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Access to Functionalized 3*H*-Pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones and Thieno[2,3-*c*]quinolin-4(5*H*)-ones via Domino Reaction of 4-Alkynyl-3-bromoquinolin-2(1*H*)-ones

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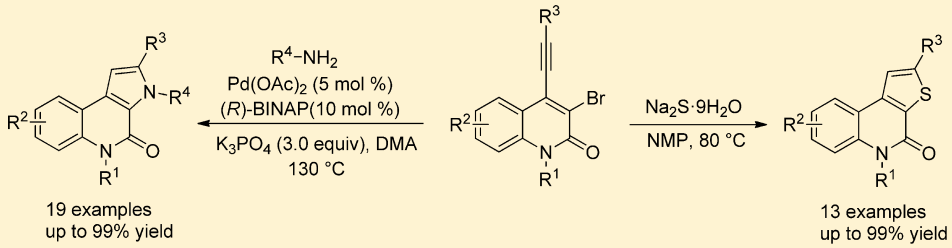
Supporting Information



ABSTRACT: We describe two efficient protocols for the straightforward synthesis of 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one and thieno[2,3-*c*]quinolin-4(5*H*)-one derivatives from readily available 4-alkynyl-3-bromoquinolin-2(1*H*)-one as precursor. The efficient synthesis of highly functionalized 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones has been achieved via a palladium-catalyzed domino reaction of 4-alkynyl-3-bromoquinolin-2(1*H*)-ones with amines. Thieno[2,3-*c*]quinolin-4(5*H*)-one derivatives were also conveniently synthesized via sequential nucleophilic aromatic substitution/5-*endo-dig* cyclization between 4-alkynyl-3-bromoquinolin-2(1*H*)-ones and sodium sulfide with good functional tolerance under mild conditions.

INTRODUCTION

Quinolin-2(1*H*)-one and its derivatives are ubiquitous subunits of numerous natural products, as well as extremely important class of heterocycles due to their wide applications in the areas of medicinal chemistry.[1−4] In particular, polycyclic pyrroloquinolines and thienoquinolines have attracted considerable attention owing to the remarkable biological activity (Figure 1). For example, martinelline and martinelline acid, which were isolated from the root bark of *Martinella iquitosensis* and contain highly substituted 1*H*-pyrrolo[3,2-*c*]quinoline core, have been reported as nonpeptide bradykinin B_1 and B_2 receptor antagonists.[2] Marinoquinolines A−F and aplidiopsamine A, which possess the tricyclic aromatic substructure 3*H*-pyrrolo[2,3-*c*]quinoline unit, exhibit high antimalarial activity and minimal toxicity toward human cells.[3] In addition, functionalized thieno[3,2-*c*]quinolines have been used as inhibitors of protein kinases for the treatment of cancer.[4a] Similarly, benzo[*b*]thieno[2,3-*c*]quinolin-6(5*H*)-ones have prominent antiproliferative activity on various tumor cell lines and were recently shown to act potent DNA binder.[4c] However, efficient and facile methods for construction of tricyclic pyrrolo- and thienoquinolones are limited so far.[5] Therefore, the pursuit of practical and efficient approaches for accessing these scaffolds from easily available precursors is in great demand and attractive.

In recent years, the domino reactions have enjoyed tremendous advances owing to their wide applications to the facile assembly of diverse hererocyclic compounds in an economically favorable way.[6−9] In particular, it is one of the most important processes in domino synthesis of various heterocycles that the transition-metal-catalyzed the process via cyclization of *ortho*-substituted ethynylbenzene derivatives.[7−9] Recently, *o*-alkynylhalobenzene has continuously drawn attention as a versatile building block in domino reactions for generation of nitrogen-containing or sulfur-containing heterocycles.[8,9] For instance, 2-substituted indoles can be formed through palladium- or copper-catalyzed transformations of *o*-alkynylhalobenzenes via amination to form *o*-alkynylanilines followed by intramolecular hydroamination.[8a,b] Halland and Lindenschmidt provided an efficient route for the synthesis 2*H*-indazoles from 2-halophenylacetylenes and hydrazines.[8e] Wu also reported the synthesis of 5*H*-cyclopenta[*c*]quinoline derivatives from a palladium-catalyzed domino reaction of *o*-alkynylhalobenzene with amine.[8f] Similarly, the domino thiolation/cyclization of *o*-alkynylhalobenzene with sodium sulfide, triisopropylsilanethiol, or thiouea as dihydrosulfide surrogate have been well developed by Takimiya,[9a] Zhang,[9b] Paradies,[9c] and Sanz et al.[9d] to access highly substituted benzo[*b*]thiophenes.

Recently, we have developed efficient method for synthesis of *N*-unsubstituted 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one start-

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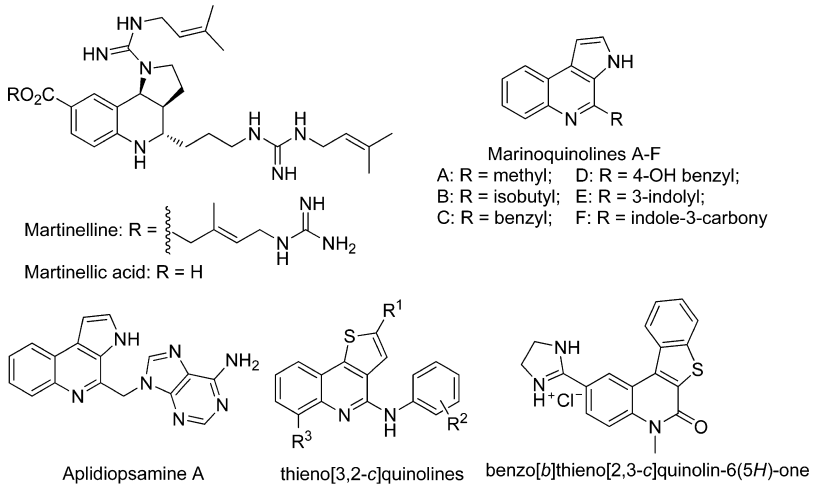
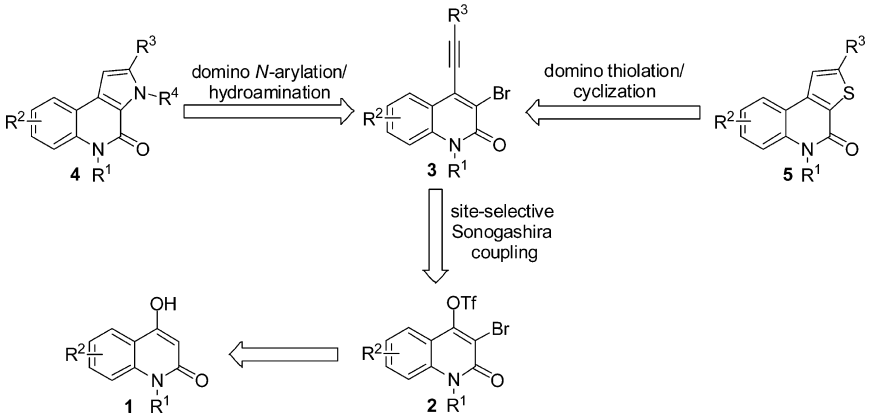


Figure 1. Selected examples of natural products and biologically active compounds containing polycyclic quinoline(quinolone)-fused heterocycles.

Scheme 1. Proposed Synthetic Route for Generation of Diverse 3*H*-Pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones 4 and Thieno[2,3-*c*]quinolin-4(5*H*)-ones 5



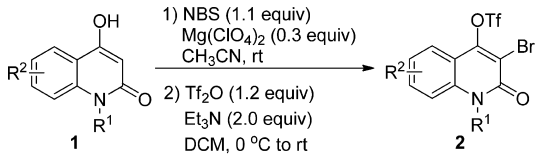
ing from readily accessible 3-nitro-4-trifloxyquinolin-2(1*H*)-one through the Songashira coupling and reduction of the nitro group, followed by an intramolecular hydroamination.[10a] Due to the importance of polycyclic pyrroloquinolines and thienoquinolines in drug discovery as well as our efforts on the development of new synthetic methods for construction of biologically interesting small molecular heterocycles,[10] we envisioned that functionalized 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one **4** and thieno[2,3-*c*]quinolin-4(5*H*)-one **5** could be produced through the domino reaction of 4-alkynyl-3-bromoquinolin-2(1*H*)-one **3** with amines and dihydrosulfide surrogates, respectively. The proposed route is described in Scheme 1. We anticipated that the key intermediate 4-alkynyl-3-bromoquinolin-2(1*H*)-one **3** could be generated from the corresponding 3-bromo-4-trifloxyquinolin-2(1*H*)-one **2** by palladium-catalyzed site-selective Sonogashira coupling reactions because of the different reactivity between the vinyl trifloxy group and vinyl bromide in cross-coupling reactions.[10d,e,11] Herein, we report a novel and flexible synthetic protocol for the synthesis of 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one **4** and thieno[2,3-*c*]quinolin-4(5*H*)-one **5** utilizing sequential palladium-catalyzed site-selective coupling and tandem C−N or C−S bond formation/heterocyclization strategy.

