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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

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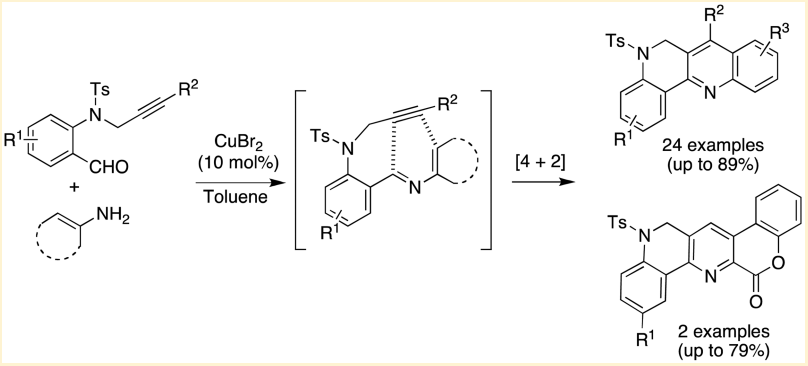
Supporting Information



ABSTRACT: A highly efficient synthesis of 5,6-dihydrodibenzo[*b*,*h*][1,6]naphthyridines was achieved by reaction between 2-(*N*-propargylamino)benzaldehydes and arylamines in the presence of $CuBr_2$. The in situ generated electron-deficient heterodienes bearing a tethered alkyne partner underwent an intramolecular inverse electron-demand hetero-Diels–Alder reaction followed by air oxidation to furnish the products in high yields. This reaction tolerated a large number of substituents to afford diverse products under mild conditions. This strategy was also successfully extended to the synthesis of 12,13-dihydro-6*H*-benzo[*h*]chromeno[3,4-*b*][1,6]naphthyridin-6-ones starting from 3-amino-2*H*-chromen-2-one, again in high yields.

INTRODUCTION

The inverse-electron-demand hetero-Diels–Alder reaction (IEDDA) between electron-deficient heterodienes (benzylidene anilines) and electron-rich dienophiles, generally known as the Povarov reaction, is a versatile transformation to access tetrahydroquinoline derivatives.[1,2] These reactions are normally catalyzed by metal Lewis acids by coordinating with the 1,3-heterodiene nitrogen to further increase its electron-deficiency and thus minimize the LUMO energy of the heterodiene to trigger the cycloaddition.[3] During the past two decades, a large number of chiral catalysts were also developed to obtain chiral tetrahydroquinolines, including natural products.[4] This powerful reaction was further extended to obtain polyheterocyclic compounds by means of intramolecular versions starting from heterodienes bearing a tethered alkene partner.[5] Although the majority of this kind of IEDDA reactions involved the use of olefins as the dienophiles and thus afforded tetrahydroquinolines, considerable effort has been devoted to the direct synthesis of quinolines by using alkynes as dienophiles.[6] The [4 + 2] cycloaddition between in situ generated benzylidene anilines and alkynes for direct access to quinolines can be catalyzed by a number of acidic catalysts including triflic acid, $SnCl_2$, $Fe(OTf)_3$, $Ga(OTf)_3$, $Sc(OTf)_3$, $Cu(OTf)_2$, molecular iodine, $HClO_4$-modified montmorillonite, K-10 under microwave irradiation, potassium dodecatungstocobaltate trihydrate, and CuI/$La(OTf)_3$ in ionic liquid, among others (Scheme 1a). Likewise, intramolecular [4 + 2] Povarov-type cycloaddition with tethered alkyne dienophiles have also been explored to access polycyclic heterocyclic compounds, normally restricted to the easily accessible salicylaldehyde-derived aryl aldehydes.[7]

[1,6]-Naphthyridines and their benzo-fused analogues dibenzo[*b*,*h*][1,6]naphthyridines are biologically significant molecules and exhibit numerous pharmacological activities. Thus, members of this class of polycyclic compounds act as potential inhibitors of telomere maintenance,[8] topoisomerase I,[9] and FGF receptor-1 tyrosine kinase.[10] In addition, 8-substituted [1,6]naphthyridines exhibit HIV-1 integrase inhibitory activity and cytotoxicity against cancer cells.[11] Furthermore, dibenzo[*b*,*h*][1,6]naphthyridines are known for their

