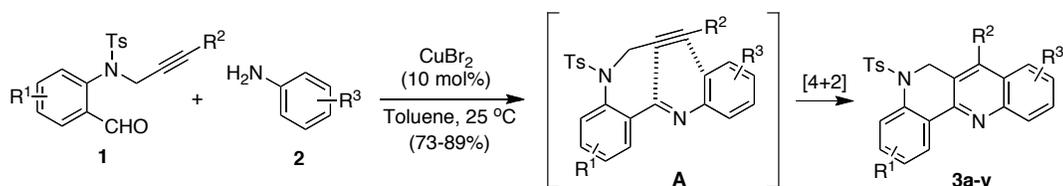
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Next we turned our attention to study the scope and limitations of the methodology and the results are summarized in Table 2. The starting 2-(*N*-tosyl-*N*-propargylamino)benzaldehydes **1a-e** were synthesized from the corresponding 2-aminobenzyl alcohols using the literature procedure.¹⁸ With the necessary starting materials in hand, our initial studies focused on the utilization of diverse arylamines **2** combining with aldehyde **1a** for the cycloaddition-oxidation sequence to obtain the corresponding dibenzo[*b,h*][1,6]naphthyridines **3**. As shown in entries 1 to 10 in Table 2, the reaction tolerated well a variety of substituents including methyl, methoxy, chloro, bromo, dimethyl (2,4- and 3,5-) and dichloro (2,4-) groups. Irrespective of the electronic nature of the substituents, the reactions were completed between 16 to 24 hours and an average of 80% yield was obtained. The nature of the substituents helps in the formation of intermediate imine A (with or without catalyst) and once the imine is formed, the Lewis acids triggered the intramolecular [4+2] reaction, where the substituents played no significant role. In order to further test the functional group tolerance, we employed *o*-aminophenol as the substrate. Interestingly, the reaction proceeded well to yield 75% of product **3j** with no traces of a benzoxazole-type side product (entry 10). Compound **3j** is an important molecule that contains the biologically significant 8-hydroxyquinoline scaffold.¹⁹

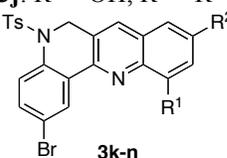
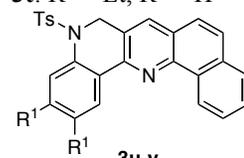
Additionally, treatment of bromoaldehyde **1b** with a set of arylamines bearing methyl, methoxy and chloro-substituents furnished the respective dibenzo[*b,h*][1,6]naphthyridines **3k-3n** in high yields (entries 11 to 14). In all cases, the maximum reaction time was 20 h and the highest yield of 85% was obtained in the case of the 4-methoxy substituted compound **3n**. In order to increase the structural diversity accessible by this methodology, we investigated the reactivity of the terminal phenyl-substituted alkyne derivatives **1d** and **1e**. In contrast to terminal alkynes, these

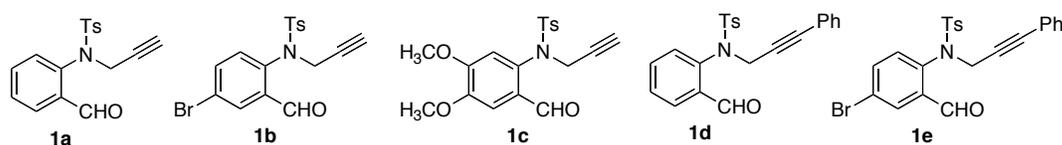
substrates were reluctant to undergo the intramolecular cycloaddition under the optimized conditions. Only traces of the product formation were observed at 25 °C together with the intermediate imines **A**. Nonetheless, increase of the reaction temperature to 70 °C triggered the reaction to afford the desired products, again in good yields (entries 15 to 18). The fluoro-substituted derivative was also synthesized with comparable yield (entry 18). The electron rich dimethoxy-substituted aldehyde **1c** was also reacted with arylamines under optimized conditions yielding 79-82% of the products (entries 19 and 20). Finally, 1-naphthylamine was tested to obtain the pentacyclic derivatives **3u** and **3v**. Although these reactions afforded the products under ambient temperature, the reactions were very slow and complete conversion was achieved only at 70 °C, affording 73-86% of isolated products.

Table 2. Scope and limitations of the methodology: Synthesis of dibenzo[*b,h*][1,6]naphthyridines **3^a**



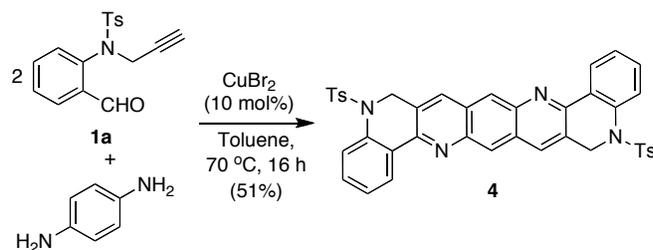
Entry	Product 3	Reaction time (h)	Yield (%) ^b	Entry	Product 3	Reaction time (h)	Yield (%) ^b
1	3a : R ¹ = R ² = H, R ³ = OMe, R ⁴ = H	20	88	15	3o : R ¹ = H, R ² = R ³ = Me	24 ^c	78
2	3b : R ¹ = R ² = R ³ = R ⁴ = H	20	83	16	3p : R ¹ = Br, R ² = R ³ = Me	24 ^c	83
3	3c : R ¹ = R ² = H, R ³ = Me, R ⁴ = H	16	76	17	3q : R ¹ = Br, R ² = OMe, R ³ = H	20 ^c	82
4	3d : R ¹ = Me, R ² = H, R ³ = Me, R ⁴ = H	16	82	18	3r : R ¹ = Br, R ² = H, R ³ = F	24 ^c	89
5	3e : R ¹ = H, R ² = Me, R ³ = H, R ⁴ = Me	16	74				
6	3f : R ¹ = OMe, R ² = R ³ = R ⁴ = H	24	79				