RESULTS AND DISCUSSION

To verify the practicability of the projected route as shown in Scheme 1, our study commenced with the preparation of the key intermediate 4-alkynyl-3-bromo-quinolin-2(1*H*)-one **3**. 3-Bromo-4-trifloxyquinolin-2(1*H*)-one **2** was easily prepared by treatment of the commercially available 4-hydroxyquinolin-2(1*H*)-one **1** with NBS/$Mg(ClO_4)_2$ and trifluoromethanesulfonic anhydride, subsequently (Scheme 2).

With this key intermediate in hand, we then attempted to the possibility of the palladium-catalyzed regioselective Sonogashira coupling for synthesis of 4-alkynyl-3-bromoqui-

Scheme 2. Synthesis of 3-Bromo-4-trifloxyquinolin-2(1*H*)-one (2)



2a R^1 = Me, R^2 = H, 54% yield
2b R^1 = Et, R^2 = H, 66% yield
2c R^1 = Ph, R^2 = H, 51% yield
2d R^1 = Me, R^2 = 6-Me, 75% yield
2e R^1 = Me, R^2 = 6-Cl, 54% yield

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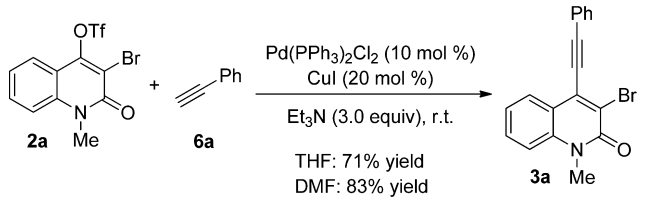
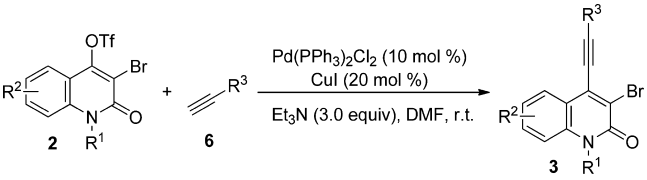
nolin-2(1*H*)-one **3**, 3-bromo-4-trifloxyquinolin-2(1*H*)-one **2a**, and phenylacetylene **6a** were used as the model substrates (Scheme 3). The reaction was initially conducted in the

Scheme 3. Conditions Screening for Sonogashira Coupling



standard Sonogashira cross-coupling reaction conditions ($Pd(PPh_3)_2Cl_2$ (10 mol %), CuI (20 mol %), Et_3N, THF, rt). Gratifyingly, the expected monoalkynylation product **3a** was isolated in 71% yield (Scheme 3). The result was improved when the reaction was conducted in DMF (83% yield). We then examined the reaction scope using a variety of 3-bromo-4-trifloxyquinolin-2(1*H*)-one **2** with various alkynes **6** at a catalyst loading of 10 mol % on a 0.5 mmol scale (Table 1). Initially, the reaction tolerance of the terminal

Table 1. Synthesis of 4-Alkynyl-3-bromoquinolin-2(1*H*)-one 3[a]



entry	R^1, R^2 (**2**)	R^3 (**6**)	product	yield[b] (%)
1	Me, H (**2a**)	Ph (**6a**)	**3a**	83
2	Me, H (**2a**)	4-$MeOC_6H_4$ (**6b**)	**3b**	82
3	Me, H (**2a**)	4-MeC_6H_4 (**6c**)	**3c**	80
4	Me, H (**2a**)	4-ClC_6H_4 (**6d**)	**3d**	79
5	Me, H (**2a**)	Thiophen-2-yl (**6e**)	**3e**	83
6	Me, H (**2a**)	*n*-Bu (**6f**)	**3f**	72
7	Me, H (**2a**)	*t*-Bu (**6g**)	**3g**	92
8	Me, H (**2a**)	*c*-Pr (**6h**)	**3h**	85
9	Me, H (**2a**)	TMS (**6i**)	**3i**	48
10	Et, H (**2b**)	Ph (**6a**)	**3j**	84
11	Ph, H (**2c**)	4-$MeOC_6H_4$ (**6b**)	**3k**	70
12	Me, 6-Me (**2d**)	Ph (**6a**)	**3l**	53
13	Me, 6-Cl (**2e**)	Ph (**6a**)	**3m**	81

[a]Reaction conditions: $Pd(PPh_3)_2Cl_2$ (0.05 mmol), CuI (0.1 mmol), Et_3N (1.5 mmol), **2** (0.5 mmol), **6** (0.6 mmol), DMF (5 mL), rt. [b]Isolated yield based on **2**.

alkynes was investigated. It was found that various alkynes are excellent partners in the reaction, aryl- and alkylacetylenes could be utilized to give the desired products in moderate to good yields (Table 1, entries 1−8), with (trimethylsilyl)-acetylene being the only one exception (Table 1, entry 9). With respect to the substituent at R^1 position of the 3-bromo-4-trifloxyquinolin-2(1*H*)-one **2**, the reaction tolerated alkyl and aryl groups, furnishing the desired products **4** in good yields (Table 1, entries 10 and 11). Moreover, it was found that substrate with an electron-deficient group as R^2 was more reactive than it with an electron-rich group (Table 1, entries 12 and 13).

Having found a reliable route to the 4-alkynyl-3-bromoquinolin-2(1*H*)-one **3**, we thus began our investigation to identify the optimized conditions of the domino reaction between 3-bromo-1-methyl-4-(phenylethynyl)quinolin-2(1*H*)-one **3a** and aniline **7a** (Table 2). The reaction was initially performed in the presence of 5 mol % of palladium acetate and 10 mol % of Sphos in DMA at 130 °C, using K_3PO_4 as the base. To our delight, the expected product **4a** was formed via Buchwald−Hartwig amination[12] and intramolecular hydroamination[7e] in 65% yield (Table 2, entry 1). This result encouraged us to examine the important reaction parameters including ligand, base, solvent, palladium source, and temperature. Different ligands such as phosphines and diphosphines were screened first (Table 2, entries 2−9). It was found that the reaction proceeded efficiently when (*R*)-BINAP was employed as ligand, leading to the desired product **4a** in an almost quantitative yield (Table 2, entry 7). Replacing K_3PO_4 with Cs_2CO_3 gave a similar yield (99% yield, Table 2, entry 11). We therefore chose to use cheap K_3PO_4 (Table 2, entries 7 and 11). Different solvents and palladium sources were evaluated subsequently (Table 2, entries 12−15). However, no better results were obtained. It is worth noting that the uncyclized product 1-methyl-3-(phenylamino)-4-(phenylethynyl)quinolin-2(1*H*)-one was isolated as the main product when the solvent was changed to toluene (Table 2, entry 13). A slightly lower yield was obtained when the reaction temperature lowered to 100 °C (Table 2, entry 16). However, noticeable amounts of Buchwald−Hartwig aminated product were observed when the reaction was conducted at 80 °C (23% yield, Table 2, entry 17).

