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$Zn(OTf)_2$-Catalyzed Formal [3+3] Cascade Annulation of Propargylic Alcohols with 2-Aminochromones: Accessing to Chromeno[2,3-*b*]pyridines

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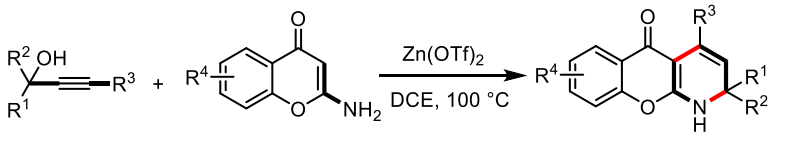
Abstract:



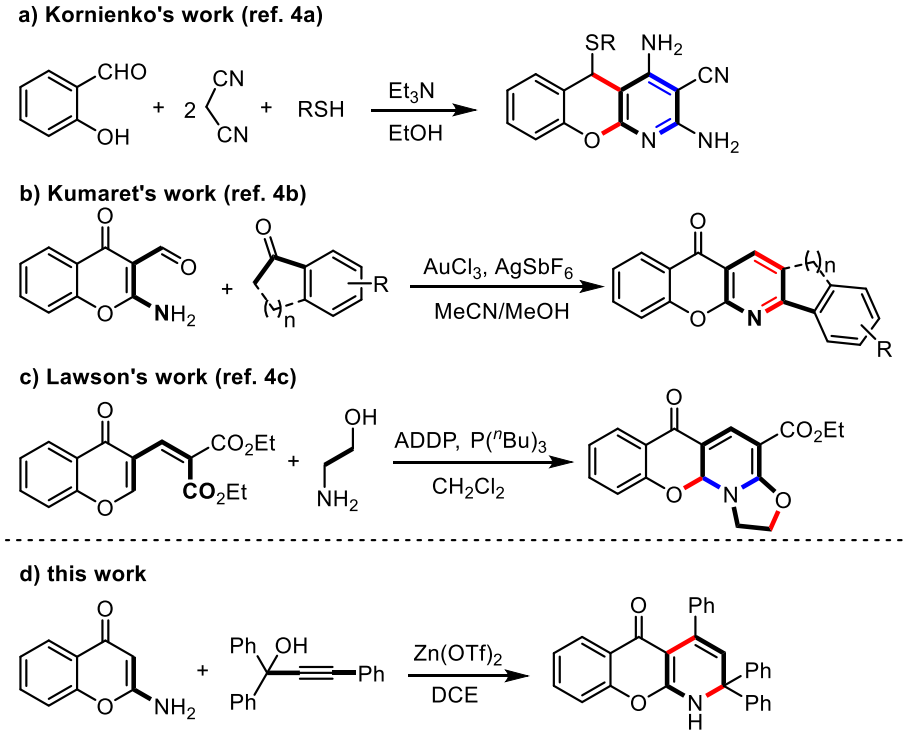
A $Zn(OTf)_2$-catalyzed formal [3+3] cascade annulation strategy for the synthesis of functionalized chromeno[2,3-*b*]pyridines has been developed using propargylic alcohols and 2-aminochromones as the substrates. The protocol provides a convenient and atom-economical method of accessing a broad range of chromeno[2,3-*b*]pyridine derivatives in excellent yields with good functional-group tolerance. The method is also effective on gram scale, which highlights the inherent practicality of this synthetic transformation.

Introduction

Functionalized 4-oxo-4*H*-chromones are of particular utility since they belong to privileged medicinal scaffolds,[1] and serve as key intermediates for the construction of a variety of novel heterocycles possessing diverse biological activities.[2] Among the family of 4-oxo-4*H*-chromones, the chromeno[2,3-*b*]pyridine scaffold is a key skeleton that exists in many pharmacologically active molecules. The derivatives of these compounds have been found to show diverse biological activities, such as glucocorticoid receptor (GR) agonists,[3a] antiinflammatory,[3b,3c] antiproliferative,[3d] antiasthmatic,[3e] antitumor,[3f] antirheumatic,[4a] antimyopic,[4a] antihistaminic,[4a] hypotensive,[4a] and antibacterial activities;[3g,3h] some chromeno[2,3-*b*]pyridine derivatives show potential application prospect for the treatment of Alzheimer's disease.[3i,3j] Owing to their

intriguing pharmaceutical and biological activities, the development of practical and efficient approaches for the synthesis of chromeno[2,3-*b*]pyridine derivatives has attracted considerable attention. In 2007, Kornienko and co-workers showed a noteworthy single-step multicomponent reaction of salicylic aldehydes with various thiols and malononitrile, delivered chromeno[2,3-*b*]pyridine derivatives (Scheme 1a).[4a] In 2008, Kumaret al. reported a gold catalyzed condensation reaction, leading to aza-xanthone frameworks from aryl alkyl ketones (Scheme 1b).[4b] Lawson and co-workers developed an efficient one-pot domino process through a 1,6-aza-Michael addition-triggered sequence and an original Mitsunobu-type concerted sequence for the synthesis of chromenopyridine systems containing a bis-*N*,*O*-acetal junction (Scheme 1c).[4c] Although these methods are effective for certain substrates,[5] the development of more versatile, convenient and efficient methods starting from easily available substrates is still highly desirable for the generation of chromeno[2,3-*b*]pyridine derivatives.

Scheme 1. Strategy for the Synthesis of Chromeno[2,3-*b*]pyridine derivatives



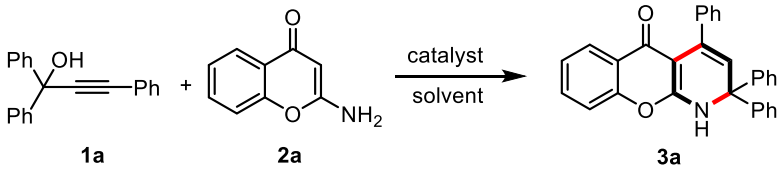
Recently, propargyl alcohols have been widely used as unique synthons in organic synthesis.[6] Upon treatment with Lewis acids, propargyl alcohols would readily undergo the Meyer-Schuster rearrangement to form allenic carbocations, which can participate in several [3+n] (n = 2, 3, 4) annulation reactions with apt partners to give a range of carbocycles and heterocycles.[7] In particular, this phenomenon has been exploited with 1,3-bis-nucleophilic enamines for the

synthesis of five,[8a] six[8b-d] and seven-membered[8e] rings. However, to the best of our knowledge, the annulation reaction involving propargylic alcohols and chromone derivatives has not been properly explored. Inspired by these intriguing discoveries for propargylic alcohols, we herein describe a $Zn(OTf)_2$-catalyzed formal [3+3] cascade annulation of propargylic alcohols with 2-aminochromones containing nonprotected free NH_2, leading to the facile formation of chromeno[2,3-*b*]pyridine derivatives in excellent yields.