7	3g : R ¹ = R ² = H, R ³ = Cl, R ⁴ = H	20	77				
8	3h : R ¹ = Cl, R ² = H, R ³ = Cl, R ⁴ = H	20	80				
9	3i : R ¹ = R ² = H, R ³ = Br, R ⁴ = H	20	78	19	3s : R ¹ = H, R ² = F	12	82
10	3j : R ¹ = OH, R ² = R ³ = R ⁴ = H	24	75	20	3t : R ¹ = Et, R ² = H	16	79
							
11	3k : R ¹ = R ² = H	20	82	21	3u : R ¹ = H	20 ^c	86
12	3l : R ¹ = R ² = Me	16	84	22	3v : R ¹ = OMe	16 ^c	73
13	3m : R ¹ = H, R ² = Cl	20	80				
14	3n : R ¹ = H, R ² = OMe	20	85				



^a Reaction conditions: unless otherwise noted, all reactions were carried out with **1** (0.5 mmol) and **2** (0.5 mmol) in the presence of CuBr₂ (10 mol%) in 3 mL toluene at 25 °C. ^b Isolated yield. ^c The reactions were carried out at 70 °C.

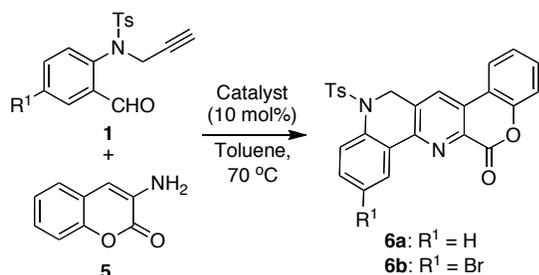
In addition to simple arylamines, the reactivity of *p*-phenylenediamine with aldehyde **1a** was also investigated (Scheme 2). Initially, we employed the optimized conditions with a 1:0.5 ratio of the aldehyde and diamine in toluene. Unexpectedly, no product formation was observed even after 24 h and only traces of the intermediate imine was noticed. However, increase of the reaction temperature afforded 51% of the heptacyclic compound **4**. Further efforts to improve the yield of the product by changing the mole ratio of the reactants and the use of CuCl as catalyst were unsuccessful.



Scheme 2. Synthesis of bis-dibenzo[*b,h*][1,6]naphthyridine **4**

Finally, to further validate the protocol, we envisioned to synthesize 12,13-dihydro-6*H*-benzo[*h*]chromeno[3,4-*b*][1,6]naphthyridin-6-ones **6** from readily available 3-amino-2*H*-chromen-2-one **5**, since coumarin and its derivatives are among the most significant heterocyclic scaffolds of wide biological interest.²⁰ The reaction between aldehydes **1a** and **1b**, and 3-amino-2*H*-chromen-2-one **5** in the presence of CuBr₂ furnished benzo[*h*]chromeno[3,4-*b*][1,6]naphthyridin-6-ones **6** albeit in moderate yields. Change of catalyst to CuCl improved the yield significantly under similar experimental conditions furnishing the products **6a** and **6b** in 74% and 79% respectively (Table 3).

Table 3. Synthesis of 12,13-dihydro-6*H*-benzo[*h*]chromeno[3,4-*b*][1,6]naphthyridin-6-ones **6**^a

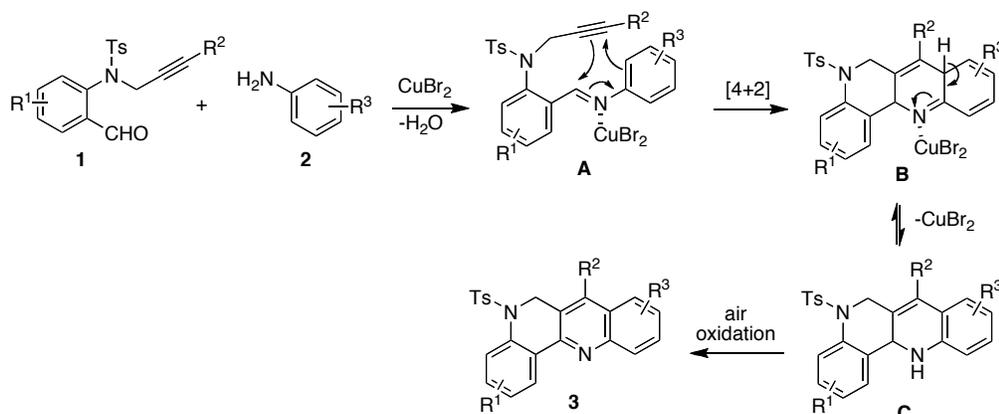


Entry	Compound	CuBr ₂ (10 mol%)		CuCl (10 mol%)	
		Reaction time (h)	Yield (%) ^b	Reaction time (h)	Yield (%) ^b
1	6a	24	60	12	74
2	6b	24	63	12	79

^a Reaction conditions: all reactions were carried out with **1** (0.5 mmol) and **5** (0.5 mmol) in the presence of catalyst (10 mol%) in 3 mL toluene at 70 °C. ^b Isolated yield.

The mechanism for the synthesis of dibenzo[*b,h*][1,6]naphthyridines **3** involves the initial formation of imine **A**, which was confirmed in several occasions during the optimization process, followed by Povarov-type intramolecular [4+2] cycloaddition catalyzed by CuBr₂. The activation of the heterodiene is attributed to the Lewis acidity of CuBr₂²¹ to trigger the addition of the tethered alkyne to the heterodiene to furnish tetrahydrodibenzo[*b,h*][1,6]naphthyridines **C**

through the intermediacy of species **B**. Subsequent air oxidation under the experimental conditions yielded products **3** (Scheme 3).