Having optimized the reaction conditions, we next surveyed the scope of this one-pot process. The results are summarized in Table 3. Reactions of 3-bromo-1-methyl-4-(phenylethynyl)-quinolin-2(1*H*)-one (**3a**) with various anilines **7** were investigated first. The use of arylamines with electron-donating or -withdrawing functionalities gave rise to the corresponding 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones **4b−g** in excellent yields (Table 3, entries 2−7). Our results suggested that the electronic nature of the arylamine does not significantly influence the outcome of the domino reaction. Furthermore, *ortho*-substituted anilines also could be tolerated under the standard conditions. For instance, *o*-toluidine and *o*-chloroaniline were good partners in this transformation, affording the desired product **4d** and **4e** in 99% and 94% yields, respectively (Table 3, entries 4 and 5). We also treated several 4-alkynyl-3-bromoquinolin-2(1*H*)-ones **3** substituted with aromatics or alkyls (*n*-butyl, *tert*-butyl, and cyclopropyl) in R^3 position with aniline **7a** under the identical conditions. The corresponding 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones **4h−4n** were formed in moderate to excellent yields (Table 3, entries 8−14). It was noteworthy that the corresponding 2-thiophene-yl-substituted acetylene **3e** was found to be a suitable substrate for the domino coupling/cyclization and gave the desired product **4k** in 97% yield (Table 3, entry 11). On the other hand, it was found that substrates **3** with an alkyl group as R^1 were more reactive than with an aryl group as R^1 (Table 3, entries 15−16). 4-Alkynyl-3-bromoquinolin-2(1*H*)-one **3l** bearing a methyl group at C6 position gave **4q** with good yield as well (Table 3, entry 17). Furthermore, we showed that aliphatic amines are also suitable partners in this domino reaction. For instance, benzylamine **7h** and 4-fluorobenzylamine **7i** were used as the reactants and gave

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Table 2. Initial Studies for the Reaction of 3-Bromo-1-methyl-4-(phenylethynyl)quinolin-2(1*H*)-one (3a) with Aniline 7a[a]

entry	[Pd]	ligand	base	solvent	temp (°C)	yield[b] (%)
1	$Pd(OAc)_2$	Sphos	K_3PO_4	DMA	130	65
2	$Pd(OAc)_2$	Xphos	K_3PO_4	DMA	130	67
3	$Pd(OAc)_2$	CyJohnphos	K_3PO_4	DMA	130	51
4	$Pd(OAc)_2$	Johnphos	K_3PO_4	DMA	130	65
5	$Pd(OAc)_2$	Xantphos	K_3PO_4	DMA	130	86
6	$Pd(OAc)_2$	DPEphos	K_3PO_4	DMA	130	74
7	**$Pd(OAc)_2$**	**(*R*)-BINAP**	**K_3PO_4**	**DMA**	**130**	**99**
8	$Pd(OAc)_2$	DPPF	K_3PO_4	DMA	130	57
9	$Pd(OAc)_2$	PPh_3	K_3PO_4	DMA	130	38
10	$Pd(OAc)_2$	(*R*)-BINAP	K_2CO_3	DMA	130	48
11	$Pd(OAc)_2$	(*R*)-BINAP	Cs_2CO_3	DMA	130	99
12	$Pd(OAc)_2$	(*R*)-BINAP	K_3PO_4	DMF	130	84
13	$Pd(OAc)_2$	(*R*)-BINAP	K_3PO_4	toluene	110	0[c]
14	$PdCl_2$	(*R*)-BINAP	K_3PO_4	DMA	130	74
15	Pd_2dba_3	(*R*)-BINAP	K_3PO_4	DMA	130	91
16	$Pd(OAc)_2$	(*R*)-BINAP	K_3PO_4	DMA	100	91
17	$Pd(OAc)_2$	(*R*)-BINAP	K_3PO_4	DMA	80	44[d]

[a]Reaction conditions: [Pd] (0.0075 mmol), ligand (0.015 mmol), base (0.45 mmol), **3a** (0.15 mmol), **7a** (0.18 mmol), solvent (1 mL). [b]Isolated yield based on **3a**. [c]1-Methyl-3-(phenylamino)-4-(phenylethynyl)quinolin-2(1*H*)-one was obtained in 78% yield. The product **4a** was formed in 99% yield when the uncyclized product was subject into the optimized reaction conditions. [d]1-Methyl-3-(phenylamino)-4-(phenylethynyl)quinolin-2(1*H*)-one was obtained in 23% yield.

the corresponding products **4r** and **4s** in 84% and 91% yields, respectively (Table 3, entries 18 and 19). However, the uncyclized product 3-(cyclohexylamino)-1-methyl-4-(phenylethynyl)quinolin-2(1*H*)-one was isolated as the main product when cyclohexylamine **7j** was used as the reactant (Table 3, entry 20). The desired cyclized product **4t** was isolated in 99% yield when the uncyclized product was carried out in DMF under reflux, in the presence of 10 mol % of $PdCl_2$.[10a]

We have also attempted to explore the reaction of 3-bromo-4-trifloxyquinolin-2(1*H*)-one **2a**, phenylacetylene **6a**, and aniline **7a** for the synthesis of 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one (**4a**) in a one-pot and sequential fashion (Scheme 4). As expected, the corresponding product **4a** was isolated in 32% yield.

To increase the diversity of 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones **4**, we attempted to introduce the substituent on the pyrrole ring of **4**, and the results are summarized in Scheme 5. Reaction of **4a** with NBS at room temperature gave the selective bromination product **4aa** in 98% yield, which was then subjected to Suzuki coupling with *p*-tolylboronic acid to afford 5-methyl-2,3-diphenyl-1-(*p*-tolyl)-3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one (**4ab**) in an almost quantitative yield.

The protocol is further illustrated by the convenient synthesis of nigalin B and lamellarin D analogues, which have possessed a variety of potentially valuable biological properties.[13] We subjected 3-bromo-4-(phenylethynyl)-2*H*-chromen-2-one **3a′** with aryl amines to the optimized reaction conditions. We were delighted to observe that chromeno[3,4-*b*]pyrrol-4(3*H*)-one derivatives **8a−c** could be isolated in reasonable yields (Scheme 6). These results demonstrate that this new protocol provides a convenient methodology to access these biologically active scaffolds.

Inspired by the recent development of synthesis of highly substituted benzo[*b*]thiophenes documented by Takimiya, Zhang, Paradies, and Sanz,[9] we turned our attention to the key thiolation/cyclization for constructing the corresponding thieno[2,3-*c*]quinolin-4(5*H*)-one backbone. First, 3-bromo-1-methyl-4-(phenylethynyl)quinolin-2(1*H*)-one **3a** was subjected to reaction with sodium sulfide using the CuI/tetramethylethylenediamine (TMEDA) catalyst system developed by Zhang et al. to obtain the desired product **5a** in 48% yield (Table 4, entry 1).[9b] The yield was increased to 85% when treatment of substrate **4a** with sodium sulfide in NMP as solvent at 180 °C (Table 4, entry 2).[9a] It is worth mentioning that the reaction temperature could be lowered to 80 °C without any loss in the yield of the isolated product (Table 4, entry 3). An evaluation of various solvents did not produce any better results (Table 4, entries 4 and 5).

The generality of this domino thiolation/cyclization reaction was then explored under the optimized conditions as shown in Table 5. We found a broad substrate scope with respect to the substituent at the terminal alkyne moiety of **3**. In all case, compound **3** reacted with sodium sulfide to afford the desired thieno[2,3-*c*]quinolin-4(5*H*)-ones **5** in moderate to excellent yields. Both aryl- and alkyl-substituted **3** proved to be good partner in the transformation (Table 5, entries 1−8). For instance, 3-bromo-1-methyl-4-(phenylethynyl)-quinolin-2(1*H*)-one **3** possessing an electron-rich (**3b**, **3c**) or electron-deficient (**3d**) group at the R^3 position showed similar efficiency in this domino thiolation/cyclization reaction

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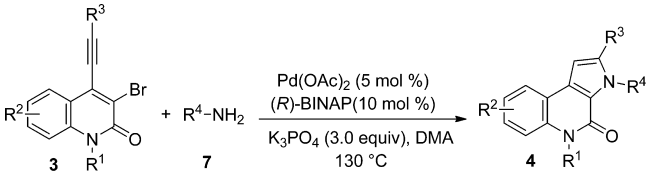
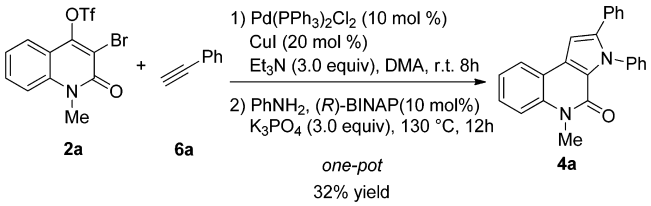
Table 3. Domino Synthesis of Various 3*H*-Pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones 4[a]