Results and Discussion

Initially, propargylic alcohol **1a** and 2-aminochromone **2a** were selected as the model substrates to screen the optimal experimental conditions (Table 1). We first screened various Lewis acids, to our delight, the expected transformation could occur in the presence of AgOTf or $Cu(OTf)_2$ in $PhCH_3$ at 100 ℃, and the desired compound **3a** was obtained in 56% and 18% yield, respectively (Table 1, entries 5–6). The structure of **3a** was further identified by the X-ray crystal structure analysis (for details see the Supporting Information).[9] Gratifyingly, the yield was notably increased when $Zn(OTf)_2$ was chosen as the catalyst (Table 1, entry 7). Among several solvents screened, DCE was found to be the best in terms of product yield (Table 1, entries 8–12). Temperature screening showed that 100 ℃ was optimal to give an 89% yield of the desired product (Table 1, entries 9, 13–15). By decreasing the catalyst loading to 10 mol %, the yield of the product slightly reduced to 80% (Table 1, entry 16). Ultimately, the optimal reaction conditions for the construction of the expected product **3a** were chosen as: the use of propargylic alcohol **1a** (0.1 mmol) and 2-aminochromone **2a** (0.15 mmol) in the presence of $Zn(OTf)_2$ (20 mol %) in DCE (2.0 mL) at 100 ℃.

Table 1. Optimization of the Reaction Conditions[a]



1a **2a** **3a**

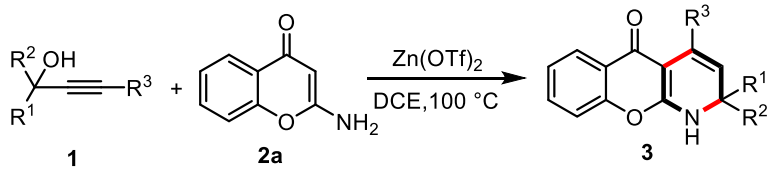
entry	catalyst	solvent	temp. (℃)	yield (%)[b]
1	$Sc(OTf)_3$	$PhCH_3$	100	0
2	$La(OTf)_3$	$PhCH_3$	100	0
3	$Y(OTf)_3$	$PhCH_3$	100	0

4	$Yb(OTf)_3$	$PhCH_3$	100	0
5	AgOTf	$PhCH_3$	100	56
6	$Cu(OTf)_2$	$PhCH_3$	100	18
7	$Zn(OTf)_2$	$PhCH_3$	100	70
8	$Zn(OTf)_2$	THF	100	81
9	$Zn(OTf)_2$	DCE	100	89
10	$Zn(OTf)_2$	CH_3NO_2	100	48
11	$Zn(OTf)_2$	CH_3CN	100	61
12	$Zn(OTf)_2$	1,4-dioxane	100	41
13	$Zn(OTf)_2$	DCE	60	52
14	$Zn(OTf)_2$	DCE	80	74
15	$Zn(OTf)_2$	DCE	120	83
16[c]	$Zn(OTf)_2$	DCE	100	80

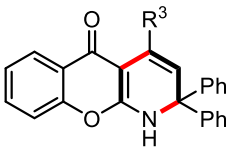
[a]Unless otherwise indicated, all reactions were carried out with **1a** (0.1 mmol), **2a** (0.15 mmol) and catalyst (20 mol %) in solvent (2.0 mL) in a sealed tube. [b]Yield of the isolated product. [c]The reaction was performed with 10 mol % catalyst.

With the optimal conditions in hand, we next examined the scope of propargylic alcohols in this annulation reaction. We first investigated the electronic effects of the aromatic substituents (R_3) of propargylic alcohols **1** (Scheme 2). Propargylic alcohols **1** bearing either electron donating or electron withdrawing groups in their aryl moiety (R_3) showed moderate to good reactivity toward the desired products **(3a**–**3l**, 71%–97%). Symmetrical propargylic alcohols containing either electron donating **(3m**, **3n**) or withdrawing **(3o**–**3q)** groups on the phenyl rings (R_1, R_2) gave high yields of the expected products **(3m**–**3q**, 75%–97%). Moreover, the unsymmetrical propargylic alcohols with a series of substituents at the ortho-, meta- and para-positions of the phenyl ring reacted readily with **2a** to provide the desired products in moderate to good yields **(3r**–**3w**, 79%–97%). Regrettably, the alkyl-substituted (R^1 = Me or cyclohexyl) propargylic alcohols led to no reaction due to their less reactivity.

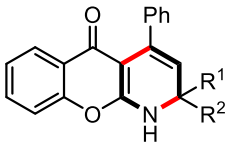
Scheme 2. Scope with Respect to Propargylic Alcohols[a,b]



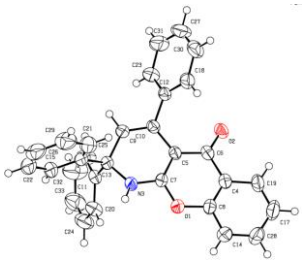
1 2a 3

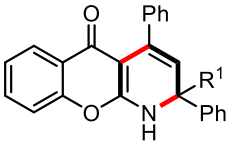


	R^3	yield		R^3	yield
3a	Ph	89%	**3g**	4-FC_6H_4	92%
3b	4-MeC_6H_4	87%	**3h**	4-ClC_6H_4	95%
3c	3-MeC_6H_4	95%	**3i**	4-BrC_6H_4	71%
3d	4-EtC_6H_4	94%	**3j**	4-$NO_2C_6H_4$	71%
3e	4-$MeOC_6H_4$	97%	**3k**	4-CNC_6H_4	96%
3f	4-PhC_6H_4	96%	**3l**	4-$COOMeC_6H_4$	95%

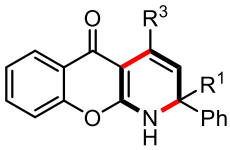


	R^1, R^2	yield
3m	4-MeC_6H_4	97%
3n	4-$MeOC_6H_4$	96%
3o	4-FC_6H_4	90%
3p	4-ClC_6H_4	95%
3q	4-BrC_6H_4	75%