Scheme 3. Proposed mechanism

CONCLUSION

In conclusion, we have developed a simple and efficient method for the synthesis of 5,6-dihydrodibenzo[*b,h*][1,6]naphthyridines from inexpensive and readily available starting materials and catalysts under mild conditions. The CuBr₂-catalyzed reaction between 2-(*N*-propargylamino)benzaldehydes and arylamines afforded the products *via* intramolecular [4+2] cycloaddition between the *in situ* generated heterodienophile and tethered alkyne dienophile. This methodology allows direct access to the products by generating two nitrogen heterocycles in a single operation besides its other significant features including high yield, simple operation and high atom economy. This protocol was also extended to the synthesis of 12,13-dihydro-6*H*-benzo[*h*]chromeno[3,4-*b*][1,6]naphthyridin-6-ones in good yields.

EXPERIMENTAL SECTION

General Information. All reagents and solvents were purchased from commercial suppliers and used without further purification. The reactions were monitored by thin-layer chromatography visualized by UV detection or using *p*-anisaldehyde stain or molecular iodine. Melting points were recorded on a melting point apparatus in capillaries and are uncorrected. ^1H - and ^{13}C -NMR spectra were recorded in CDCl_3 or DMSO-d_6 at room temperature in a spectrometer operating at 300 MHz for ^1H and 75 MHz for ^{13}C . Chemical shifts (δ) are expressed in ppm using TMS as internal standard and coupling constants (J) are given in Hz. Infrared (IR) spectra were obtained in a FTIR spectrometer with a diamond ATR accessory for solid and liquid samples, requiring no sample preparation and the major frequencies were reported in cm^{-1} . Elemental analyses were determined by using a CHNS combustion microanalyzer.

General procedure for the synthesis of compounds **3**, **4** and **6**.

To a stirred solution of 2-(*N*-propargylamino)benzaldehydes **1** (0.5 mmol) and arylamines **2** or 3-amino-2*H*-chromen-2-one **5** (0.5 mmol) in toluene (3 mL) was added CuBr_2 or CuCl (10 mol%) and stirring was continued at 25 °C or 70 °C for the time periods given in Tables 2 and 3. After completion of the reaction, as indicated by TLC, the reaction mixture was diluted with dichloromethane (15 mL), washed with water (10 mL) and brine solution (10 mL). The organic layer was dried over anhyd. Na_2SO_4 and the solvent was removed under reduced pressure. The crude was purified through flash silica gel column chromatography using petroleum ether: ethyl acetate as eluent (90:10 to 60:40, v/v).

Characterization data for compounds 3, 4 and 6.

9-Methoxy-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3a). Colourless solid; mp: 183-185 °C; yield: 184 mg, 88%; IR (neat) 2980.5, 2945.0, 1620.2, 1596.7, 1494.6, 1345.5, 1226.8, 1160.1, 1064.4 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.81 (s, 3H), 3.92 (s, 3H), 4.99 (s, 2H), 6.53 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 2.7 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.26 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.38-7.50 (m, 2H), 7.58 (s, 1H), 7.78 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.84 (d, *J* = 9.3 Hz, 1H), 8.26 (dd, *J* = 7.5, 2.1 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃)*: δ 20.9, 49.7, 55.6, 104.6, 122.1, 125.0, 125.6, 127.2, 127.8, 128.3, 128.6, 130.1, 130.6, 130.8, 131.0, 134.3, 137.9, 143.6, 143.7, 147.1, 157.9. Anal Calcd for C₂₄H₂₀N₂O₃S: C, 69.21; H, 4.84; N, 6.73. Found: C, 68.96; H, 4.88; N, 6.98. *One aromatic carbon is merged with others.

5-Tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3b). Colourless solid; mp: 174-177 °C; yield: 160 mg, 83%; IR (neat) 3033.6, 1596.8, 1449.4, 1343.0, 1161.5, 1061.1 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.80 (s, 3H), 5.07 (s, 2H), 6.56 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 2H), 7.46-7.59 (m, 3H), 7.67 (td, *J* = 8.4, 1.2 Hz, 1H), 7.72 (s, 1H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.85 (dd, *J* = 7.8, 0.9 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 8.38 (dd, *J* = 7.8, 1.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃)*: δ 20.9, 49.7, 124.6, 126.0, 126.6, 127.1, 127.2, 127.8, 127.9, 128.6, 129.2, 129.4, 130.6, 132.2, 134.4, 138.4, 143.7, 147.7, 149.5. Anal Calcd for C₂₃H₁₈N₂O₂S: C, 71.48; H, 4.69; N, 7.25. Found: C, 71.16; H, 4.68; N, 7.38. *Two aromatic carbons are merged with others.

9-Methyl-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3c). Brown solid; mp: 179-181 °C; yield: 152 mg, 76%; IR (neat) 3027.0, 2920.0, 1597.8, 1491.7, 1348.3, 1161.1, 1064.5 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.74 (s, 3H), 2.47 (s, 3H), 4.96 (s, 2H), 6.49 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 7.36-7.48 (m, 4H), 7.54 (s, 1H), 7.75 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.80 (d,

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3 $J = 9.3$ Hz, 1H), 8.27 (dd, $J = 7.5, 1.5$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3)*: δ 20.9, 21.6, 49.7,
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5 124.6, 125.8, 125.9, 127.2, 127.3, 127.8, 128.6, 128.9, 130.4, 130.8, 131.5, 131.7, 134.4, 136.6,
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7 138.2, 143.6, 146.3, 148.6. Anal Calcd for $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$: C, 71.98; H, 5.03; N, 6.99. Found: C,
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9 71.67; H, 5.10; N, 7.01. *One aromatic carbon is merged with others.