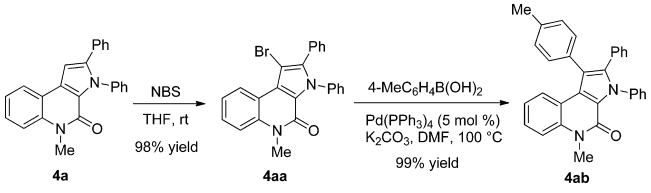
entry	R^1, R^2, R^3 (3)	R^4 (7)	product	yield[b] (%)
1	Me, H, Ph (**3a**)	Ph (**7a**)	**4a**	99
2	Me, H, Ph (**3a**)	4-MeC_6H_4 (**7b**)	**4b**	99
3	Me, H, Ph (**3a**)	4-$MeOC_6H_4$ (**7c**)	**4c**	96
4	Me, H, Ph (**3a**)	2-MeC_6H_4 (**7d**)	**4d**	99
5	Me, H, Ph (**3a**)	2-ClC_6H_4 (**7e**)	**4e**	94
6	Me, H, Ph (**3a**)	3-ClC_6H_4 (**7f**)	**4f**	94
7	Me, H, Ph (**3a**)	4-FC_6H_4 (**7g**)	**4g**	99
8	Me, H, 4-$MeOC_6H_4$ (**3b**)	Ph (**7a**)	**4h**	89
9	Me, H, 4-MeC_6H_4 (**3c**)	Ph (**7a**)	**4i**	86
10	Me, H, 4-ClC_6H_4 (**3d**)	Ph (**7a**)	**4j**	45
11	Me, H, thiophene-2-yl (**3e**)	Ph (**7a**)	**4k**	97
12	Me, H, *n*-Bu (**3f**)	Ph (**7a**)	**4l**	53
13	Me, H, *t*-Bu (**3g**)	Ph (**7a**)	**4m**	95
14	Me, H, *c*-Pr (**3h**)	Ph (**7a**)	**4n**	55
15	Et, H, Ph (**3j**)	Ph (**7a**)	**4o**	99
16	Ph, H, 4-$MeOC_6H_4$ (**3k**)	Ph (**7a**)	**4p**	63
17	Me, 6-Me, Ph (**3l**)	Ph (**7a**)	**4q**	88
18	Me, H, Ph (**3a**)	Bn (**7h**)	**4r**	84
19	Me, H, Ph (**3a**)	4-$FC_6H_4CH_2$ (**7i**)	**4s**	91
20	Me, H, Ph (**3a**)	*c*-hexyl (**7j**)	**4t**	0[c]

[a]Reaction conditions: $Pd(OAc)_2$ (0.0075 mmol), (*R*)-BINAP (0.015 mmol), K_3PO_4 (0.45 mmol), **3** (0.15 mmol), 7 (0.18 mmol), DMA (1 mL), 130 °C. [b]Isolated yield based on **3**. [c]3-(Cyclohexylamino)-1-methyl-4-(phenylethynyl)quinolin-2(1*H*)-one was obtained in 69% yield.

Scheme 4. One-Pot 3*H*-Pyrrolo[2,3-*c*]quinolin-4(5*H*)-one (4a) Synthesis

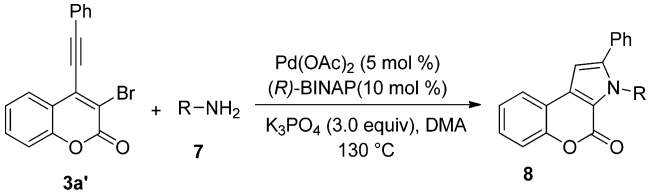


Scheme 5. Synthesis of 5-Methyl-2,3-diphenyl-1-(*p*-tolyl)-3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one (4ab)



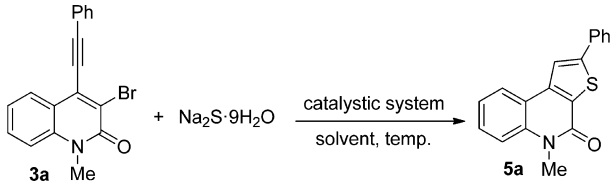
(Table 5, entries 2–4). Furthermore, heterocyclic substrate **3e** also underwent this transformation, with a satisfactory yield (Table 5, entry 5). Interestingly, it was found that the substrate **3i** bearing a TMS group at the terminal of the triple bond was compatible with this reaction, and the desilyl

Scheme 6. Domino Synthesis of Various Chromeno[3,4-*b*]pyrrol-4(3*H*)-ones (Nigalin B and Lamellarin D Analogues)



8a: R = C_6H_5, 34% yield
8b: R = 4-$MeOC_6H_4$, 53% yield
8c: R = 4-FC_6H_4, 36% yield

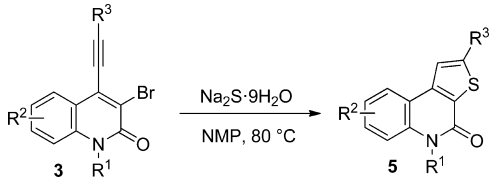
Table 4. Initial Studies for the Reaction of 3-Bromo-1-methyl-4-(phenylethynyl)quinolin-2(1*H*)-one (3a) with Na_2S[a]



entry	catalytic system	solvent	temp (°C)	yield[b] (%)
1	CuI/TMEDA	DMF	80	48[c]
2		NMP	180	85
3		**NMP**	**80**	**85**
4		DMF	80	82
5		EtOH	80	14

[a]Reaction conditions: **3a** (0.15 mmol), $Na_2S·9H_2O$ (0.30 mmol), solvent (1 mL). [b]Isolated yield based on **3a**. [c]10 mol % of CuI and 20 mol % of TMEDA were added.

Table 5. Domino Synthesis of Various Thieno[2,3-*c*]quinolin-4(5*H*)-ones 5[a]



entry	R^1, R^2, R^3 (3)	product	yield[b] (%)
1	Me, H, Ph (**3a**)	**5a**	85
2	Me, H, 4-$MeOC_6H_4$ (**3b**)	**5b**	99
3	Me, H, 4-MeC_6H_4 (**3c**)	**5c**	79
4	Me, H, 4-ClC_6H_4 (**3d**)	**5d**	94
5	Me, H, thiophene-2-yl (**3e**)	**5e**	83
6	Me, H, *n*-Bu (**3f**)	**5f**	59
7	Me, H, *t*-Bu (**3g**)	**5g**	86
8	Me, H, *c*-Pr (**3h**)	**5h**	99
9	Me, H, TMS (**3i**)	**5i**	36[c]
10	Et, H, Ph (**3j**)	**5j**	98
11	Ph, H, 4-$MeOC_6H_4$ (**3k**)	**5k**	82
12	Me, 6-Me, Ph (**3l**)	**5l**	94
13	Me, 6-Cl, Ph (**3m**)	**5m**	99

[a]Reaction conditions: **3** (0.15 mmol), $Na_2S·9H_2O$ (0.30 mmol), NMP (1 mL), 80 °C. [b]Isolated yield based on **3**. [c]The desilyl product was obtained.

product **5i** was generated (Table 5, entry 9). Next, a series of 4-alkynyl-3-bromo-quinolin-2(1*H*)-one **3** derivatives by differ-

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ing the nature of the R^1 and R^2 substituent were tested. The corresponding thieno[2,3-*c*]quinolin-4(5*H*)-ones **5j−m** were formed in good to excellent yields (Table 5, entries 10−13). For example, substrate **3l** or **3m** was reacted with sodium sulfide under the standard conditions to provide the corresponding product **5l** or **5m** in 94 and 99% yields, respectively (Table 5, entries 12 and 13).

CONCLUSIONS

In summary, we have developed two efficient approaches to construct biologically important 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one and thieno[2,3-*c*]quinolin-4(5*H*)-one derivatives from the readily available 4-alkynyl-3-bromoquinolin-2(1*H*)-one as precursor by the domino process. Palladium-catalyzed domino reaction of 4-alkynyl-3-bromoquinolin-2(1*H*)-one with amine provided a practical synthesis of highly functionalized 3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones in good yields. While thieno[2,3-*c*]quinolin-4(5*H*)-one derivatives could be obtained via a domino substitution/cyclization process between 4-alkynyl-3-bromoquinolin-2(1*H*)-one and sodium hydrosulfide with good functional tolerance under mild conditions. Application of the developed method has been successfully extended for the synthesis of nigalin B and lamellarin D analogues, chromeno[3,4-*b*]pyrrol-4(3*H*)-one derivatives. These protocols provide straightforward access to more diversity in the scaffold for drug discovery and material sciences. Additionally, the related library construction as well as evaluation of all these small molecules for biological effects are currently underway in our laboratory, and the results will be reported in due course.