	R^1	yield
3r	4-MeC_6H_4	97%
3s	3-MeC_6H_4	79%
3t	4-$MeOC_6H_4$	97%

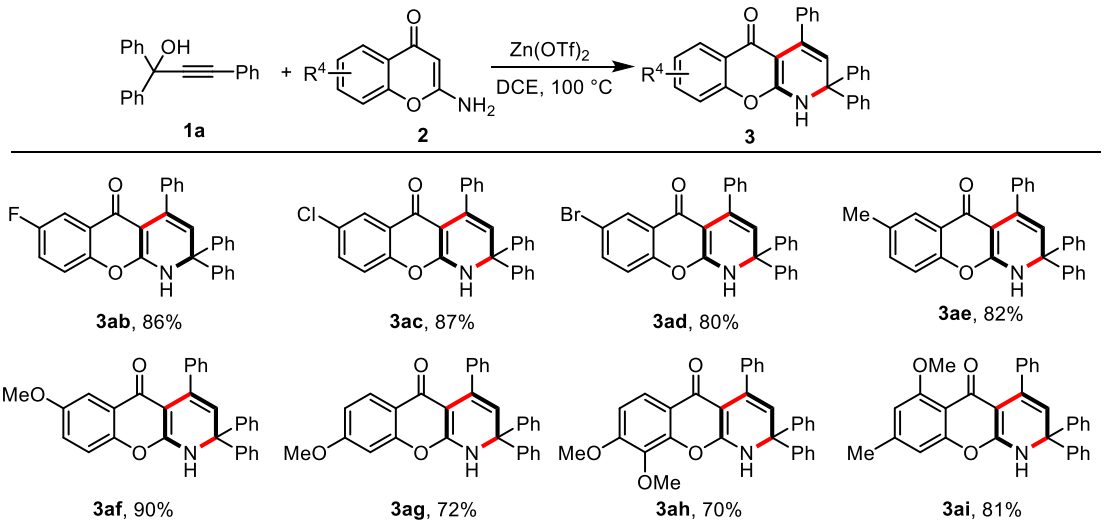


	R^1	R^3	yield
3u	2-ClC_6H_4	4-$MeOC_6H_4$	95%
3v	3-ClC_6H_4	4-$MeOC_6H_4$	93%
3w	4-ClC_6H_4	4-$MeOC_6H_4$	87%

[a]Unless otherwise indicated, all reactions were carried out with **1** (0.1 mmol), **2a** (0.15 mmol), and $Zn(OTf)_2$ (20 mol %) in DCE (2.0 mL) at 100 ℃ in a sealed tube. [b]Yield of the isolated product.

The scope of 2-aminochromones **2** was subsequently investigated with propargylic alcohols **1a** as partners (Scheme 3). Halogen-containing substrates (**2b**–**2d**) were well tolerated, and the annulated products (**3ab**–**3ad**) were obtained in good yields (80–87%). Likewise, 2-aminochromones (**2e**–**2g**) possessing 6-Me, 6-MeO and 7-MeO groups efficiently cyclized into the corresponding products (**3ae**–**3ag**) in 72–90% yields. Moreover, 2-amino-7,8-dimethoxy-4*H*-chromen-4-one **2h** and 2-amino-5-methoxy-7-methyl-4*H*-chromen-4-one **2i** led to the formation of expected products **3ah** and **3ai** in good yields respectively.

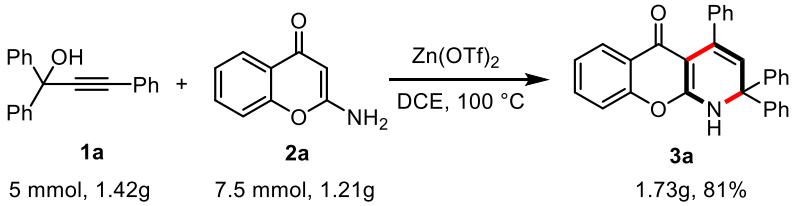
Scheme 3. Scope with Respect to 2-Aminochromones[a,b]



[a]Unless otherwise indicated, all reactions were carried out with **1a** (0.1 mmol), **2** (0.15 mmol), and $Zn(OTf)_2$ (20 mol %) in DCE (2.0 mL) at 100 ℃ in a sealed tube. [b]Yield of the isolated product.

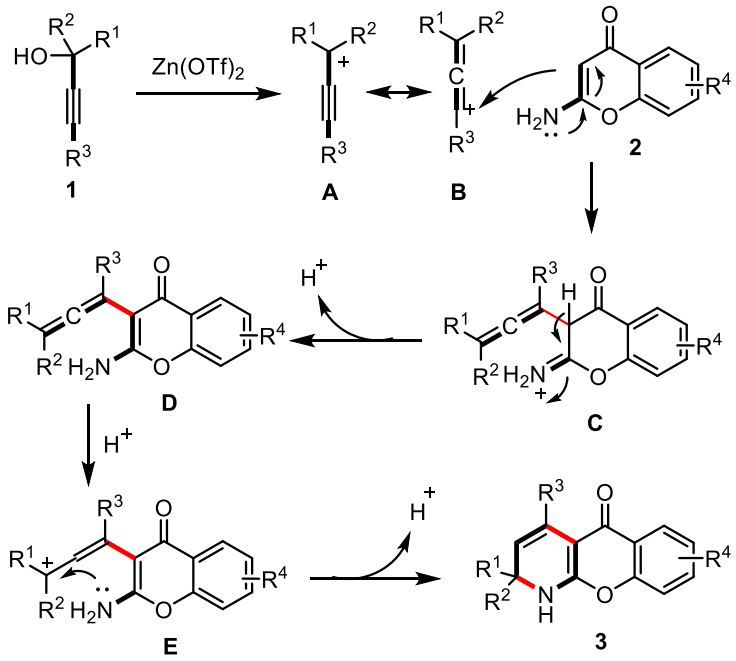
In order to expand the synthetic competence of our strategy, a gram-scale synthesis of **3a** was performed under the standard conditions. The desired chromeno[2,3-*b*]pyridine **3a** was isolated in 81% yield, which demonstrated the potential applicability of our strategy (Scheme 4).

Scheme 4. Large-Scale Synthesis of 3a



A plausible mechanism based on the precedent literatures is illustrated in Scheme 5.[10] Initially, the Lewis acid catalyst $Zn(OTf)_2$ promotes the formation of active propargyl intermediate **A** from propargylic alcohol **1**, which could afford the allenic carbocation **B** formed in situ through the Meyer-Schuster rearrangement. Subsequently, the allenic carbocation **B** undergoes a nucleophilic attack by the 2-aminochromone **2** to furnish iminium intermediate **C**, which could readily transform to intermediate **D** by the removal of a proton. Finally, the protonation of intermediate **D** delivers intermediate **E**, which could undergo an intramolecular nucleophilic attack to afford the desired product **3**.[8b]

Scheme 5. Proposed Mechanism for the Formation of Chromeno[2,3-*b*]pyridine Derivatives



Conclusion

In summary, we have developed a $Zn(OTf)_2$ catalyzed formal [3+3] cascade annulation of propargylic alcohols with 2-aminochromones that provides a practical, convenient and efficient method for the formation of chromeno[2,3-*b*]pyridine derivatives in good to excellent yields. The reaction conditions tolerate a wide scope of typical organic functional groups. The highly efficient catalytic system, operational simplicity and good functional group compatibility of this strategy can be ranked the sustainable and convenient alternatives for the synthesis of chromeno[2,3-*b*]pyridine derivatives.