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12 **9,11-Dimethyl-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3d)**. Colourless solid; mp:
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14 184-186 °C; yield: 170 mg, 82%; IR (neat) 3044.5, 2905.6, 1594.6, 1488.7, 1350.6, 1166.2,
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16 1081.5 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.79 (s, 3H), 2.44 (s, 3H), 2.67 (s, 3H), 4.98 (s, 2H),
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18 6.48 (d, $J = 8.1$ Hz, 2H), 6.93 (d, $J = 8.1$ Hz, 2H), 7.26 (s, 1H), 7.29 (s, 1H), 7.37-7.48 (m, 2H),
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20 7.52 (s, 1H), 7.75 (d, $J = 7.5$ Hz, 1H), 8.34 (dd, $J = 7.5, 1.8$ Hz, 1H); ^{13}C NMR (75 MHz,
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22 CDCl_3): δ 17.6, 20.8, 21.6, 49.7, 123.9, 124.1, 125.9, 127.2, 127.3, 127.5, 127.6, 128.5, 130.0,
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24 131.4, 131.5, 131.7, 134.3, 136.1, 136.9, 138.1, 143.5, 145.2, 147.1. Anal Calcd for
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26 $\text{C}_{25}\text{H}_{22}\text{N}_2\text{O}_2\text{S}$: C, 72.44; H, 5.35; N, 6.76. Found: C, 72.17; H, 5.39; N, 6.93.

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29 **8,10-Dimethyl-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3e)**. Colourless solid; mp:
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31 159-160 °C; yield: 153 mg, 74%; IR (neat) 3035.3, 2898.7, 1596.3, 1459.8, 1340.6, 1160.8,
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33 1051.3 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.74 (s, 3H), 2.42 (s, 3H), 2.55 (s, 3H), 4.98 (s, 2H),
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35 6.49 (d, $J = 8.4$ Hz, 2H), 6.96 (d, $J = 8.4$ Hz, 2H), 7.10 (s, 1H), 7.41 (td, $J = 7.2, 1.5$ Hz, 1H),
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37 7.45 (td, $J = 8.1, 1.5$ Hz, 1H), 7.57 (s, 1H), 7.70 (s, 1H), 7.75 (dd, $J = 7.8, 1.2$ Hz, 1H), 8.29 (dd,
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39 $J = 7.8, 1.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3)*: δ 18.5, 20.9, 21.7, 49.9, 123.3, 124.6, 125.9,
40
41 126.4, 127.2, 127.7, 128.6, 128.7, 129.4, 130.4, 130.6, 133.5, 134.7, 138.3, 139.3, 143.7, 148.2,
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43 148.9. Anal Calcd for $\text{C}_{25}\text{H}_{22}\text{N}_2\text{O}_2\text{S}$: C, 72.44; H, 5.35; N, 6.76. Found: C, 72.09; H, 5.38; N,
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45 6.91. *One aromatic carbon is merged with others.

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48 **11-Methoxy-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3f)**. Colourless solid; mp:
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50 179-180 °C; yield: 165 mg, 79%; IR (neat) 2918.5, 1598.4, 1558.0, 1488.3, 1345.9, 1161.9,
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3 1067.0 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.81 (s, 3H), 4.06 (s, 3H), 5.05 (s, 2H), 6.63 (d, $J =$
4 8.1 Hz, 2H), 7.00 (d, 7.5 Hz, 1H), 7.10 (d, $J = 8.1$ Hz, 2H), 7.28 (d, $J = 7.5$ Hz, 1H), 7.42 (t, $J =$
5 7.8 Hz, 1H), 7.43-7.56 (m, 2H), 7.65 (s, 1H), 7.82 (d, $J = 7.5$ Hz, 1H), 8.46 (dd, $J = 7.5, 1.8$ Hz,
6 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 20.8, 49.5, 56.1, 107.8, 119.0, 125.2, 126.4, 126.9, 127.2,
7 127.6, 127.7, 128.4, 128.8, 130.3, 130.5, 132.3, 134.8, 138.2, 139.5, 143.8, 148.5, 155.3. Anal
8 Calcd for $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_3\text{S}$: C, 69.21; H, 4.84; N, 6.73. Found: C, 68.91; H, 4.94; N, 6.84.

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17 **9-Chloro-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3g)**. Colourless solid; mp: 182-
18 185 $^\circ\text{C}$; yield: 162 mg, 77%; IR (neat) 3039.7, 1598.3, 1482.9, 1349.9, 1165.2, 1063.4 cm^{-1} ; ^1H
19 NMR (300 MHz, CDCl_3): δ 1.85 (s, 3H), 5.04 (s, 2H), 6.59 (d, $J = 8.1$ Hz, 2H), 7.01 (d, $J = 8.1$
20 Hz, 2H), 7.47 (td, $J = 7.5, 0.9$ Hz, 1H), 7.53-7.61 (m, 2H), 7.63 (s, 1H), 7.69 (d, $J = 2.1$ Hz, 1H),
21 7.83 (d, $J = 8.1$ Hz, 1H), 7.92 (d, $J = 9.0$ Hz, 1H), 8.34 (dd, $J = 7.8, 1.5$ Hz, 1H); ^{13}C NMR (75
22 MHz, CDCl_3)*: δ 20.9, 49.6, 125.7, 126.0, 127.2, 127.7, 127.8, 127.9, 129.7, 130.2, 130.3,
23 130.7, 130.9, 131.2, 132.2, 134.3, 138.4, 143.8, 145.9, 149.8. Anal Calcd for $\text{C}_{23}\text{H}_{17}\text{ClN}_2\text{O}_2\text{S}$: C,
24 65.63; H, 4.07; N, 6.66. Found: C, 65.29; H, 4.05; N, 6.70. *One aromatic carbon is merged with
25 others.

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38 **9,11-Dichloro-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3h)**. Colourless solid; mp
39 243-246 $^\circ\text{C}$; yield: 182 mg, 80%; IR (neat) 3065.8, 2919.3, 1594.7, 1474.4, 1338.3, 1159.1,
40 1061.8 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.93 (s, 3H), 5.07 (s, 2H), 6.62 (d, $J = 7.8$ Hz, 2H),
41 7.01 (d, $J = 7.8$ Hz, 2H), 7.48-7.60 (m, 4H), 7.77 (s, 1H), 7.84 (d, $J = 7.5$ Hz, 1H), 8.45 (d, $J =$
42 7.2 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 20.9, 49.4, 124.8, 126.5, 126.7, 127.3, 127.7, 128.0,
43 128.5, 128.7, 130.0, 130.1, 131.2, 131.4, 131.5, 134.1, 134.9, 138.5, 142.3, 144.0, 150.2. Anal
44 Calcd for $\text{C}_{23}\text{H}_{16}\text{Cl}_2\text{N}_2\text{O}_2\text{S}$: C, 60.67; H, 3.54; N, 6.15. Found: C, 60.41; H, 3.62; N, 6.37.