EXPERIMENTAL SECTION

General Information. The ^{1}H and ^{13}C NMR spectra were recorded on a 400, 500, or 600 MHz spectrometer with chloroform-*d* as a solvent at 20−25 °C. High-resolution mass spectra (HRMS) were recorded on a Q-TOF or FT-ICR MS spectrometer. Melting points are uncorrected. All anaerobic manipulations were carried out with standard Schlenk techniques under an inert atmosphere of argon. All commercial materials were used without further purification. Column chromatography was performed using silica gel (200−300 mesh).

General Procedure for Synthesis of 3-Bromo-4-trifloxyquinolin-2(1*H*)-one 2. A mixture of 4-hydroxyquinolin-2(1*H*)-one **1** (5 mmol), NBS (974 mg, 5.5 mmol), and $Mg(ClO_4)_2$ (333 mg, 1.5 mmol) in acetonitrile (25 mL) was stirred overnight at room temperature. After the solvent was evaporated under vacuum, the remaining solid was dried and used without further purification. The crude 3-bromo-4-hydroxyquinolin-2(1*H*)-one and Et_3N (606 mg, 6 mmol) were dissolved in DCM (50 mL), and Tf_2O (1.692 g, 6 mmol) was subsequently slowly added into the mixture at 0 °C. The reaction mixture was stirred until TLC indicated completion of reaction. The reaction solution was concentrated under vacuo and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 4:1 to 2:1) to afford the corresponding products **2b−e**.

*3-Bromo-1-ethyl-2-oxo-1,2-dihydroquinolin-4-yl trifluoromethanesulfonate (**2b**):* pale yellow solid (1.316 g, 66% yield); mp 93−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.1 Hz, 1H), 7.75−7.71 (m, 1H), 7.49 (d, J = 8.6 Hz, 1H), 7.39 (t, J = 7.7 Hz, 1H), 4.45 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 151.6, 137.5, 132.6, 123.4, 123.3, 118.4 (q, J = 319.4 Hz), 116.0, 114.6, 112.8, 39.8, 12.5; HRMS (ESI) calcd for $C_{12}H_{10}BrF_3NO_4S[M + H]^+$ 399.9461, found 399.9472.

*3-Bromo-2-oxo-1-phenyl-1,2-dihydroquinolin-4-yl trifluoromethanesulfonate (**2c**):* white solid (1.139 g, 51% yield); mp 173−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.1 Hz, 1H), 7.65−7.55 (m, 3H), 7.49 (t, J = 7.9 Hz, 1H), 7.37−7.28 (m, 3H), 6.77 (d, J = 8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 152.2, 139.5, 136.9, 132.2, 130.4, 129.6, 128.4, 123.6, 122.8, 118.5 (q, J = 319.0 Hz), 116.6, 115.6, 113.2; HRMS (ESI) calcd for $C_{16}H_{10}BrF_3NO_4S[M + H]^+$ 447.9461, found 447.9439.

*3-Bromo-1,6-dimethyl-2-oxo-1,2-dihydroquinolin-4-yl trifluoromethanesulfonate (**2d**):* white solid (1.496 g, 75% yield); mp 122−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.54 (d, J = 8.7 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 3.81 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 151.5, 136.6, 134.0, 133.4, 123.1, 122.8, 118.5 (q, J = 319.4 Hz), 115.6, 114.7, 114.5, 112.7, 31.5, 20.9; HRMS (ESI) calcd for $C_{12}H_{10}BrF_3NO_4S[M + H]^+$ 399.9461, found 399.9447.

*3-Bromo-6-chloro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl trifluoromethanesulfonate (**2e**):* pale yellow solid (1.19 g, 54% yield); mp 107−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.81 (m, 1H), 7.68−7.66 (m, 1H), 7.41 (d, J = 9.1 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 150.4, 136.9, 132.7, 129.4, 122.6, 118.4 (q, J = 319.4 Hz), 116.7, 116.3, 114.5, 31.8; HRMS (ESI) calcd for $C_{11}H_6BrClF_3NNaO_4S[M + Na]^+$ 441.8734, found 441.8743.

General Procedure for Synthesis of 4-Alkynyl-3-bromoquinolin-2(1*H*)-ones 3. A mixture of 3-bromo-4-trifloxyquinolin-2(1*H*)-one **2** (0.5 mmol), Pd $(PPh_3)_2Cl_2$ (35 mg, 0.05 mmol), CuI (19 mg, 0.10 mmol), and Et_3N (152 mg, 1.5 mmol) in a Schlenk flask under argon atmosphere was added 5 mL of freshly distilled DMF and terminal alkyne (0.6 mmol). The mixture was stirred until TLC indicated completion of reaction. The reaction solution was concentrated under vacuo, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 4:1 to 2:1) to afford products **3a−m**.

*3-Bromo-1-methyl-4-(phenylethynyl)quinolin-2(1H)-one (**3a**):* white solid (140 mg, 83% yield); mp 172−173 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18−8.16 (m, 1H), 7.71−7.69 (m, 2H), 7.65−7.62 (m, 1H), 7.48−7.42 (m, 3H), 7.39 (d, J = 8.5 Hz, 1H), 7.35−7.32 (m, 1H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.0, 138.6, 133.3, 132.1, 131.1, 129.9, 128.6, 127.7, 122.9, 122.0, 121.8, 120.1, 114.4, 104.1, 84.4, 31.1; HRMS (ESI) calcd for $C_{18}H_{13}BrNO$ $[M + H]^+$ 338.0175, found 338.0177.

*3-Bromo-4-((4-methoxyphenyl)ethynyl)-1-methylquinolin-2(1H)-one (**3b**):* brown solid (150 mg, 82% yield); mp 195−196 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17−8.15 (m, 1H), 7.65−7.61 (m, 3H), 7.37 (d, J = 8.4 Hz, 1H), 7.34−7.31 (m, 1H), 6.96−6.93 (m, 2H), 3.87 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.8, 158.0, 138.5, 133.8, 133.6, 131.0, 127.7, 122.8, 121.1, 120.0, 114.3, 114.2, 113.7, 104.7, 83.7, 55.4, 31.0; HRMS (ESI) calcd for $C_{19}H_{15}BrNO_2$ $[M + H]^+$ 368.0281, found 368.0271.

*3-Bromo-1-methyl-4-(p-tolylethynyl)quinolin-2(1H)-one (**3c**):* pale pink solid (140 mg, 80% yield); mp 160−161 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18−8.16 (m, 1H), 7.65−7.61 (m, 1H), 7.59 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.4 Hz, 1H), 7.35−7.31 (m, 1H), 7.24 (d, J = 7.9 Hz, 2H), 3.82 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.0, 140.4, 138.6, 133.5, 132.0, 131.1, 129.4, 127.7, 122.9, 121.6, 120.1, 118.7, 114.4, 104.6, 84.0, 31.1, 21.7; HRMS (ESI) calcd for $C_{19}H_{15}BrNO$ $[M + H]^+$ 352.0332, found 352.0317.

*3-Bromo-4-((4-chlorophenyl)ethynyl)-1-methylquinolin-2(1H)-one (**3d**):* pale brown solid (147 mg, 79% yield); mp 188−189 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13−8.11 (m, 1H), 7.66−7.61 (m, 3H), 7.42−7.38 (m, 3H), 7.35−7.32 (m, 1H), 3.82 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.9, 138.6, 136.1, 133.3, 133.0, 131.2, 129.0, 127.5, 122.9, 122.2, 120.2, 119.9, 114.5, 102.6, 85.3, 31.2; HRMS (ESI) calcd for $C_{18}H_{12}BrClNO$ $[M + H]^+$ 371.9786, found 371.9793.