EXPERIMENTAL SECTION

General Experimental Procedures

All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on GF254 plates. Silica gel (200−300 mesh) was used for column chromatography. Unless otherwise noted, commercially available reagents and solvents were used without any purification. The distillation range of petroleum ether was 60–90 ℃. Liquid ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a 400 MHz spectrometer. The data were reported as follows: chemical shift on the δ scale using the residual proton solvent as the internal standard [δ 0.00 (TMS)], multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration,

and coupling constant(s) *J* in hertz. High-resolution mass spectras (HRMS) were obtained on a mass spectrometer using electrospray ionization (ESI) analyzed by quadrupole time-of-flight (QToF). Melting points were determined on a microscopic apparatus and were uncorrected. The required propargyl alcohols were prepared by following the literature procedure.[11]

General Procedure for the synthesis of 2-aminochromones 2. The required 2-aminochromones were prepared by following the literature procedure.[12] *o*-Hydroxyacetophenone (10 mmol) and dimethylformamide dimethyl acetal (DMFDA, 15 mmol, 1.5 equiv) were heated at 90–100 ℃ for 2h. The reaction mixture was cooled to room temperature and excess methanol and DMFDA were removed in vacuo to leave a light brown solid. This solid was purified by column chromatography on silica gel using petroleum ether/ethyl acetate to obtain the desired enamino ketones.

To an EtOH solution (50 mL) of enamino ketone (5 mmol), NH_2OH ·HCl (7.5 mmol, 1.5 equiv) was added. The reaction mixture was heated under reflux for 30 min. Solvent was removed under reduced pressure. Ice-cold H_2O (50 mL) was added to the residue, the precipitated solid was filtered off, washed with H_2O, dried in air and recrystallized (ethyl acetate–light petroleum) to afford crystalline isoxazole solids.

Et_3N (5 mmol, 1.0 equiv) was added to a solution of isoxazole (5 mmol) in DMF (30 mL). The reaction mixture was heated in an oil bath at 140–150 ℃ for 8 h. DMF was removed under reduced pressure and ice-cold H_2O was added to the residue. The separated solid was filtered off and recrystallized from MeOH to get crystalline compounds **2**.

2-Amino-4*H*-chromen-4-one (2a). Pale yellow solid, mp 254–255 ℃, 0.65 g, 81% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.91 (d, J = 7.5 Hz, 1H), 7.65 – 7.54 (m, 3H), 7.43 – 7.28 (m, 2H), 5.21 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 175.0, 165.4, 153.7, 132.5, 25.1, 124.9, 123.4, 116.9, 85.5. HRMS (ESI): calcd for $C_9H_8NO_2$ $(M+H)^+$ 162.0550, found 162.0551.

2-Amino-6-fluoro-4*H*-chromen-4-one (2b). Brown solid, mp 257–258 ℃, 0.54 g, 60% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.63 (s, 2H), 7.55 (d, J = 5.5 Hz, 1H), 7.45 (s, 2H), 5.19 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 173.9, 165.5, 159.1 (d, J(C, F) = 243.4 Hz), 149.9, 124.9, 119.9 (d, J(C, F) = 25.3 Hz), 119.3 (d, J(C, F) = 8.1 Hz), 110.1 (d, J(C, F) = 24.2 Hz), 85.2. ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6) δ -117.4. HRMS (ESI): calcd for $C_9H_7FNO_2$ $(M+H)^+$ 180.0455, found 180.0459.

2-Amino-6-chloro-4*H*-chromen-4-one (2c). Pale grey solid, mp 284–285 ℃, 0.76 g, 78% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 (s, 1H), 7.75 – 7.58 (m, 3H), 7.42 (d, J = 8.7 Hz, 1H), 5.19 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 173.4, 165.5, 152.2, 132.3, 129.3, 124.9, 124.2, 119.3, 85.5. HRMS (ESI): calcd for $C_9H_7ClNO_2$ $(M+H)^+$ 196.0160, found 196.0163.

2-Amino-6-bromo-4*H*-chromen-4-one (2d). Pale grey solid, mp 282–283 ℃, 0.80 g, 67% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.95 (s, 1H), 7.78 – 7.61 (m, 3H), 7.36 (d, J = 8.0 Hz, 1H), 5.19 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 173.3, 165.4, 152.6, 135.0, 127.3, 125.2, 119.6, 117.2, 85.5. HRMS (ESI): calcd for $C_9H_7BrNO_2$ $(M+H)^+$ 239.9655, found 239.9658.

2-Amino-6-methyl-4*H*-chromen-4-one (2e). Pale yellow solid, mp 281–283 ℃, 0.67 g, 77% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.68 (s, 1H), 7.48 (s, 2H), 7.40 (d, J = 8.1 Hz, 1H), 7.25 (d, J = 8.3 Hz, 1H), 5.14 (s, 1H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 175.0, 165.3, 151.9, 134.1, 133.3, 124.7, 123.1, 116.7, 85.5, 20.9. HRMS (ESI): calcd for $C_{10}H_{10}NO_2$ $(M+H)^+$ 176.0706, found 176.0709.

2-Amino-6-methoxy-4*H*-chromen-4-one (2f). Yellow solid, mp 250–252 ℃, 0.74 g, 77% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49 (s, 2H), 7.35 – 7.29 (m, 2H), 7.16 (dd, J = 8.9, 2.8 Hz, 1H), 5.17 (s, 1H), 3.80 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 174.7, 165.3, 156.3, 148.0, 124.1, 120.4, 118.3, 106.3, 85.3, 56.0. HRMS (ESI): calcd for $C_{10}H_{10}NO_3$ $(M+H)^+$ 192.0655, found 192.0660.

2-Amino-7-methoxy-4*H*-chromen-4-one (2g). Yellow solid, mp 254–256 ℃, 0.72 g, 75% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.80 (d, J = 8.7 Hz, 1H), 7.40 (s, 2H), 6.94 – 6.87 (m, 1H), 6.83 (s, 1H), 5.10 (s, 1H), 3.83 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 175.0, 165.3, 162.7, 155.2, 126.4, 117.0, 112.7, 100.7, 84.9, 56.2. HRMS (ESI): calcd for $C_{10}H_{10}NO_3$ $(M+H)^+$ 192.0655, found 192.0659.

2-Amino-7,8-dimethoxy-4*H*-chromen-4-one (2h). Yellow solid, mp 212–213 ℃, 0.72 g, 65% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 – 7.42 (m, 3H), 7.08 (s, 1H), 5.08 (s, 1H), 3.84 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 174.9, 165.2, 155.3, 147.6, 136.0, 119.9, 117.9, 109.5, 84.6, 61.3, 56.6. HRMS (ESI): calcd for $C_{11}H_{12}NO_4$ $(M+H)^+$ 222.0761, found 222.0765.

2-Amino-5-methoxy-7-methyl-4*H*-chromen-4-one (2i). Brown solid, mp >350 ℃, 0.75 g, 73% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.11 (s, 2H), 6.69 (s, 2H), 4.94 (s, 1H), 3.75 (s, 3H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 175.5, 163.3, 159.1, 155.9, 143.1, 111.0, 109.3, 108.8, 86.6, 56.4, 21.9. HRMS (ESI): calcd for $C_{11}H_{12}NO_3$ $(M+H)^+$ 206.0812, found 206.0817.