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3 **9-Bromo-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3i).** Colourless solid; mp 167-
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5 168 °C; yield: 182 mg, 78%; IR (neat) 3048.5, 2933.2, 1596.7, 1479.5, 1339.0, 1156.0, 1078.1
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7 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.87 (s, 3H), 5.06 (s, 2H), 6.61 (d, $J = 8.1$ Hz, 2H), 7.02 (d,
8
9 $J = 8.1$ Hz, 2H), 7.49 (t, $J = 7.5$ Hz, 1H), 7.57 (t, $J = 6.9$ Hz, 1H), 7.63 (s, 1H), 7.73 (d, $J = 9.0$
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11 Hz, 1H), 7.83-7.89 (m, 3H), 8.35 (d, $J = 6.9$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3)*: δ 20.9, 49.5,
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13 120.4, 125.7, 126.0, 127.2, 127.9, 128.2, 128.7, 129.1, 130.3, 130.8, 130.9, 131.1, 132.8, 134.3,
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15 138.4, 143.8, 146.2, 149.9. Anal Calcd for $\text{C}_{23}\text{H}_{17}\text{BrN}_2\text{O}_2\text{S}$: C, 59.36; H, 3.68; N, 6.02. Found:
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17 C, 58.99; H, 3.64; N, 6.13. *One aromatic carbon is merged with others.

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21 **5-Tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridin-11-ol (3j).** Colourless solid; mp 184-185
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23 °C; yield: 151 mg, 75%; IR (neat) 3354.3, 2958.5, 1601.9, 1487.0, 1351.0, 1332.6, 1154.6,
24
25 1058.5 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.86 (s, 3H), 5.06 (s, 2H), 6.52 (d, $J = 8.1$ Hz, 2H),
26
27 6.95 (d, 8.1 Hz, 2H), 7.13 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.24 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.42 (t, $J =$
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29 7.8 Hz, 1H), 7.48 (td, $J = 7.5, 1.2$ Hz, 1H), 7.56 (td, $J = 7.8, 1.5$ Hz, 1H), 7.73 (s, 1H), 7.83 (dd, J
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31 = 8.1, 1.2 Hz, 1H), 8.03 (brs, 1H), 8.28 (dd, $J = 7.5, 1.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ
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33 20.9, 49.7, 110.0, 117.4, 125.5, 125.7, 127.2, 127.5, 127.8, 127.9, 128.0, 128.5, 130.2, 130.8,
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35 132.4, 134.0, 137.3, 138.5, 143.9, 147.4, 152.0. Anal Calcd for $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_3\text{S}$: C, 68.64; H, 4.51;
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37 N, 6.96. Found: C, 68.50; H, 4.61; N, 7.05.

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41 **2-Bromo-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3k).** Colourless solid; mp 185-
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43 188 °C; yield: 191 mg, 82%; IR (neat) 2938.4, 1592.5, 1434.3, 1354.6, 1161.8, 1051.3 cm^{-1} ; ^1H
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45 NMR (300 MHz, CDCl_3): δ 1.80 (s, 3H), 5.03 (s, 2H), 6.58 (d, $J = 8.1$ Hz, 2H), 7.04 (d, $J = 8.1$
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47 Hz, 2H), 7.52 (td, $J = 8.1, 1.2$ Hz, 1H), 7.62-7.73 (m, 5H), 7.99 (d, $J = 8.4$ Hz, 1H), 8.51 (d, $J =$
48
49 2.1 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3)*: δ 20.9, 49.5, 121.7, 124.3, 127.0, 127.1, 127.2, 127.3,
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51 128.8, 129.2, 129.5, 129.6, 132.2, 132.4, 133.4, 134.1, 137.3, 144.0, 147.5, 148.1. Anal Calcd for
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$C_{23}H_{17}BrN_2O_2S$: C, 59.36; H, 3.68; N, 6.02. Found: 59.02; H, 3.66; N, 6.19. *One aromatic carbon is merged with others.

2-Bromo-9,11-dimethyl-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3l). Colourless solid; mp 213-218 °C; yield: 207 mg, 84%; IR (neat) 2915.9, 1593.1, 1485.9, 1349.2, 1161.2, 1046.0 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 1.66 (s, 3H), 2.31 (s, 3H), 2.54 (s, 3H), 4.83 (s, 2H), 6.38 (d, $J = 8.1$ Hz, 2H), 6.82 (d, $J = 8.1$ Hz, 2H), 7.12 (s, 1H), 7.17 (s, 1H), 7.38 (s, 1H), 7.40 (dd, $J = 8.4, 2.1$ Hz, 1H), 7.49 (d, $J = 8.4$ Hz, 1H), 8.30 (d, $J = 2.1$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.7, 20.9, 21.7, 49.5, 121.5, 123.7, 123.8, 127.2, 127.5, 128.5, 128.6, 129.3, 131.7, 131.9, 132.8, 133.0, 134.1, 136.6, 137.0, 137.1, 143.8, 145.1, 145.8. Anal Calcd for $C_{25}H_{21}BrN_2O_2S$: C, 60.86; H, 4.29; N, 5.68. Found: C, 60.57; H, 4.24; N, 5.86.