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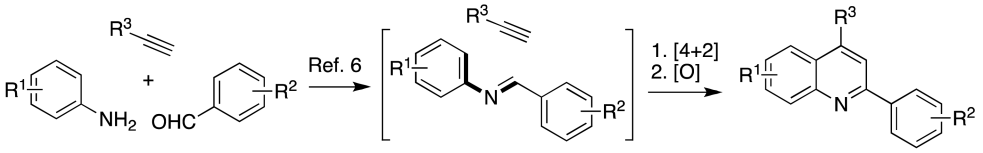
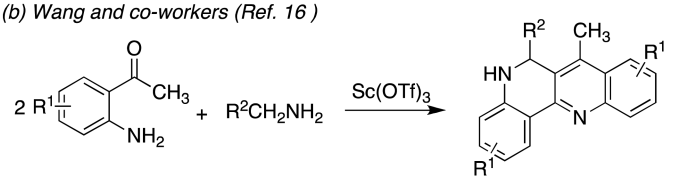
Scheme 1. One-Pot Access to Quinolines and Dibenzo[*b*,*h*][1,6]naphthyridines

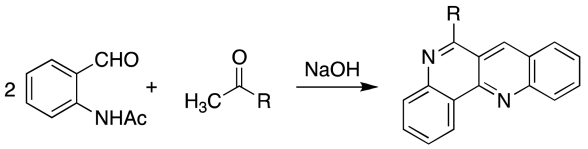
(a) [4 + 2] Cycloaddition of benzylidene anilines and alkynes



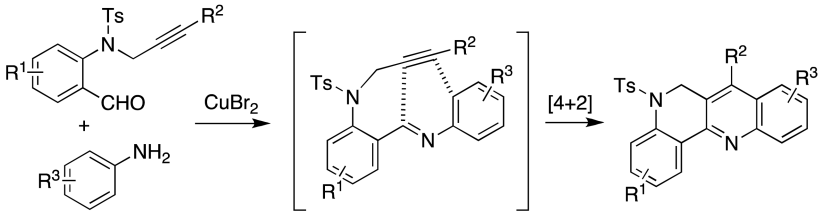
(b) Wang and co-workers (Ref. 16)



(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



florescence properties; for instance, the 2-acetylaminobenzaldehyde-derived dibenzo[*b*,*h*][1,6]naphthyridines have found application in fluorescent DNA labeling.[12] Despite the significance of dibenzo[*b*,*h*][1,6]naphthyridines in biology, only a limited number of reports deal with the direct synthesis of these compounds. The main methodologies developed with this purpose include the silica gel catalyzed, three-component reaction between 2-hydroxyacetophenone, aryl aldehydes, and malononitrile,[13] the neat reaction between 4-chloro-2-methylquinoline and amino ketones,[14] and a few others.[15] Recently, Wang and co-workers reported the synthesis of dibenzo[*b*,*h*]-[1,6]naphthyridines involving the $Sc(OTf)_3$-catalyzed cascade reaction between *o*-aminoacetophenone with methanamine in moderate to good yields (Scheme 1b).[16] A one-pot synthesis of these compounds starting from 2-acetylaminobenzaldehydes was also reported (Scheme 1c).[12] Notwithstanding these few reports, no efficient, general methods are available to access these significant compounds.

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 benzylidene anilines derived from 2-aminoaryl aldehydes 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]

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, $InCl_3$, $BiCl_3$, 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, formation of the intermediate imine **A** was observed from the crude ^{1}H NMR spectra in all cases. To our delight, elevation of temperature to 80 °C triggered the [4 + 2] cycloaddition−oxidation sequence furnishing the product dibenzo[*b*,*h*][1,6]naphthyridine **3a** in moderate yields (entries 1−8). However, in all of the tested Lewis acids, the reactions were fairly slow, and even after 24 h, some unreacted intermediate imine was observed. $InCl_3$ and $Sc(OTf)_3$ were superior, yielding 75% and 67% of the product, respectively (entries 4 and 8). On the other hand, changing the solvent did not significantly improve the yield (entries 9−12). Encouraged by these preliminary results, we subsequently moved to copper salts as catalysts. Gratifyingly, switching the catalyst to CuCl (10 mol %) increased the rate of the reaction remarkably,