General Procedure for the synthesis of chromeno [2,3-*b*]pyridine derivatives 3. A mixture of of propargylic alcohols **1** (0.1 mmol), substituted 2-aminochromones **2** (0.15 mmol, 1.5 equiv), and $Zn(OTf)_2$ (20 mol %) in dry DCE (2.0 mL) was stirred in a sealed tube under an air atmosphere at 100 ℃ for 24 h (monitored by TLC). The resulting mixture was cooled down to room temperature. The solvent was evaporated under reduced pressure, and the residues were further purified by chromatography on silica gel (column chromatography eluent, petroleum ether/ethyl acetate = 2/1) to afford the corresponding products **3**.

2,2,4-Triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3a). Pale yellow solid, mp 243 – 244 ℃, 38.3 mg, 89% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 7.83 (d, J = 6.7 Hz, 1H), 7.62 (t, J = 7.7 Hz, 1H), 7.44 – 7.38 (m, 9H), 7.37 – 7.29 (m, 3H), 7.28 – 7.24 (m, 5H), 5.48 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 169.6, 161.5, 152.8, 146.5, 140.2, 134.3, 132.7, 128.8, 128.1, 127.7, 127.6, 127.5, 127.0, 125.8, 125.2, 124.1, 123.1, 116.9, 93.4, 65.3. HRMS (ESI): calcd for $C_{30}H_{22}NO_2$ $(M+H)^+$ 428.1645, found 428.1649.

2,2-Diphenyl-4-(*p*-tolyl)-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3b). Pale yellow solid, mp 232 – 234 ℃, 38.6 mg, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.8, 1.3 Hz, 1H), 7.47 (dd, J = 11.2, 4.2 Hz, 1H), 7.35 (d, J = 4.2 Hz, 7H), 7.31 – 7.26 (m, 3H), 7.26 – 7.22 (m, 3H), 7.18 (d, J = 8.3 Hz, 1H), 7.12 (d, J = 7.9 Hz, 2H), 5.83 (s, 1H), 5.52 (d, J = 1.8 Hz, 1H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.1, 160.0, 152.7, 145.6, 137.0, 136.6, 134.5, 131.7, 128.6, 128.1, 127.6, 127.6, 127.0, 126.4, 124.7, 124.4, 121.6, 116.0, 94.7, 65.6, 21.3. HRMS (ESI): calcd for $C_{31}H_{24}NO_2$ $(M+H)^+$ 442.1802, found 442.1807.

2,2-Diphenyl-4-(*m*-tolyl)-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3c). Pale yellow solid, mp 227 – 228 ℃, 42.0 mg, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, J = 7.9, 1.6 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.39 – 7.35 (m, 7H), 7.34 – 7.20 (m, 6H), 7.17 – 7.07 (m, 3H), 5.62 (s, 1H), 5.52 (d, J = 2.0 Hz, 1H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.1, 159.9, 152.8, 145.6, 139.9, 136.9, 134.8, 131.8, 128.7, 128.2, 127.9, 127.7, 127.3, 127.0, 126.5, 125.0, 124.8, 124.4, 121.8, 116.0, 94.9, 65.7, 21.6. HRMS (ESI): calcd for $C_{31}H_{24}NO_2$ $(M+H)^+$ 442.1802, found 442.1815.

4-(4-Ethylphenyl)-2,2-diphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3d). White solid, mp 131 – 132 ℃, 42.9 mg, 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.9, 1.5

Hz, 1H), 7.48 – 7.43 (m, 1H), 7.36 – 7.33 (m, 6H), 7.29 – 7.23 (m, 7H), 7.16 (t, *J* = 8.2 Hz, 3H), 5.95 (s, 1H), 5.51 (d, *J* = 1.9 Hz, 1H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.1, 160.1, 152.7, 145.7, 142.8, 137.2, 134.5, 131.7, 128.8, 128.7, 128.6, 127.6, 127.6, 127.0, 126.9, 124.7, 121.8, 116.0, 94.7, 65.7, 28.6, 15.3. HRMS (ESI): calcd for $C_{32}H_{26}NO_2$ $(M+H)^+$ 456.1958, found 456.1971.

4-(4-Methoxyphenyl)-2,2-diphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3e). Yellow solid, mp 222 – 223 ℃, 44.5 mg, 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.45 (dd, *J* = 11.2, 4.2 Hz, 1H), 7.37 – 7.31 (m, 8H), 7.30 – 7.25 (m, 4H), 7.24 – 7.20 (m, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.03 (s, 1H), 5.49 (d, *J* = 1.9 Hz, 1H), 3.77 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.1, 160.1, 158.6, 152.7, 145.6, 134.1, 132.3, 131.7, 128.8, 128.6, 127.6, 127.0, 126.4, 124.7, 124.3, 121.4, 116.0, 112.8, 94.6, 65.6, 55.1. HRMS (ESI): calcd for $C_{31}H_{24}NO_3$ $(M+H)^+$ 458.1751, found 458.1762.

4-([1,1'-Biphenyl]-4-yl)-2,2-diphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3f). White solid, mp 246 – 247 ℃, 48.4 mg, 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.57 – 7.53 (m, 2H), 7.51 – 7.46 (m, 1H), 7.44 – 7.40 (m, 3H), 7.39 – 7.34 (m, 8H), 7.33 – 7.24 (m, 5H), 7.21 (d, *J* = 7.8 Hz, 1H), 5.78 (s, 1H), 5.59 (d, *J* = 2.0 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.2, 160.1, 152.8, 145.6, 141.2, 139.8, 139.0, 134.3, 131.9, 128.7, 128.6, 128.2, 127.7, 127.1, 127.0, 127.0, 126.5, 126.2, 124.8, 124.3, 122.2, 116.1, 94.6, 65.7. HRMS (ESI): calcd for $C_{36}H_{26}NO_2$ $(M+H)^+$ 504.1958, found 504.1973.

4-(4-Fluorophenyl)-2,2-diphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3g). Yellow solid, mp 237 – 239 ℃, 41.2 mg, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.9, 1H), 7.48 – 7.43 (m, 1H), 7.39 – 7.32 (m, 8H), 7.32 – 7.22 (m, 5H), 7.17 (d, *J* = 8.3 Hz, 1H), 6.98 (t, *J* = 8.7 Hz, 2H), 6.02 (s, 1H), 5.49 (d, *J* = 1.9 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.1, 162.0 (d, *J*(C, F) = 245.4 Hz), 160.1, 152.7, 145.5, 135.8 (d, *J*(C, F) = 3.0 Hz), 133.7, 131.9, 129.3 (d, *J*(C, F) = 8.1 Hz), 128.6, 127.7, 127.0, 126.3, 124.8, 124.2, 122.0, 116.0, 114.2 (d, *J*(C, F) = 21.2 Hz), 94.4, 65.7. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -115.7. HRMS (ESI): calcd for $C_{30}H_{21}FNO_2$ $(M+H)^+$ 446.1551, found 446.1560.