2-Bromo-9-chloro-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3m). Colourless solid; mp 195-197 °C; yield: 200 mg, 80%; IR (neat) 3048.6, 2900.0, 1597.1, 1484.0, 1343.3, 1163.8, 1048.3 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 1.86 (s, 3H), 5.03 (s, 2H), 6.62 (d, $J = 8.4$ Hz, 2H), 7.03 (d, $J = 8.4$ Hz, 2H), 7.59-7.68 (m, 3H), 7.69-7.72 (m, 2H), 7.92 (d, $J = 9.0$ Hz, 1H), 8.48 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9, 49.3, 121.7, 125.4, 125.7, 127.2, 127.9, 128.7, 128.8, 129.5, 130.6, 130.8, 131.4, 131.7, 132.7, 133.7, 134.0, 137.3, 144.0, 145.8, 148.4. Anal Calcd for $C_{23}H_{16}BrClN_2O_2S$: C, 55.27; H, 3.23; N, 5.60. Found: C, 55.04; H, 3.16; N, 5.57.

2-Bromo-9-methoxy-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3n). Colourless solid; mp 201-204 °C; yield: 211 mg, 85%; IR (neat) 3045.3, 2958.5, 1622.9, 1497.4, 1345.2, 1246.7, 1156.8, 1037.6 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 1.88 (s, 3H), 3.97 (s, 3H), 5.03 (s, 2H), 6.61 (d, $J = 8.1$ Hz, 2H), 6.99 (d, $J = 2.7$ Hz, 1H), 7.04 (d, $J = 8.1$ Hz, 2H), 7.33 (dd, $J = 9.3, 2.7$ Hz, 1H), 7.61 (dd, $J = 8.7, 2.4$ Hz, 1H), 7.63 (s, 1H), 7.70 (d, $J = 8.4$ Hz, 1H), 7.88 (d, $J = 8.4$ Hz, 1H), 8.45 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$)*: δ 21.0, 49.5, 55.6, 104.6,

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3 121.6, 122.4, 124.6, 127.2, 128.3, 128.5, 128.7, 129.3, 130.7, 131.1, 132.4, 132.8, 134.1, 136.8,
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5 143.7, 143.9, 145.7 . Anal Calcd for C₂₄H₁₉BrN₂O₃S: C, 58.19; H, 3.87; N, 5.65. Found: C,
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7 57.81; H, 3.84; N, 5.79. *One aromatic carbon is merged with others.
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10 **9,11-Dimethyl-6-phenyl-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3o).** Colourless
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12 solid; mp 210-212 °C; yield: 191 mg, 78%; IR (neat) 3030.6, 2915.9, 1578.7, 1486.1, 1345.2,
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14 1161.9, 1084.5 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.95 (s, 3H), 2.37 (s, 3H), 2.77 (s, 3H), 4.79
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16 (s, 2H), 6.65 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 1H), 7.03 (s, 1H), 7.27 (dd, *J* = 7.5, 1.8 Hz,
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18 2H), 7.33 (s, 1H), 7.43-7.53 (m, 2H), 7.56-7.64 (m, 3H), 7.77 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.42 (dd,
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20 *J* = 7.5, 2.4 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃)*: δ 18.0, 21.0, 21.9, 47.9, 121.1, 122.6, 126.1,
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22 126.5, 127.0, 127.4, 127.5, 128.5, 128.6, 128.9, 129.4, 129.9, 131.5, 131.9, 134.4, 135.4, 136.0,
23
24 137.0, 137.9, 143.5, 145.1, 146.7. Anal Calcd for C₃₁H₂₆N₂O₂S: C, 75.89; H, 5.34; N, 5.71.
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26 Found: C, 75.61; H, 5.40; N, 5.80. *One aromatic carbon is merged with others.
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30 **2-Bromo-9,11-dimethyl-6-phenyl-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3p).**
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32 Colourless solid; mp 221-224 °C; yield: 236 mg, 83%; IR (neat) 2919.0, 1583.1, 1483.1, 1344.5,
33
34 1161.9, 1083.6 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.96 (s, 3H), 2.37 (s, 3H), 2.77 (s, 3H), 4.77
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36 (s, 2H), 6.69 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 7.03 (s, 1H), 7.23-7.26 (m, 2H), 7.35
37
38 (s, 1H), 7.57-7.66 (m, 5H), 8.52 (d, *J* = 2.1 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃)*: δ 18.0, 21.0,
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40 21.9, 47.7, 121.4, 121.9, 122.6, 126.7, 127.0, 128.7, 128.9, 129.0, 129.1, 129.3, 131.7, 132.7,
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42 133.6, 134.1, 135.1, 136.5, 136.8, 137.2, 143.7, 143.8, 145.0, 145.4. Anal Calcd for
43
44 C₃₁H₂₅BrN₂O₂S: C, 65.38; H, 4.42; N, 4.92. Found: C, 65.07; H, 4.41; N, 5.05. *One aromatic
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46 carbon is merged with others.
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52 **2-Bromo-11-methoxy-6-phenyl-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3q).**
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54 Colourless solid; mp 220-222 °C; yield: 234 mg, 82%; IR (neat) 2932.9, 1593.7, 1485.3, 1344.7,
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3 1257.8, 1161.1, 1072.6 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.96 (s, 3H), 4.09 (s, 3H), 4.82 (s,
4 2H), 6.78 (d, $J = 8.1$ Hz, 2H), 7.00-7.05 (m, 2H), 7.08 (d, $J = 8.1$ Hz, 2H), 7.24-7.27 (m, 2H),
5 7.33 (t, $J = 7.8$ Hz, 1H), 7.58-7.69 (m, 5H), 8.60 (d, $J = 2.1$ Hz, 1H); ^{13}C NMR (75 MHz,
6 CDCl_3)*: δ 21.0, 47.5, 56.2, 107.7, 117.8, 121.7, 123.1, 126.9, 127.0, 127.8, 129.0, 129.1, 129.3,
7 132.5, 133.2, 134.6, 134.7, 136.8, 139.5, 143.9, 144.5, 146.8, 155.4. Anal Calcd for
8 $\text{C}_{30}\text{H}_{23}\text{BrN}_2\text{O}_3\text{S}$: C, 63.05; H, 4.06; N, 4.90. Found: C, 62.90; H, 3.95; N, 4.97. *Three aromatic
9 carbons are merged with others.