*3-Bromo-1-methyl-4-(thiophene-2-ylethynyl)quinolin-2(1H)-one (**3e**):* pale yellow solid (142 mg, 83% yield); mp 156−157 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10−8.08 (m, 1H), 7.65−7.62 (m, 1H), 7.52 (d, J = 3.4 Hz, 1H), 7.48 (d, J = 5.1 Hz, 1H), 7.38 (d, J = 8.5 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.12−7.10 (m, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 138.6, 134.1, 133.0, 131.1,

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129.8, 127.6, 127.5, 122.9, 121.5, 121.4, 119.8, 114.4, 97.3, 88.3, 31.1; HRMS (ESI) calcd for $C_{16}H_{11}BrNOS$ $[M + H]^+$ 343.9739, found 343.9726.

3-Bromo-4-(hex-1-yn-1-yl)-1-methylquinolin-2(1H)-one (**3f**): yellow solid (114 mg, 72% yield); mp 102−103 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08−8.06 (m, 1H), 7.62−7.59 (m, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.31−7.28 (m, 1H), 3.80 (s, 3H), 2.64 (t, J = 7.1 Hz, 2H), 1.75−1.70 (m, 2H), 1.61−1.56 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.1, 138.5, 134.0, 130.9, 127.8, 122.7, 121.5, 120.5, 114.2, 107.1, 76.2, 31.0, 30.3, 22.0, 19.7, 13.6; HRMS (ESI) calcd for $C_{16}H_{17}BrNO$ $[M + H]^+$ 318.0488, found 318.0484.

3-Bromo-4-(3,3-dimethylbut-1-yn-1-yl)-1-methylquinolin-2(1H)-one (**3g**): white solid (146 mg, 92% yield); mp 138−139 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04−8.03 (m,1H), 7.62−7.59 (m, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.31−7.28 (m, 1H), 3.80 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.1, 138.5, 133.9, 130.9, 127.8, 122.8, 121.6, 120.4, 114.8, 114.3, 74.9, 31.0, 30.6, 28.9; HRMS (ESI) calcd for $C_{16}H_{17}BrNO$ $[M + H]^+$ 318.0488, found 318.0501.

3-Bromo-4-(cyclopropylethynyl)-1-methylquinolin-2(1H)-one (**3h**): white solid (128 mg, 85% yield); mp 120−121 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02−8.01 (m, 1H), 7.61−7.58 (m, 1H), 7.34 (d, J = 8.5 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 3.79 (s, 3H), 1.69−1.64 (m, 1H), 1.09−1.02 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 138.5, 133.8, 130.9, 127.7, 122.7, 121.2, 120.4, 114.2, 110.5, 71.4, 31.0, 9.8, 0.9; HRMS (ESI) calcd for $C_{15}H_{13}BrNO$ $[M + H]^+$ 302.0175, found 302.0176.

3-Bromo-1-methyl-4-((trimethylsilyl)ethynyl)quinolin-2(1H)-one (**3i**): white solid (80 mg, 48% yield); mp 243−244 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09−8.07 (m, 1H), 7.64−7.60 (m, 1H), 7.36 (d, J = 8.5 Hz, 1H), 7.33−7.30 (m, 1H), 3.81 (s, 3H), 0.36 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.0, 138.6, 133.1, 131.1, 127.8, 122.9, 122.6, 120.1, 114.4, 111.6, 98.7, 31.2, −0.35; HRMS (ESI) calcd for $C_{15}H_{17}BrNOSi$ $[M + H]^+$ 334.0258, found 334.0246

3-Bromo-1-ethyl-4-(phenylethynyl)quinolin-2(1H)-one (**3j**): yellow solid (147 mg, 84% yield); mp 116−117 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20−8.18 (m, 1H), 7.71−7.69 (m, 2H), 7.65−7.62 (m, 1H), 7.48−7.40 (m, 4H), 7.33 (t, J = 7.6 Hz, 1H), 4.45 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 137.6, 133.2, 132.0, 131.0, 129.8, 128.5, 127.9, 122.6, 122.0, 121.8, 120.3, 114.2, 104.0, 84.4, 39.1, 12.6; HRMS (ESI) calcd for $C_{19}H_{15}BrNO$ $[M + H]^+$ 352.0332, found 352.0333.

3-Bromo-4-((4-methoxyphenyl)ethynyl)-1-phenylquinolin-2(1H)-one (**3k**): white solid (150 mg, 70% yield); mp 198−199 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20−8.18 (m, 1H), 7.69−7.66 (m, 2H), 7.62−7.59 (m, 2H), 7.55−7.52 (m, 1H), 7.40−7.37 (m, 1H), 7.31−7.28 (m, 3H), 6.97−6.95 (m, 2H), 6.67 (d, J = 8.5 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 157.9, 139.8, 137.6, 134.4, 133.9, 130.5, 130.2, 129.1, 128.7, 127.3, 122.9, 121.5, 119.9, 116.3, 114.3, 113.8, 105.3, 83.9, 55.4; HRMS (ESI) calcd for $C_{24}H_{17}BrNO_2$ $[M + H]^+$ 430.0437, found 430.0447.

3-Bromo-1,6-dimethyl-4-(phenylethynyl)quinolin-2(1H)-one (**3l**): yellow solid (93 mg, 53% yield); mp 193−194 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.72−7.70 (m, 2H), 7.47−7.42 (m, 4H), 7.28 (d, J = 8.6 Hz, 1H), 3.81 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 136.7, 133.0, 132.6, 132.4, 132.1, 129.8, 128.6, 127.4, 122.1, 121.9, 120.0, 114.4, 103.9, 84.6, 31.1, 20.8; HRMS (ESI) calcd for $C_{19}H_{15}BrNO$ $[M + H]^+$ 352.0332, found 352.0328.

3-Bromo-6-chloro-1-methyl-4-(phenylethynyl)quinolin-2(1H)-one (**3m**): pale yellow solid (150 mg, 81% yield); mp 207−208 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 2.4 Hz, 1H), 7.71−7.69 (m, 2H), 7.58−7.56 (m, 1H), 7.49−7.43 (m, 3H), 7.31 (d, J = 9.0 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 137.2, 132.3, 132.2, 131.1, 130.1, 128.7, 128.6, 126.9, 123.3, 121.5, 121.0, 115.9, 104.7, 83.9, 31.3; HRMS (ESI) calcd for $C_{18}H_{12}BrClNO$ $[M + H]^+$ 371.9786, found 371.9775.

3-Bromo-4-(phenylethynyl)-2H-chromen-2-one (**3a′**): white solid (111 mg, 68% yield); mp 134−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98−7.96 (m, 1H), 7.71−7.69 (m, 2H), 7.62−7.58 (m, 1H), 7.52−7.43 (m, 3H), 7.40−7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 152.2, 137.3, 132.4, 132.2, 130.6, 128.8, 126.8, 125.0, 121.1, 118.8, 116.9, 115.3, 107.8, 83.5; HRMS (ESI) calcd for $C_{17}H_{10}BrO_2$ $[M + H]^+$ 324.9859, found 324.9852.

General Procedure for Synthesis of 3*H*-Pyrrolo[2,3-*c*]quinolin-4(5*H*)-ones 4. To a mixture of 4-alkynyl-3-bromoquinolin-2(1*H*)-ones **3** (0.15 mmol), $Pd(OAc)_2$ (1.7 mg, 0.0075 mmol), (*R*)-BINAP (9.4 mg, 0.015 mmol), and K_3PO_4 (95 mg, 0.45 mmol) in a Schlenk flask under argon atmosphere were added an amine (0.18 mmol) and dimethylacetamide (1 mL). The reaction mixture was heated to 130 °C for 8 h. After being quenched with water, the reaction mixture was extracted with ethyl acetate and the organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 4:1 to 2:1) to afford products **4a**−**t**.

5-Methyl-2,3-diphenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4a**): white solid (52 mg, 99% yield); mp 235−236 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−8.00 (m, 1H), 7.50−7.46 (m, 1H), 7.42−7.37 (m, 4H), 7.33−7.29 (m, 3H), 7.23 (s, 5H), 7.01 (s, 1H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 143.1, 138.6, 137.0, 131.6, 129.2, 128.9, 128.2, 128.1, 128.0, 127.8, 127.2, 123.5, 123.1, 122.0, 118.0, 114.9, 102.6, 29.0; HRMS (ESI) calcd for $C_{24}H_{19}N_2O$ $[M + H]^+$ 351.1492, found 351.1508.