4-(4-Chlorophenyl)-2,2-diphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3h). Pale yellow solid, mp 223 – 224 ℃, 43.8 mg, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.50 – 7.45 (m, 1H), 7.39 – 7.33 (m, 8H), 7.32 – 7.24 (m, 7H), 7.20 (d, *J* = 8.3

Hz, 1H), 5.83 (s, 1H), 5.51 (d, *J* = 1.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.1, 160.0, 152.8, 145.4, 138.4, 133.7, 132.8, 131.9, 129.1, 128.7, 127.8, 127.5, 126.9, 126.5, 124.9, 124.2, 122.2, 116.1, 94.3, 65.7. HRMS (ESI): calcd for $C_{30}H_{21}ClNO_2$ $(M+H)^+$ 462.1255, found 462.1267.

4-(4-Bromophenyl)-2,2-diphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3i). Yellow solid, mp 235 – 236 ℃, 36.2 mg, 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.41 – 7.35 (m, 7H), 7.34 – 7.28 (m, 4H), 7.24 – 7.19 (m, 3H), 5.71 (s, 1H), 5.52 (d, *J* = 1.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.2, 160.0, 152.8, 145.4, 138.8, 133.7, 132.0, 130.5, 129.5, 128.7, 127.8, 126.9, 126.4, 124.9, 124.2, 122.1, 121.0, 116.0, 94.3, 65.7. HRMS (ESI): calcd for $C_{30}H_{21}BrNO_2$ $(M+H)^+$ 506.0750, found 506.0766.

4-(4-Nitrophenyl)-2,2-diphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3j). Red solid, mp 161 – 162 ℃, 33.7 mg, 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.5Hz, 2H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.57 – 7.49 (m, 1H), 7.48 – 7.45 (m, 2H), 7.41 – 7.33 (m, 11H), 7.24 – 7.23 (m, 1H), 5.84 (s, 1H), 5.59 (d, *J* = 1.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.1, 160.0, 152.8, 146.9, 146.8, 145.1, 133.1, 132.3, 128.9, 128.6, 128.0, 126.9, 126.3, 125.1, 123.9, 123.2, 122.8, 116.2, 93.9, 65.9. HRMS (ESI): calcd for $C_{30}H_{21}N_2O_4$ $(M+H)^+$ 473.1496, found 473.1511.

4-(5-Oxo-2,2-diphenyl-1,5-dihydro-2*H*-chromeno[2,3-*b*]pyridin-4-yl) benzonitrile (3k). Pale yellow solid, mp 157 – 158 ℃, 43.5 mg, 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.54 – 7.47 (m, 2H), 7.43 – 7.32 (m, 11H), 7.24 – 7.21 (m, 2H), 5.89 (s, 1H), 5.55 (d, *J* = 1.8 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.1, 160.0, 152.8, 145.2, 144.9, 133.4, 132.2, 131.2, 128.8, 128.6, 128.0, 126.9, 126.3, 125.1, 124.0, 123.0, 119.2, 116.1, 110.6, 93.9, 65.9. HRMS (ESI): calcd for $C_{31}H_{21}N_2O_2$ $(M+H)^+$ 453.1598, found 453.1606.

Methyl 4-(5-oxo-2,2-diphenyl-1,5-dihydro-2*H*-chromeno[2,3-*b*]pyridin-4-yl) benzoate (3l). Pale yellow solid, mp 220 – 221 ℃, 46.1 mg, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.00 (m, 1H), 7.98 (d, *J* = 8.3 Hz, 2H), 7.48 – 7.45 (m, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.36 – 7.33 (m, 7H), 7.31 – 7.26 (m, 2H), 7.26 – 7.20 (m, 2H), 7.18 – 7.14 (m, 1H), 6.31 (br, 1H), 5.55 (d, *J* = 1.9 Hz, 1H), 3.85 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.0, 167.1, 160.1, 152.7, 145.4,

145.0, 134.0, 131.9, 128.8, 128.7, 128.6, 128.5, 127.7, 127.0, 126.3, 124.8, 124.1, 122.6, 116.1, 94.2, 65.7, 51.9. HRMS (ESI): calcd for $C_{32}H_{24}NO_4$ $(M+H)^+$ 486.1700, found 486.1705.

4-Phenyl-2,2-di-p-tolyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3m). White solid, mp 236 – 237 ℃, 44.2 mg, 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.02 (m, 1H), 7.49 – 7.43 (m, 1H), 7.37 – 7.28 (m, 5H), 7.26 – 7.23 (m, 5H), 7.17 (t, J = 9.9 Hz, 5H), 5.68 (s, 1H), 5.49 (d, J = 1.6 Hz, 1H), 2.34 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.0, 160.0, 152.7, 142.9, 140.0, 137.4, 134.3, 131.7, 129.3, 127.7, 127.3, 126.9, 126.9, 126.5, 124.7, 124.4, 122.3, 116.0, 94.6, 65.3, 21.0. HRMS (ESI): calcd for $C_{32}H_{26}NO_2$ $(M+H)^+$ 456.1958, found 456.1965.

2,2-Bis(4-methoxyphenyl)-4-phenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3n). Yellow solid, mp 230 – 231 ℃, 46.8 mg, 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.9, 1.5 Hz, 1H), 7.49 – 7. 43 (m, 1H), 7.36 – 7.24 (m, 10H), 7.18 (d, J = 8.3 Hz, 1H), 6.90 – 6.84 (m, 4H), 5.75 (s, 1H), 5.47 (d, J = 1.5 Hz, 1H), 3.79 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.1, 160.0, 158.9, 152.8, 140.0, 138.0, 134.1, 131.7, 128.2, 127.7, 127.4, 127.0, 126.5, 124.7, 124.4, 122.5, 116.0, 113.9, 94.6, 64.9, 55.3. HRMS (ESI): calcd for $C_{32}H_{26}NO_4$ $(M+H)^+$ 488.1856, found 488.1866.

2,2-Bis(4-fluorophenyl)-4-phenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3o). Pale yellow solid, mp 244 – 245 ℃, 41.8 mg, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, J = 7.8, 1.2 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.35 – 7.27 (m, 9H), 7.26 – 7.21 (m, 1H), 7.16 (d, J = 8.3 Hz, 1H), 7.06 – 6.98 (m, 4H), 6.05 (s, 1H), 5.45 (d, J = 1.7 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.2, 162.1 (d, J(C, F) = 249.5 Hz), 159.9, 152.7, 141.3 (d, J(C, F) = 3.0 Hz), 139.6, 135.0, 131.9, 128.8 (d, J(C, F) = 8.1 Hz), 127.7, 127.4, 127.2, 126.4, 124.9, 124.2, 121.6, 116.0, 115.6 (d, J(C, F) = 21.2 Hz), 94.7, 64.8. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -114.1. HRMS (ESI): calcd for $C_{30}H_{20}F_2NO_2$ $(M+H)^+$ 464.1457, found 464.1467.