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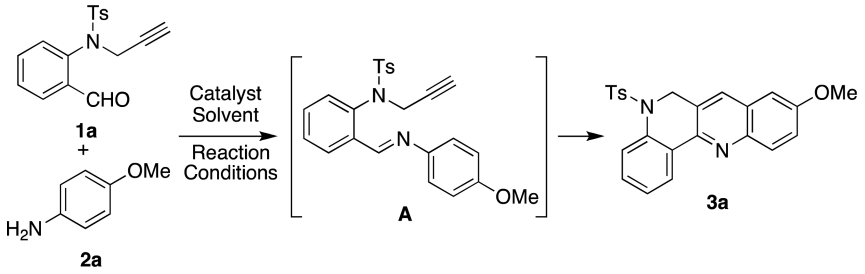
Table 1. Optimization of Reaction Conditions[a]



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[e]
26[f]	**$CuBr_2$**	**10**	**toluene**	**25**	**20**	**88**
27	$CuBr_2$	30	toluene	25	12	89
28	$Cu(OAc)_2$	10	toluene	25	12	22[e]
29	$CuCl_2$	10	toluene	25	8	82

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

affording 80% of the product in just 1 h reaction time at 25 °C. Indeed, 5 mol % of the catalyst was sufficient to allow complete conversion and to yield 81% of the product in toluene (entries 13 and 14). In order to improve the isolated yield and to avoid the byproducts of decomposition, we carried out the reaction at 5 °C, but only imine formation was noticed with traces of the product **3a** (entry 15). A subsequent solvent screening revealed that acetonitrile, dioxane, DCM, DCE, ethanol, and THF were inefficient to improve the yield (entries 16−23). Among the other tested cuprous halides, CuI failed to afford the product, and CuBr yielded 56% of **3a** in 1 h (entries 24 and 25). On the other hand, the last copper halide to be tested $CuBr_2$ (10 mol %) was the most efficient one in terms of yield providing 88% of the isolated product. Although the reaction time was 20 h, the reaction was clean and no side products or decomposition was observed (entry 26). The reaction time was reduced to 12 h with 30 mol % of the catalyst, and $Cu(OAc)_2$ was inefficient (entries 27 and 28). The reaction was also carried out in the presence 10 mol % of $CuCl_2$, and a comparable yield with CuCl was obtained albeit in longer reaction time (entry 29). Finally, we settled on $CuBr_2$ (10 mol %) as the catalyst and toluene as the solvent for subsequent studies due to the high yield and neatness of the reaction.

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 1−10 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

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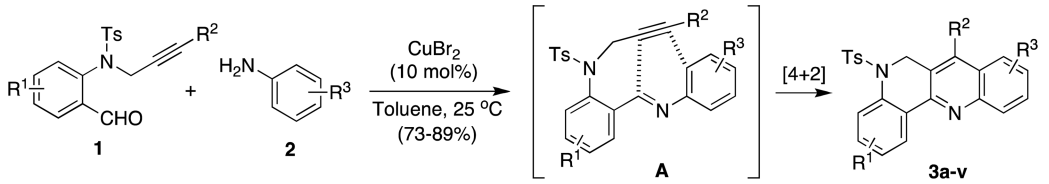
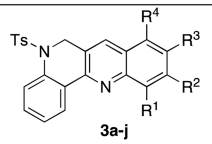
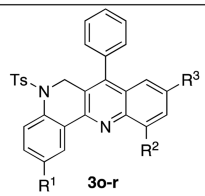
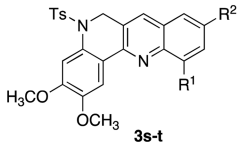
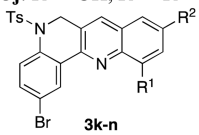
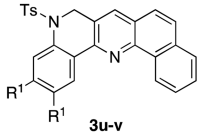
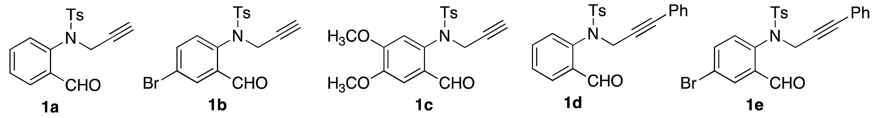
Table 2. Scope and Limitations of the Methodology: Synthesis of Dibenzo[*b*,*h*][1,6]naphthyridines 3[a]



Entry	Product **3**	Reaction time (h)	Yield (%)[b]	Entry	Product **3**	Reaction time (h)	Yield (%)[b]
	 **3a-j**				 **3o-r**		
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		 **3s-t**		
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
	 **3k-n**				 **3u-v**		
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 $CuBr_2$ (10 mol %) in 3 mL of toluene at 25 °C. [b]Isolated yield. [c]The reactions were carried out at 70 °C.