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20 **2-Bromo-9-fluoro-6-phenyl-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3r).**

21 Colourless solid; mp 228-230 $^\circ\text{C}$; yield: 249 mg, 89%; IR (neat) 3030.8, 1619.2, 1489.0, 1333.3,
22 1229.7, 1159.7, 1079.9 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.96 (s, 3H), 4.81 (s, 2H), 6.73 (d, J
23 = 8.4 Hz, 2H), 7.00 (d, $J = 8.4$ Hz, 2H), 7.10 (dd, $J = 9.9, 2.7$ Hz, 1H), 7.25-7.28 (m, 2H), 7.40-
24 7.46 (m, 1H), 7.57-7.69 (m, 5H), 8.03 (dd, $J = 9.0, 5.4$ Hz, 1H), 8.51 (d, $J = 1.8$ Hz, 1H); ^{13}C
25 NMR (75 MHz, CDCl_3)*: δ 21.1, 47.6, 109.4 (d, $J = 23.3$ Hz), 119.7 (d, $J = 26.3$ Hz), 121.7,
26 123.2, 127.0, 127.5 (d, $J = 9.0$ Hz), 128.8, 128.9, 129.1, 129.2, 129.3, 131.9 (d, $J = 9.0$ Hz),
27 132.5, 133.4, 134.0, 134.1, 137.0, 143.9, 144.1, 144.5, 147.3 (d, $J = 2.3$ Hz), 160.7 (d, $J = 8.4$
28 Hz). Anal Calcd for $\text{C}_{29}\text{H}_{20}\text{BrFN}_2\text{O}_2\text{S}$: C, 62.26; H, 3.60; N, 5.01. Found: C, 61.97; H, 3.56; N,
29 5.22. *One aromatic carbon is merged with others.

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43 **9-Fluoro-2,3-dimethoxy-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3s).** Colourless
44 solid; mp 206-209 $^\circ\text{C}$; yield: 191 mg, 82%; IR (neat) 3002.8, 2934.6, 1602.0, 1507.4, 1357.5,
45 1283.9, 1212.5, 1160.7 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 1.85 (s, 3H), 4.05 (s, 3H), 4.06 (s,
46 3H), 5.00 (s, 2H), 6.60 (d, $J = 8.4$ Hz, 2H), 7.05 (d, $J = 8.4$ Hz, 2H), 7.31 (dd, $J = 8.7, 2.7$ Hz,
47 1H), 7.33 (s, 1H), 7.40 (td, $J = 9.0, 2.7$ Hz, 1H), 7.61 (s, 1H), 7.79 (s, 1H), 7.95 (dd, $J = 9.0, 5.1$
48 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3)*: δ 20.9, 49.9, 56.2, 56.4, 107.0, 110.2 (d, $J = 21.0$ Hz),
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3 110.6, 119.4 (d, $J = 18.0$ Hz), 123.2, 125.0, 126.9, 127.3, 127.5 (d, $J = 9.8$ Hz), 128.6, 131.2 (d, J
4 = 15.8 Hz), 131.3, 132.2, 134.0, 143.7, 144.6, 148.9, 149.0, 150.9, 160.2 (d, $J = 246.8$ Hz), Anal
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6 Calcd for $C_{25}H_{21}FN_2O_4S$: C, 64.64; H, 4.56; N, 6.03. Found: C, 64.32; H, 4.44; N, 6.00.
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10 **11-Ethyl-2,3-dimethoxy-5-tosyl-5,6-dihydrodibenzo[*b,h*][1,6]naphthyridine (3t).** Colourless
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12 solid; mp 192-196 °C; yield: 188 mg, 79%; IR (neat) 3011.5, 2967.4, 2928.1, 1602.7, 1510.6,
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14 1346.4, 1210.2, 1160.6 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, $J = 7.5$ Hz, 3H), 1.77 (s,
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16 3H), 3.23 (q, $J = 7.5$ Hz, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 5.01 (s, 2H), 6.52 (d, $J = 7.8$ Hz, 2H),
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18 7.00 (d, $J = 7.8$ Hz, 2H), 7.31 (s, 1H), 7.37 (t, $J = 7.2$ Hz, 1H), 7.47 (d, $J = 7.2$ Hz, 1H), 7.52 (d,
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20 $J = 8.1$ Hz, 1H), 7.61 (s, 1H), 7.87 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$)*: δ 15.2, 20.8, 24.9,
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22 50.0, 56.1, 56.4, 107.3, 110.6, 123.4, 124.3, 125.0, 126.0, 127.0, 127.4, 127.8, 128.4, 132.1,
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24 133.9, 142.8, 143.5, 145.8, 147.8, 148.8, 150.7. Anal Calcd for $C_{27}H_{26}N_2O_4S$: C, 68.33; H, 5.52;
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26 N, 5.90. Found: C, 68.01; H, 5.44; N, 5.79. *One aromatic carbon is merged with others.
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31 **5-Tosyl-5,6-dihydrobenzo[*h*]naphtho[1,2-*b*][1,6]naphthyridine (3u).** Pale yellow solid; mp
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33 201-203 °C; yield: 188 mg, 86%; IR (neat) 3058.7, 2977.3, 1593.7, 1398.2, 1341.8, 1159.6,
34
35 1073.9 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 1.52 (s, 3H), 5.03 (s, 2H), 6.43 (d, $J = 8.1$ Hz, 2H),
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37 6.93 (d, $J = 8.1$ Hz, 2H), 7.41-7.50 (m, 2H), 7.53 (d, $J = 8.7$ Hz, 1H), 7.64-7.68 (m, 3H), 7.71 (d,
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39 $J = 8.7$ Hz, 1H), 7.77-7.84 (m, 2H), 8.48 (dd, $J = 7.5, 2.4$ Hz, 1H), 9.22 (dd, $J = 7.2, 1.8$ Hz, 1H);
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41 ^{13}C NMR (75 MHz, $CDCl_3$)*: δ 20.7, 49.6, 124.5, 124.7, 124.8, 125.4, 125.9, 126.9, 127.2,
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43 127.7, 127.8, 127.9, 128.2, 128.5, 130.3, 131.2, 131.4, 132.1, 133.5, 134.3, 138.1, 143.7, 145.6,
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45 147.8. Anal Calcd for $C_{27}H_{20}N_2O_2S$: C, 74.29; H, 4.62; N, 6.42. Found: 73.98; H, 4.63; N, 6.64.
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49 *One aromatic carbon is merged with others.
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53 **2,3-Dimethoxy-5-tosyl-5,6-dihydrobenzo[*h*]naphtho[1,2-*b*][1,6]naphthyridine (3v).**
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55 Colourless solid; mp 203-206°C; yield: 181 mg, 73%; IR (neat) 3004.6, 2931.2, 1598.2, 1514.0,
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3 1341.2, 1284.7, 1208.2, 1161.2 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.60 (s, 3H), 4.06 (s, 3H),
4 4.13 (s, 3H), 5.07 (s, 2H), 6.51 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 7.36 (s, 1H), 7.58
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6 (d, *J* = 8.7 Hz, 1H), 7.68-7.77 (m, 4H), 7.90 (dd, *J* = 6.6, 2.4 Hz, 1H), 8.00 (s, 1H), 9.26 (dd, *J* =
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8 7.2, 2.1 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃)*: δ 20.7, 49.8, 56.3, 56.4, 107.2, 110.5, 124.0,
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10 124.3, 124.8, 124.9, 126.8, 127.2, 127.3, 127.8, 128.1, 128.4, 131.3, 131.9, 133.5, 134.0, 143.7,
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12 145.4, 147.8, 148.8, 150.7. Anal Calcd for C₂₉H₂₄N₂O₄S: C, 70.14; H, 4.87; N, 5.64. Found:
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14 69.88; H, 4.81; N, 5.56. *Two aromatic carbons are merged with others.
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20 **bis-Dibenzo[*b,h*][1,6]naphthyridine (4).*** Colourless solid; mp 269-271 °C; yield: 177 mg,
21
22 51%; IR (neat) 3065.9, 2922.5, 1599.8, 1483.2, 1418.1, 1349.3, 1163.5 cm⁻¹; ¹H NMR (300
23
24 MHz, CDCl₃): δ 1.77 (s, 6H), 5.24 (s, 4H), 6.57 (d, *J* = 8.1 Hz, 4H), 7.04 (d, *J* = 8.1 Hz, 4H),
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26 7.51 (t, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.8 Hz, 2H), 7.77 (d, *J* = 7.2 Hz, 2H), 8.01 (s, 2H), 8.38 (dd,
27
28 *J* = 7.8, 1.8 Hz, 2H), 8.89 (s, 2H); Anal Calcd for C₄₀H₃₀N₄O₄S₂: C, 69.15; H, 4.35; N, 8.06.
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30 Found: 68.88; H, 4.31; N, 7.97. *This compound is insoluble in common NMR solvents and
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32 sparingly soluble only in CDCl₃. The concentration in CDCl₃ was not sufficient enough to record
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34 ¹³C NMR.
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39 **12-Tosyl-12,13-dihydro-6*H*-benzo[*h*]chromeno[3,4-*b*][1,6]naphthyridin-6-one (6a).**
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41 Colourless solid; mp 254-256 °C; yield: 168 mg, 74%; IR (neat) 3071.0, 2917.5, 1742.5, 1602.7,
42
43 1468.8, 1435.3, 1348.2, 1166.6, 1091.5 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.97 (s, 3H), 5.12
44
45 (s, 2H), 6.73 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 7.42-7.50 (m, 3H), 7.54-7.62 (m,
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47 2H), 7.83 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 8.04 (s, 1H), 8.42 (dd, *J* = 7.8, 1.5
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49 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃)*: δ 21.1, 49.3, 116.4, 118.0, 122.8, 125.1, 126.6, 126.9,
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51 127.2, 127.4, 128.0, 128.8, 129.0, 130.4, 131.5, 132.2, 134.4, 136.9, 137.7, 144.3, 150.9, 151.1,
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3 158.5. Anal Calcd for C₂₆H₁₈N₂O₄S: C, 68.71; H, 3.99; N, 6.16. Found: 68.48; H, 3.82; N, 6.11.