2,2-Bis(4-chlorophenyl)-4-phenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3p). Pale yellow solid, mp 235 – 236 ℃, 44.3 mg, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 7.9, 1.5 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.35 – 7.31 (m, 8H), 7.30 – 7.26 (m, 6H), 7.19 (d, J = 8.9 Hz, 1H), 5.75 (s, 1H), 5.42 (d, J = 1.4 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.2, 159.8, 152.8, 143.7, 139.5, 135.5, 134.0, 132.0, 130.0, 128.9, 128.4, 127.6, 127.5, 127.3, 126.5, 125.0, 120.9, 116.1, 94.8, 65.0. HRMS (ESI): calcd for $C_{30}H_{20}Cl_2NO_2$ $(M+H)^+$ 496.0866, found 496.0878.

2,2-Bis(4-bromophenyl)-4-phenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3q). White solid, mp 245 – 246 ℃, 43.8 mg, 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.8, 1.3 Hz, 1H), 7.52 – 7.45 (m, 5H), 7.34 – 7.27 (m, 6H), 7.24 – 7.17 (m, 5H), 5.69 (s, 1H), 5.41 (d, J = 1.5 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.3, 159.8, 152.8, 144.1, 139.4, 135.5, 132.1, 131.9, 128.7, 127.6, 127.5, 127.3, 126.5, 125.0, 124.2, 122.2, 120.8, 116.1, 94.8, 65.1. HRMS (ESI): calcd for $C_{30}H_{20}Br_2NO_2$ $(M+H)^+$ 583.9855, found 583.9868.

2,4-Diphenyl-2-(*p*-tolyl)-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3r). Yellow solid, mp 247 – 248 ℃, 42.9 mg, 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 7.8, 1.1 Hz, 1H), 7.49 – 7.43 (m, 1H), 7.38 – 7.27 (m, 10H), 7.26 – 7.22 (m, 3H), 7.21 – 7.13 (m, 3H), 5.76 (s, 1H), 5.51 (d, J = 1.7 Hz, 1H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.1, 160.0, 152.8, 145.8, 142.8, 140.0, 137.5, 134.5, 131.7, 129.3, 128.6, 127.7, 127.6, 127.4, 127.0, 126.9, 126.5, 124.7, 124.4, 122.1, 116.0, 94.6, 65.5, 21.0. HRMS (ESI): calcd for $C_{31}H_{24}NO_2$ $(M+H)^+$ 442.1802, found 442.1810.

2,4-Diphenyl-2-(*m*-tolyl)-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3s). Pale yellow solid, mp 218 – 219 ℃, 35.0 mg, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.9, 1.5 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.36 – 7.33 (m, 6H), 7.31 (s, 1H), 7.30 – 7.20 (m, 5H), 7.19 – 7.16 (m, 2H), 7.10 (t, J = 8.5 Hz, 2H), 5.94 (d, J = 1.5 Hz, 1H), 5.51 (d, J = 2.0 Hz, 1H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.0, 160.0, 152.7, 145.7, 145.6, 139.9, 138.3, 134.4, 131.7, 128.6, 128.5, 128.4, 127.7, 127.7, 127.5, 127.3, 126.9, 126.4, 124.7, 124.3, 124.1, 122.1, 116.0, 94.5, 65.6, 21.6. HRMS (ESI): calcd for $C_{31}H_{24}NO_2$ $(M+H)^+$ 442.1802, found 442.1808.

2-(4-Methoxyphenyl)-2,4-diphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3t). Pale yellow solid, mp 248 – 249 ℃, 43.5 mg, 95% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.69 (s, 1H), 7.83 (d, J = 7.4 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.44 – 7.36 (m, 5H), 7.35 (d, J = 7.8 Hz, 1H), 7.32 – 7.28 (m, 3H), 7.28 – 7.22 (m, 5H), 6.95 (d, J = 8.6 Hz, 2H), 5.44 (s, 1H), 3.73 (s, 3H). ^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 169.6, 161.5, 158.8, 152.8, 146.7, 140.3, 138.6, 134.0, 132.7, 128.8, 128.7, 128.1, 127.6, 127.5, 127.4, 127.0, 125.8, 125.2, 124.1, 123.3, 116.8, 114.1, 93.4, 64.9, 55.6. HRMS (ESI): calcd for $C_{31}H_{24}NO_3$ $(M+H)^+$ 458.1751, found 458.1761.

2-(2-Chlorophenyl)-4-(4-methoxyphenyl)-2-phenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3u). White solid, mp 141– 142 ℃, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 7.8, 1.5 Hz, 1H), 7.91– 7.83 (m, 1H), 7.53 – 7.47 (m, 1H), 7.41 – 7.35 (m, 2H), 7.34 – 7.24 (m,

10H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.60 (s, 1H), 5.38 (d, *J* = 1.9 Hz, 1H), 3.81 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.4, 160.7, 158.9, 152.8, 145.5, 141.0, 134.5, 132.0, 131.9, 131.9, 131.7, 130.5, 129.6, 128.8, 128.7, 127.3, 127.1, 126.5, 125.9, 124.8, 124.4, 120.3, 116.1, 113.0, 94.8, 65.6, 55.2. HRMS (ESI): calcd for $C_{31}H_{23}ClNO_3$ $(M+H)^+$ 492.1361, found 492.1374.

2-(3-Chlorophenyl)-4-(4-methoxyphenyl)-2-phenyl-1,2-dihydro-5H-chromeno[2,3-b]pyridin-5-one (3v). Off white solid, mp 151 – 152 ℃, 45.8 mg, 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.48 – 7.43 (m, 1H), 7.39 – 7.23 (m, 12H), 7.21 (d, *J* = 8.5 Hz, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.75 (s, 1H), 5.45 (d, *J* = 1.5 Hz, 1H), 3.79 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.3, 160.1, 158.8, 152.7, 147.8, 145.0, 134.7, 134.6, 132.1, 131.8, 129.9, 128.8, 128.7, 127.9, 127.8, 127.2, 127.0, 126.4, 125.3, 124.8, 124.3, 120.7, 116.1, 112.9, 94.1, 65.4, 55.1. HRMS (ESI): calcd for $C_{31}H_{23}ClNO_3$ $(M+H)^+$ 492.1361, found 492.1375.

(4-Chlorophenyl)-4-(4-methoxyphenyl)-2-phenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3w). Pale yellow solid, mp 234 – 235 ℃, 42.7 mg, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.38 – 7.30 (m, 8H), 7.30 – 7.26 (m, 2H), 7.26 – 7.23 (m, 2H), 7.19 (d, *J* = 8.2 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.88 (s, 1H), 5.45 (s, 1H), 3.79 (s, 3H).$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.3, 160.1, 158.8, 152.7, 145.2, 144.2, 134.6, 133.7, 132.0, 131.9, 128.8, 128.8, 128.5, 127.9, 126.9, 126.5, 124.9, 124.3, 121.0, 116.0, 112.9, 94.9, 65.3, 55.2. HRMS (ESI): calcd for $C_{31}H_{23}ClNO_3$ $(M+H)^+$ 492.1361, found 492.1375.