reactions were completed between 16 and 24 h, 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**–**n** in high yields (entries 11–14). 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 15–18). 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

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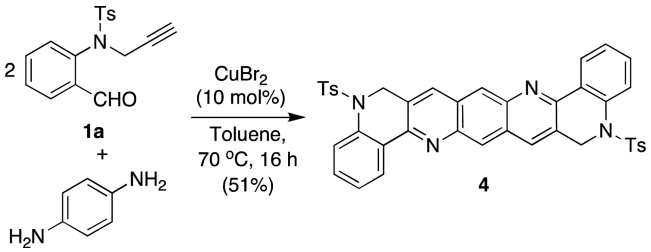
pentacyclic derivatives **3u** and **3v**. Although these reactions afforded the products under ambient temperature, the reactions were very slow, and complete conversion was achieved only at 70 °C, affording 73−86% of isolated products.

In addition to simple arylamines, the reactivity of *p*-phenylenediamine with aldehyde **1a** was also investigated (Scheme 2). Initially, we employed the optimized conditions

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

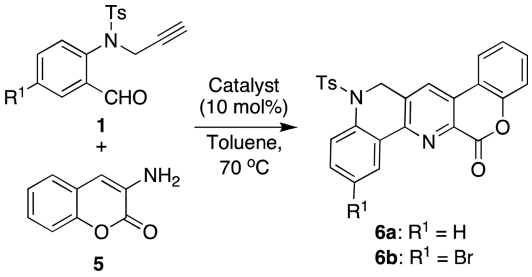


with a 1:0.5 ratio of the aldehyde and diamine in toluene. Unexpectedly, no product formation was observed even after 24 h, and only traces of the intermediate imine was noticed. However, increase of the reaction temperature afforded 51% of the heptacyclic compound **4**. Further efforts to improve the yield of the product by changing the mole ratio of the reactants, and the use of CuCl as catalyst were unsuccessful.

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 $CuBr_2$ 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).

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 $CuBr_2$. The activation of the heterodiene is attributed to the Lewis acidity of $CuBr_2$[21] to

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



		$CuBr_2$ (10 mol %)		CuCl (10 mol %)	
entry	compd	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 of toluene at 70 °C. [b]Isolated yield.

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).

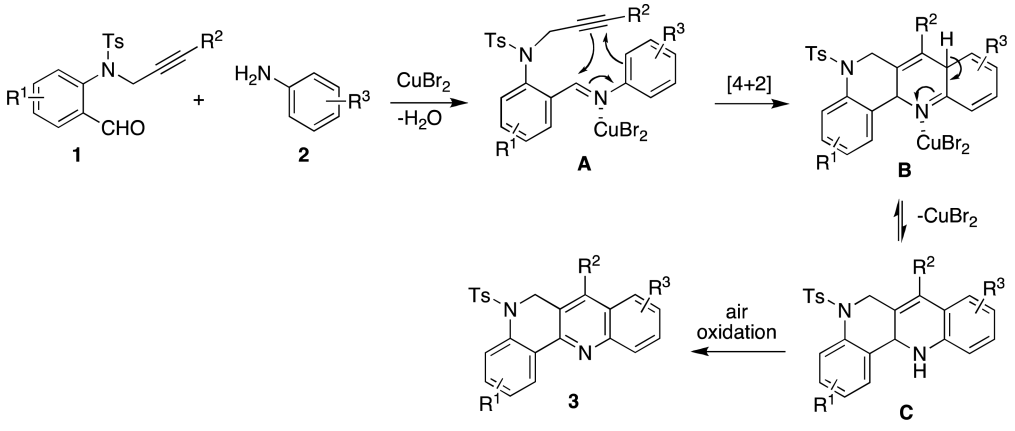
CONCLUSION

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 $CuBr_2$-catalyzed reaction between 2-(*N*-propargylamino)benzaldehydes and arylamines afforded the products via intramolecular [4 + 2] cycloaddition between the in situ generated heterodiene 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

Scheme 3. Proposed Mechanism



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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. ^{1}H 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 ^{1}H 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 hertz. 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 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) and 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**):* colorless 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}; ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$)* 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 $C_{24}H_{20}N_2O_3S$: 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**):* colorless 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}; ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$)* 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 $C_{23}H_{18}N_2O_2S$: 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}; ^{1}H NMR (300 MHz, $CDCl_3$) 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, 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, 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, 138.2, 143.6, 146.3, 148.6. Anal. Calcd for $C_{24}H_{20}N_2O_2S$: C, 71.98; H, 5.03; N, 6.99. Found: C, 71.67; H, 5.10; N, 7.01. *One aromatic carbon is merged with others.