5-Methyl-2-phenyl-3-(p-tolyl)-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4b**): white solid (54 mg, 99% yield); mp 228−229 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.8 Hz, 1H), 7.48−7.44 (m, 1H), 7.41−7.39 (m, 1H), 7.31−7.24 (m, 6H), 7.19−7.15 (m, 4H), 6.99 (s, 1H), 3.72 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 143.1, 137.8, 136.9, 136.0, 131.7, 129.2, 128.9, 128.5, 128.1, 127.9, 127.7, 127.1, 123.5, 123.1, 121.9, 118.0, 114.8, 102.4, 28.9, 21.3; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ $[M + H]^+$ 365.1648, found 365.1643.

3-(4-Methoxyphenyl)-5-methyl-2-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4c**): white solid (55 mg, 96% yield); mp 232−233 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.99 (m, 1H), 7.48−7.44 (m, 1H), 7.41−7.39 (m, 1H), 7.32−7.20 (m, 8H), 6.99 (s, 1H), 6.88 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.0, 155.3, 143.2, 136.9, 131.7, 131.5, 129.7, 129.2, 128.2, 127.9, 127.7, 127.2, 123.5, 123.2, 122.0, 118.0, 114.9, 113.5, 102.3, 55.3, 29.0; HRMS (ESI) calcd for $C_{25}H_{21}N_2O_2$ $[M + H]^+$ 381.1598, found 381.1592.

5-Methyl-2-phenyl-3-(o-tolyl)-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4d**): yellow solid (54 mg, 99% yield); mp 49−50 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−8.01 (m, 1H), 7.49−7.45 (m, 1H), 7.42−7.40 (m, 1H), 7.33−7.22 (m, 10H), 7.05 (s, 1H), 3.71 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 142.8, 138.2, 137.0, 136.4, 131.6, 130.3, 129.1, 128.7, 128.6, 128.2, 127.9, 127.2, 126.0, 123.5, 123.0, 122.0, 118.1, 114.9, 102.2, 29.0, 17.6; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ $[M + H]^+$ 365.1648, found 365.1640.

3-(2-Chlorophenyl)-5-methyl-2-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4e**): brown solid (54 mg, 94% yield); mp 76−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.7 Hz, 1H), 7.51−7.47 (m, 2H), 7.43−7.41 (m, 1H), 7.38−7.25 (m, 9H), 7.05 (s, 1H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 143.1, 137.1, 137.0, 133.8, 131.3, 130.6, 129.7, 129.5, 128.9, 128.2, 128.1, 127.4, 126.9, 123.6, 123.2, 122.1, 118.0, 115.0, 102.6, 29.0; HRMS (ESI) calcd for $C_{24}H_{18}ClN_2O$ $[M + H]^+$ 385.1102, found 385.1095.

3-(3-Chlorophenyl)-5-methyl-2-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4f**): white solid (54 mg, 94% yield); mp 225−226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.8 Hz, 1H), 7.50−7.46 (m, 1H), 7.42−7.40 (m, 1H), 7.36−7.22 (m, 10H), 7.00 (s, 1H), 3.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.1, 143.1, 139.7, 137.0, 133.7, 131.2, 129.2, 129.1, 129.0, 128.3, 128.2, 128.1, 128.0, 127.4, 127.3, 123.6, 123.0, 122.1, 117.8, 114.9, 103.0, 29.0; HRMS (ESI) calcd for $C_{24}H_{18}ClN_2O$ $[M + H]^+$ 385.1102, found 385.1108.

3-(4-Fluorophenyl)-5-methyl-2-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4g**): white solid (55 mg, 99% yield); mp 218−219 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−8.00 (m, 1H), 7.51−7.47 (m,

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1H), 7.43−7.41 (m, 1H), 7.34−7.22 (m, 8H), 7.06 (t, J = 8.6 Hz, 2H), 7.01 (s, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0 (d, J = 246.3 Hz), 155.2, 143.2, 136.9, 134.6 (d, J = 3.3 Hz), 131.4, 130.4 (d, J = 8.6 Hz), 129.2, 128.2, 128.1, 128.0, 127.4, 123.5, 123.1, 122.1, 117.9, 115.2 (d, J = 22.8 Hz), 114.9, 102.7, 29.0; HRMS (ESI) calcd for $C_{24}H_{18}FN_2O$ $[M + H]^+$ 369.1398, found 369.1391.

2-(4-Methoxyphenyl)-5-methyl-3-phenyl-3H-pyrrolo[2,3-c]-quinolin-4(5H)-one (**4h**): white solid (51 mg, 89% yield); mp 219−220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.7 Hz, 1H), 7.48−7.45 (m, 1H), 7.41−7.37 (m, 4H), 7.31−7.28 (m, 3H), 7.15 (d, J = 8.8 Hz, 2H), 6.94 (s, 1H), 6.76 (d, J = 8.7 Hz, 2H), 3.76 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 155.2, 143.0, 138.8, 136.9, 130.4, 128.9, 128.2, 128.0, 127.9, 127.2, 124.1, 123.5, 122.8, 121.9, 118.0, 114.9, 113.6, 101.9, 55.2, 29.0; HRMS (ESI) calcd for $C_{25}H_{21}N_2O_2$ $[M + H]^+$ 381.1598, found 381.1580.

5-Methyl-3-phenyl-2-(p-tolyl)-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4i**): white solid (47 mg, 86% yield); mp 242−243 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00−7.98 (m, 1H), 7.48−7.44 (m, 1H), 7.41−7.37 (m, 4H), 7.32−7.28 (m, 3H), 7.13−7.11 (m, 2H), 7.04−7.02 (m, 2H), 6.97 (s, 1H), 3.72 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 143.2, 138.7, 137.7, 136.9, 129.0, 128.9, 128.8, 128.7, 128.2, 128.0, 127.2, 123.5, 122.9, 121.9, 118.0, 114.9, 102.2, 29.0, 21.2; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ $[M + H]^+$ 365.1648, found 365.1663.

2-(4-Chlorophenyl)-5-methyl-3-phenyl-3H-pyrrolo[2,3-c]-quinolin-4(5H)-one (**4j**): pale yellow solid (26 mg, 45% yield); mp 268−269 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00−7.98 (m, 1H), 7.50−7.46 (m, 1H), 7.42−7.37 (m, 4H), 7.33−7.28 (m, 3H), 7.23−7.19 (m, 2H), 7.16−7.14 (m, 2H), 6.99 (s, 1H), 3.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.1, 141.7, 138.4, 137.0, 133.9, 130.3, 130.1, 128.8, 128.4, 128.3, 128.2, 128.0, 127.4, 123.5, 123.3, 122.1, 117.8, 114.9, 102.8, 29.0; HRMS (ESI) calcd for $C_{24}H_{18}ClN_2O$ $[M + H]^+$ 385.1102, found 385.1093.

5-Methyl-3-phenyl-2-(thiophene-2-yl)-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4k**): white solid (52 mg, 97% yield); mp 208−209 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.97 (m, 1H), 7.53−7.44 (m, 4H), 7.41−7.38 (m, 3H), 7.30 (t, J = 7.4 Hz, 1H), 7.19 (d, J = 5.0 Hz, 1H), 7.09 (s, 1H), 6.89 (m, 1H), 6.76−6.75 (m, 1H), 3.70 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.0, 138.6, 137.0, 136.6, 133.2, 129.0, 128.9, 128.7, 127.8, 127.3, 127.2, 126.6, 126.2, 123.6, 123.5, 122.0, 117.8, 114.9, 101.9, 28.9; HRMS (ESI) calcd for $C_{22}H_{17}N_2OS$ $[M + H]^+$ 357.1056, found 357.1064.

2-Butyl-5-methyl-3-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4l**): white solid (26 mg, 53% yield); mp 122−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96−7.94 (m, 1H), 7.53−7.48 (m, 3H), 7.46−7.42 (m, 1H), 7.39−7.37 (m, 1H), 7.34−7.32 (m, 2H), 7.30−7.28 (m, 1H), 6.67 (s, 1H), 3.69 (s, 3H), 2.51 (t, J = 7.7 Hz, 2H), 1.63−1.55 (m, 2H), 1.36−1.27 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.0, 144.5, 138.6, 136.9, 128.6, 128.3, 128.2, 127.7, 126.9, 123.4, 122.1, 121.8, 118.2, 114.8, 99.8, 30.8, 28.8, 26.4, 22.3, 13.8; HRMS (ESI) calcd for $C_{22}H_{23}N_2O$ $[M + H]^+$ 331.1805, found 331.1794.