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5 *One aromatic carbon is merged with others.

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8 **9-Bromo-12-tosyl-12,13-dihydro-6H-benzo[h]chromeno[3,4-b][1,6]naphthyridin-6-one (6b).**

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10 Colourless solid; mp 262-264 °C; yield: 211 mg, 79%; IR (neat) 3060.8, 2967.4, 1746.7, 1601.5,
11 1463.5, 1340.3, 1164.1, 1088.0 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.98 (s, 3H), 5.11 (s, 2H),
12 6.77 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.41-7.48 (m, 2H), 7.58-7.73 (m, 3H), 7.98
13 (dd, *J* = 8.1, 1.2 Hz, 1H), 8.06 (s, 1H), 8.51 (d, *J* = 2.1 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ
14 21.1, 49.0, 116.1, 118.0, 121.9, 123.0, 125.2, 127.1, 127.2, 128.9, 129.0, 129.1, 130.2, 130.9,
15 131.8, 132.2, 134.3, 134.4, 136.6, 136.8, 144.5, 149.8, 150.9, 158.2. Anal Calcd for
16 C₂₆H₁₇BrN₂O₄S: C, 58.55; H, 3.21; N, 5.25. Found: 58.24; H, 3.17; N, 5.16.
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29 **ASSOCIATED CONTENT**

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31 **Supporting information**

32 The Supporting Information is available free of charge on the ACS Publications website at DOI:

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36 Copies of ¹H and ¹³C NMR spectra of compounds **3**, **4** and **6**.
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41 **AUTHOR INFORMATION**

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43 **Corresponding Author**

44 *Email: vsridharan@scbt.sastra.edu; vesridharan@gmail.com
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48 **Notes**

49 The authors declare no competing financial interest.
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