*9,11-Dimethyl-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]naphthyridine (**3d**):* colorless solid; mp 184−186 °C; yield 170 mg, 82%; IR (neat) 3044.5, 2905.6, 1594.6, 1488.7, 1350.6, 1166.2, 1081.5 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 3H), 2.44 (s, 3H), 2.67 (s, 3H), 4.98 (s, 2H), 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), 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, $CDCl_3$) 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, 131.4, 131.5, 131.7, 134.3, 136.1, 136.9, 138.1, 143.5, 145.2, 147.1. Anal. Calcd for $C_{25}H_{22}N_2O_2S$: C, 72.44; H, 5.35; N, 6.76. Found: C, 72.17; H, 5.39; N, 6.93.

*8,10-Dimethyl-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]naphthyridine (**3e**):* colorless solid; mp 159−160 °C; yield 153 mg, 74%; IR (neat) 3035.3, 2898.7, 1596.3, 1459.8, 1340.6, 1160.8, 1051.3 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.74 (s, 3H), 2.42 (s, 3H), 2.55 (s, 3H), 4.98 (s, 2H), 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), 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, 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, 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, 148.9. Anal. Calcd for $C_{25}H_{22}N_2O_2S$: C, 72.44; H, 5.35; N, 6.76. Found: C, 72.09; H, 5.38; N, 6.91. *One aromatic carbon is merged with others.

*11-Methoxy-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]naphthyridine (**3f**):* colorless solid; mp 179−180 °C; yield 165 mg, 79%; IR (neat) 2918.5, 1598.4, 1558.0, 1488.3, 1345.9, 1161.9, 1067.0 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.81 (s, 3H), 4.06 (s, 3H), 5.05 (s, 2H), 6.63 (d, J = 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 = 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, 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, 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. Calcd for $C_{24}H_{20}N_2O_3S$: C, 69.21; H, 4.84; N, 6.73. Found: C, 68.91; H, 4.94; N, 6.84.

*9-Chloro-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]naphthyridine (**3g**):* colorless solid; mp 182−185 °C; yield 162 mg, 77%; IR (neat) 3039.7, 1598.3, 1482.9, 1349.9, 1165.2, 1063.4 cm^{-1}; ^{1}H 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 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), 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 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, 130.7, 130.9, 131.2, 132.2, 134.3, 138.4, 143.8, 145.9, 149.8. Anal. Calcd for $C_{23}H_{17}ClN_2O_2S$: C, 65.63; H, 4.07; N, 6.66. Found: C, 65.29; H, 4.05; N, 6.70. *One aromatic carbon is merged with others.

*9,11-Dichloro-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]naphthyridine (**3h**):* colorless solid; mp 243−246 °C; yield 182 mg, 80%; IR (neat) 3065.8, 2919.3, 1594.7, 1474.4, 1338.3, 1159.1, 1061.8 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.93 (s, 3H), 5.07 (s, 2H), 6.62 (d, J = 7.8 Hz, 2H), 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 = 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, 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. Calcd for $C_{23}H_{16}Cl_2N_2O_2S$: C, 60.67; H, 3.54; N, 6.15. Found: C, 60.41; H, 3.62; N, 6.37.

*9-Bromo-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]naphthyridine (**3i**):* colorless solid; mp 167−168 °C; yield 182 mg, 78%; IR (neat) 3048.5, 2933.2, 1596.7, 1479.5, 1339.0, 1156.0, 1078.1 cm^{-1}; ^{1}H 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, 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 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, 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, 138.4, 143.8, 146.2, 149.9. Anal. Calcd for $C_{23}H_{17}BrN_2O_2S$: C, 59.36; H, 3.68; N, 6.02. Found: C, 58.99; H, 3.64; N, 6.13. *One aromatic carbon is merged with others.