7-Fluoro-2,2,4-triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3ab). Yellow solid, mp 235 – 236 ℃, 38.4 mg, 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.65 (m, 1H), 7.39 – 7.27 (m, 15H), 7.19 – 7.13 (m, 2H), 5.93 (s, 1H), 5.54 (d, *J* = 1.9 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 170.2, 160.3, 159.5 (d, *J*(C, F) = 245.4 Hz), 148.8, 145.5, 139.8, 134.4, 128.7, 127.8, 127.8, 127.5, 127.2, 127.1, 125.8 (d, *J*(C, F) = 7.1 Hz), 122.4, 119.4(d, *J*(C, F) = 28.3 Hz), 117.9 (d, *J*(C, F) = 8.1 Hz), 111.9 (d, *J*(C, F) = 24.2 Hz), 94.4, 65.9. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -116.3. HRMS (ESI): calcd for $C_{30}H_{21}FNO_2$ $(M+H)^+$ 446.1551, found 446.1561.

7-Chloro-2,2,4-triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3ac). Pale yellow solid, mp 237 – 238 ℃, 40.3 mg, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 2.3 Hz, 1H), 7.43 – 7.39(m, 1H), 7.38 – 7.26 (m, 15H), 7.16 (d, *J* = 8.8 Hz, 1H), 5.79 (s, 1H), 5.55 (d, *J* = 1.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 169.8, 160.1, 151.0, 145.4, 139.6, 134.3, 131.8,

130.6, 128.7, 127.8, 127.7, 127.4, 127.1, 127.0, 126.0, 125.5, 122.3, 117.7, 94.6, 65.8. HRMS (ESI): calcd for $C_{30}H_{21}ClNO_2$ $(M+H)^+$ 462.1255, found 462.1266.

7-Bromo-2,2,4-triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3ad). Pale yellow solid, mp 240 – 241 ℃, 40.4 mg, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 1.9 Hz, 1H), 7.56 (dd, J = 8.8, 2.4 Hz, 1H), 7.39 – 7.35 (m, 7H), 7.34 – 7.29 (m, 8H), 7.10 (d, J = 8.7 Hz, 1H), 5.74 (s, 1H), 5.55 (d, J = 1.9 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.7, 160.0, 151.5, 145.4, 139.5, 134.6, 134.3, 129.2, 128.7, 127.8, 127.7, 127.4, 127.2, 127.0, 125.8, 122.3, 118.1, 117.9, 94.7, 65.8. HRMS (ESI): calcd for $C_{30}H_{21}BrNO_2$ $(M+H)^+$ 506.0750, found 506.0762.

7-Methyl-2,2,4-triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3ae). Yellow solid, mp 238 – 239 ℃, 36.1 mg, 82% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.69 (s, 1H), 7.61 (s, 1H), 7.46 – 7.35 (m, 10H), 7.32 – 7.28 (m, 3H), 7.26 – 7.23 (m, 4H), 5.47 (s, 1H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 169.8, 161.5, 151.0, 146.6, 140.2, 134.5, 133.4, 128.8, 128.1, 127.7, 127.5, 127.0, 125.5, 123.8, 123.0, 116.7, 93.4, 65.2, 20.9. HRMS (ESI): calcd for $C_{31}H_{24}NO_2$ $(M+H)^+$ 442.1802, found 442.1809.

7-Methoxy-2,2,4-triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3af). Pale yellow solid, mp 232 – 234 ℃, 41.2 mg, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 3.0 Hz, 1H), 7.38 – 7.33 (m, 10H), 7.33 – 7.24 (m, 5H), 7.11 (d, J = 9.0 Hz, 1H), 7.04 (dd, J = 9.0, 3.0 Hz, 1H), 5.76 (s, 1H), 5.53 (d, J = 1.9 Hz, 1H), 3.75 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.0, 160.0, 156.6, 147.2, 145.6, 140.0, 134.7, 128.6, 127.7, 127.6, 127.4, 127.0, 124.9, 122.0, 120.9, 117.2, 106.7, 94.4, 65.7, 55.8. HRMS (ESI): calcd for $C_{31}H_{24}NO_3$ $(M+H)^+$ 458.1751, found 458.1759.

8-Methoxy-2,2,4-triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3ag). Yellow solid, mp 231 – 232 ℃, 33.1 mg, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.8 Hz, 1H), 7.38 – 7.25 (m, 15H), 6.81 (dd, J = 8.8, 2.3 Hz, 1H), 6.65 (d, J = 2.3 Hz, 1H), 5.73 (s, 1H), 5.50 (d, J = 1.9 Hz, 1H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.1, 162.7, 160.0, 154.1, 145.7, 140.0, 134.8, 128.6, 127.7, 127.6, 127.3, 127.0, 127.0, 121.7, 117.9, 112.4, 100.1, 94.2, 65.7, 55.7. HRMS (ESI): calcd for $C_{31}H_{24}NO_3$ $(M+H)^+$ 458.1751, found 458.1759.

8,9-Dimethoxy-2,2,4-triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3ah). Pale yellow solid, mp 202 – 203 ℃, 34.3 mg, 70% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.71 (s,

1H), 7.52 (d, *J* = 8.9 Hz, 1H), 7.43 – 7.35 (m, 9H), 7.33 – 7.28 (m, 2H), 7.26 – 7.22 (m, 4H), 7.08 (d, *J* = 8.9 Hz, 1H), 5.45 (s, 1H), 3.91 (s, 3H), 3.88 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6) δ 169.7, 161.4, 155.5, 146.8, 146.6, 140.4, 136.0, 134.4, 128.8, 128.1, 127.7, 127.6, 127.5, 127.0, 122.7, 120.6, 118.5, 109.9, 92.6, 65.3, 61.6, 56.8. HRMS (ESI): calcd for $C_{32}H_{26}NO_4$ $(M+H)^+$ 488.1856, found 488.1866.

6-Methoxy-8-methyl-2,2,4-triphenyl-1,2-dihydro-5*H*-chromeno[2,3-*b*]pyridin-5-one (3ai). Yellow solid, mp 236 – 237 ℃, 38.2 mg, 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 10H), 7.29 – 7.21 (m, 5H), 6.58 (s, 1H), 6.51 (s, 1H), 5.48 (s, 1H), 5.44 (d, *J* = 1.5 Hz, 1H), 3.78 (s, 3H), 2.35 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.6, 160.0, 158.4, 154.8, 145.9, 142.8, 140.5, 135.2, 128.5, 127.6, 127.5, 127.3, 127.0, 126.7, 121.9, 111.9, 108.8, 108.3, 95.4, 65.4, 56.2, 21.9. HRMS(ESI): calcd for $C_{32}H_{26}NO_3$ $(M+H)^+$ 472.1907, found 472.1917.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge via the Internet at http://pubs.acs.org. X-Ray Single Crystal Diffraction Data for **3a**; Copies of ^{1}H and ^{13}C NMR spectra of synthetic compounds.

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Notes

The authors declare no competing financial interest.

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