*5-Tosyl-5,6-dihydrodibenzo[b,h][1,6]naphthyridin-11-ol (**3j**):* colorless solid; mp 184−185 °C; yield 151 mg, 75%; IR (neat) 3354.3, 2958.5, 1601.9, 1487.0, 1351.0, 1332.6, 1154.6, 1058.5 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.86 (s, 3H), 5.06 (s, 2H), 6.52 (d, J = 8.1 Hz, 2H), 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 = 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 = 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 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, 132.4, 134.0, 137.3, 138.5, 143.9, 147.4, 152.0. Anal. Calcd for $C_{23}H_{18}N_2O_3S$: C, 68.64; H, 4.51; N, 6.96. Found: C, 68.50; H, 4.61; N, 7.05.

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*2-Bromo-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]naphthyridine (**3k**):* colorless solid; mp 185−188 °C; yield 191 mg, 82%; IR (neat) 2938.4, 1592.5, 1434.3, 1354.6, 1161.8, 1051.3 cm^{-1}; ^1H 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 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 = 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, 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 $C_{23}H_{17}BrN_2O_2S$: 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**):* colorless 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**):* colorless 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**):* colorless 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, 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, 143.7, 143.9, 145.7. Anal. Calcd for $C_{24}H_{19}BrN_2O_3S$: C, 58.19; H, 3.87; N, 5.65. Found: C, 57.81; H, 3.84; N, 5.79. *One aromatic carbon is merged with others.

*9,11-Dimethyl-6-phenyl-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]-naphthyridine (**3o**):* colorless solid; mp 210−212 °C; yield 191 mg, 78%; IR (neat) 3030.6, 2915.9, 1578.7, 1486.1, 1345.2, 1161.9, 1084.5 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.95 (s, 3H), 2.37 (s, 3H), 2.77 (s, 3H), 4.79 (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, 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, J = 7.5, 2.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$)* δ 18.0, 21.0, 21.9, 47.9, 121.1, 122.6, 126.1, 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, 137.0, 137.9, 143.5, 145.1, 146.7. Anal. Calcd for $C_{31}H_{26}N_2O_2S$: C, 75.89; H, 5.34; N, 5.71. Found: C, 75.61; H, 5.40; N, 5.80. *One aromatic carbon is merged with others.

*2-Bromo-9,11-dimethyl-6-phenyl-5-tosyl-5,6-dihydrodibenzo-[b,h][1,6]naphthyridine (**3p**):* colorless solid; mp 221−224 °C; yield 236 mg, 83%; IR (neat) 2919.0, 1583.1, 1483.1, 1344.5, 1161.9, 1083.6 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.96 (s, 3H), 2.37 (s, 3H), 2.77 (s, 3H), 4.77 (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 (s, 1H), 7.57−7.66 (m, 5H), 8.52 (d, J = 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$)* δ 18.0, 21.0, 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, 133.6, 134.1, 135.1, 136.5, 136.8, 137.2, 143.7, 143.8, 145.0, 145.4. Anal. Calcd for $C_{31}H_{25}BrN_2O_2S$: C, 65.38; H, 4.42; N, 4.92. Found: C, 65.07; H, 4.41; N, 5.05. *One aromatic carbon is merged with others.

*2-Bromo-11-methoxy-6-phenyl-5-tosyl-5,6-dihydrodibenzo[b,h]-[1,6]naphthyridine (**3q**):* Colorless solid; mp 220−222 °C; yield 234 mg, 82%; IR (neat) 2932.9, 1593.7, 1485.3, 1344.7, 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, 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), 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, $CDCl_3$)* 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, 132.5, 133.2, 134.6, 134.7, 136.8, 139.5, 143.9, 144.5, 146.8, 155.4. Anal. Calcd for $C_{30}H_{23}BrN_2O_3S$: C, 63.05; H, 4.06; N, 4.90. Found: C, 62.90; H, 3.95; N, 4.97. *Three aromatic carbons are merged with others.

*2-Bromo-9-fluoro-6-phenyl-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]-naphthyridine (**3r**):* colorless solid; mp 228−230 °C; yield 249 mg, 89%; IR (neat) 3030.8, 1619.2, 1489.0, 1333.3, 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 = 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), 7.40−7.46 (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 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, 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), 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 Hz). Anal. Calcd for $C_{29}H_{20}BrFN_2O_2S$: C, 62.26; H, 3.60; N, 5.01. Found: C, 61.97; H, 3.56; N, 5.22. *One aromatic carbon is merged with others.

*9-Fluoro-2,3-dimethoxy-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]-naphthyridine (**3s**):* colorless solid; mp 206−209 °C; yield 191 mg, 82%; IR (neat) 3002.8, 2934.6, 1602.0, 1507.4, 1357.5, 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, 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, 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 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), 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 = 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. 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.

*11-Ethyl-2,3-dimethoxy-5-tosyl-5,6-dihydrodibenzo[b,h][1,6]-naphthyridine (**3t**):* Colorless solid; mp 192−196 °C; yield 188 mg, 79%; IR (neat) 3011.5, 2967.4, 2928.1, 1602.7, 1510.6, 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, 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), 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, 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, 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, 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; N, 5.90. Found: C, 68.01; H, 5.44; N, 5.79. *One aromatic carbon is merged with others.

*5-Tosyl-5,6-dihydrobenzo[h]naphtho[1,2-b][1,6]naphthyridine (**3u**):* pale yellow solid; mp 201−203 °C; yield 188 mg, 86%; IR (neat) 3058.7, 2977.3, 1593.7, 1398.2, 1341.8, 1159.6, 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), 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, 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); ^{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, 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, 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. *One aromatic carbon is merged with others.

*2,3-Dimethoxy-5-tosyl-5,6-dihydrobenzo[h]naphtho[1,2-b][1,6]-naphthyridine (**3v**):* colorless solid; mp 203−206 °C; yield 181 mg, 73%; IR (neat) 3004.6, 2931.2, 1598.2, 1514.0, 1341.2, 1284.7, 1208.2, 1161.2 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.60 (s, 3H), 4.06 (s, 3H), 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 (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 = 7.2, 2.1

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Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$)* δ 20.7, 49.8, 56.3, 56.4, 107.2, 110.5, 124.0, 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, 145.4, 147.8, 148.8, 150.7. Anal. Calcd for $C_{29}H_{24}N_2O_4S$: C, 70.14; H, 4.87; N, 5.64. Found: 69.88; H, 4.81; N, 5.56. *Two aromatic carbons are merged with others.

*Bis-dibenzo[b,h][1,6]naphthyridine (**4**):*. colorless solid; mp 269−271 °C; yield 177 mg, 51%; IR (neat) 3065.9, 2922.5, 1599.8, 1483.2, 1418.1, 1349.3, 1163.5 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 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), 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, J = 7.8, 1.8 Hz, 2H), 8.89 (s, 2H). Anal. Calcd for $C_{40}H_{30}N_4O_4S_2$: C, 69.15; H, 4.35; N, 8.06. Found: 68.88; H, 4.31; N, 7.97. *This compound is insoluble in common NMR solvents and sparingly soluble only in $CDCl_3$. The concentration in $CDCl_3$ was not sufficient enough to record ^{13}C NMR.

*12-Tosyl-12,13-dihydro-6H-benzo[h]chromeno[3,4-b][1,6]-naphthyridin-6-one (**6a**):* colorless solid; mp 254−256 °C; yield 168 mg, 74%; IR (neat) 3071.0, 2917.5, 1742.5, 1602.7, 1468.8, 1435.3, 1348.2, 1166.6, 1091.5 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 5.12 (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, 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 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$)* δ 21.1, 49.3, 116.4, 118.0, 122.8, 125.1, 126.6, 126.9, 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, 158.5. Anal. Calcd for $C_{26}H_{18}N_2O_4S$: C, 68.71; H, 3.99; N, 6.16. Found: 68.48; H, 3.82; N, 6.11. *One aromatic carbon is merged with others.

*9-Bromo-12-tosyl-12,13-dihydro-6H-benzo[h]chromeno[3,4-b]-[1,6]naphthyridin-6-one (**6b**):* colorless solid; mp 262−264 °C; yield 211 mg, 79%; IR (neat) 3060.8, 2967.4, 1746.7, 1601.5, 1463.5, 1340.3, 1164.1, 1088.0 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.98 (s, 3H), 5.11 (s, 2H), 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 (dd, J = 8.1, 1.2 Hz, 1H), 8.06 (s, 1H), 8.51 (d, J = 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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, 131.8, 132.2, 134.3, 134.4, 136.6, 136.8, 144.5, 149.8, 150.9, 158.2. Anal. Calcd for $C_{26}H_{17}BrN_2O_4S$: C, 58.55; H, 3.21; N, 5.25. Found: 58.24; H, 3.17; N, 5.16.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02669.

^{1}H and ^{13}C NMR spectra of compounds **3**, **4**, and **6** (PDF)

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to Professor Shanmugam Muthusubramanian on the occasion of his retirement.

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