2-tert-Butyl-5-methyl-3-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4m**): brown solid (47 mg, 95% yield); mp 142−143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98−7.95 (m, 1H), 7.53−7.41 (m, 6H), 7.37−7.35 (m, 1H), 7.30−7.26 (m, 1H), 6.75 (s, 1H), 3.65 (s, 3H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 152.2, 140.6, 136.9, 129.8, 128.7, 128.0, 126.8, 126.6, 123.6, 123.2, 121.7, 118.1, 114.7, 99.3, 33.6, 31.1, 28.8; HRMS (ESI) calcd for $C_{22}H_{23}N_2O$ $[M + H]^+$ 331.1805, found 331.1798.

2-Cyclopropyl-5-methyl-3-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4n**): brown solid (26 mg, 55% yield); mp 132−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.8 Hz, 1H), 7.53−7.41 (m, 6H), 7.38−7.36 (m, 1H), 7.28−7.24 (m, 1H), 6.41 (s, 1H), 3.69 (s, 3H), 1.62−1.55 (m, 1H), 0.89−0.84 (m, 2H), 0.82−0.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 146.5, 138.7, 136.9, 128.5, 128.3, 128.1, 127.7, 126.9, 123.3, 122.2, 121.8, 118.1, 114.8, 96.6, 28.8, 8.5, 8.1; HRMS (ESI) calcd for $C_{21}H_{19}N_2O$ $[M + H]^+$ 315.1492, found 315.1484.

5-Ethyl-2,3-diphenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4o**): white solid (54 mg, 99% yield); mp 204−205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.8 Hz, 1H), 7.49−7.42 (m, 2H), 7.38−7.36 (m, 3H), 7.32−7.27 (m, 3H), 7.23 (s, 5H), 7.00 (s, 1H), 4.39 (q, J = 7.0 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 143.1, 138.6, 135.8, 131.7, 129.2, 128.9, 128.2, 128.1, 128.0, 127.8, 127.2, 123.7, 123.0, 121.7, 118.2, 114.8, 102.5, 36.6, 13.2; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ $[M + H]^+$ 365.1648, found 365.1646.

2-(4-Methoxyphenyl)-3,5-diphenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4p**): yellow solid (42 mg, 63% yield); mp 243−244 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.5 Hz, 1H), 7.53−7.50 (m, 2H), 7.44−7.41 (m, 1H), 7.29−7.15 (m, 11H), 7.01 (s, 1H), 6.77 (d, J = 7.4 Hz, 2H), 6.64 (d, J = 8.1 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.3, 155.2, 143.5, 138.5, 138.4, 138.3, 130.4, 129.9, 129.6, 128.9, 128.7, 128.3, 128.2, 127.8, 126.7, 124.1, 123.1, 122.6, 122.0, 117.6, 116.7, 113.7, 102.2, 55.2; HRMS (ESI) calcd for $C_{30}H_{23}N_2O_2$ $[M + H]^+$ 443.1754, found 443.1774.

5,8-Dimethyl-2,3-diphenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4q**): pale yellow solid (48 mg, 88% yield); mp 259−260 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.38−7.36 (m, 3H), 7.31−7.26 (m, 4H), 7.23 (s,5H), 7.00 (s, 1H), 3.70 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.1, 143.0, 138.7, 134.9, 131.7, 131.4, 129.2, 128.9, 128.4, 128.2, 128.1, 128.0, 127.9, 127.7, 123.5, 123.2, 117.8, 114.8, 102.5, 29.0, 20.8; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ $[M + H]^+$ 365.1648, found 365.1665.

3-Benzyl-5-methyl-2-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4r**): white solid (46 mg, 84% yield); mp 179−180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.93 (m, 1H), 7.46−7.39 (m, 7H), 7.29−7.26 (m, 1H), 7.21−7.12 (m, 3H), 6.89 (d, J = 6.9 Hz, 2H), 6.84 (s, 1H), 5.91 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 143.7, 139.5, 136.9, 131.8, 129.6, 128.6, 128.5, 128.4, 127.9, 127.0, 126.8, 126.0, 123.4, 122.0, 118.2, 114.8, 102.4, 49.0, 29.1; HRMS (ESI) calcd for $C_{25}H_{21}N_2O$ $[M + H]^+$ 365.1648, found 365.1644.

3-(4-Fluorobenzyl)-5-methyl-2-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4s**): white solid (52 mg, 91% yield); mp 193−194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96−7.93 (m, 1H), 7.48−7.37 (m, 7H), 7.31−7.27 (m, 1H), 6.88−6.84 (m, 5H), 5.88 (s, 2H), 3.78 (s,3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8 (d, J = 243.3 Hz), 155.9, 143.6, 136.9, 135.1 (d, J = 2.9 Hz), 131.8, 129.6, 128.7, 128.6, 128.1, 127.9 (d, J = 8.0 Hz), 127.1, 123.4, 122.1, 121.8, 118.1, 115.3 (d, J = 21.4 Hz), 114.9, 102.6, 48.2, 29.1; HRMS (ESI) calcd for $C_{25}H_{20}FN_2O$ $[M + H]^+$ 383.1554, found 383.1539.

3-Cyclohexyl-5-methyl-2-phenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4t**): white solid (36 mg, 68% yield); mp 84−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.8 Hz, 1H), 7.50−7.39 (m, 7H), 7.25−7.23 (m, 1H), 6.73 (s, 1H), 3.84 (s, 3H), 2.66 (s, 1H), 1.81 (s, 4H), 1.61 (s, 2H), 1.36−1.23 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 143.9, 136.9, 133.6, 129.8, 128.5, 128.4, 126.9, 123.2, 121.9, 121.8, 118.0, 114.6, 102.3, 58.6, 32.3, 29.6, 26.3, 24.9; HRMS (ESI) calcd for $C_{24}H_{24}N_2NaO$ $[M + Na]^+$ 379.1781, found 379.1792.

Synthesis of 1-Bromo-5-methyl-2,3-diphenyl-3*H*-pyrrolo-[2,3-*c*]quinolin-4(5*H*)-one (4aa). A mixture of 5-methyl-2,3-diphenyl-3*H*-pyrrolo[2,3-*c*]quinolin-4(5*H*)-one (**4a**) (0.3 mmol) and NBS (0.6 mmol) was stirred in THF (8 mL) and water (2 mL) at room temperature until the starting material disappeared. The reaction mixture was poured into water and extracted with ethyl acetate. The combined extract was washed with brine and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was chromatographed by silica gel (petroleum ether/ethyl acetate, 4:1) to afford the desired product **4aa**.

1-Bromo-5-methyl-2,3-diphenyl-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4aa**): white solid (126 mg, 98% yield); mp 234−235 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06−9.04 (m, 1H), 7.51−7.47 (m, 1H), 7.40 (d, J = 8.3 Hz, 1H), 7.35−7.18 (m, 11H), 3.69 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.4, 141.0, 138.2, 137.0, 131.1, 129.5, 128.6, 128.5, 128.1, 128.0, 127.9, 127.5, 123.6, 123.3, 122.1, 121.8,

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117.7, 114.8, 92.3, 29.2; HRMS (ESI) calcd for $C_{24}H_{18}BrN_2O$ [M + H]$^+$ 429.0597, found 429.0611.

Synthesis of 5-Methyl-2,3-diphenyl-1-(*p*-tolyl)-3*H*-pyrrolo-[2,3-*c*]quinolin-4(5*H*)-one (4ab). Under an argon atmosphere, to a mixture of **4aa** (86 mg, 0.2 mmol), $Pd(PPh_3)_4$ (23 mg, 0.02 mmol), *p*-tolylboronic acid (54 mg, 0.4 mmol), and K_2CO_3 (83 mg, 0.6 mmol) was added DMF (8 mL). The resulting mixture was heated to 100 °C for 2 h. The reaction mixture was cooled to room temperature and diluted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the desired product **4ab**.

*5-Methyl-2,3-diphenyl-1-(p-tolyl)-3H-pyrrolo[2,3-c]quinolin-4(5H)-one (**4ab**):* white solid (87 mg, 99% yield); mp 247−248 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 7.9 Hz, 1H), 7.40−7.24 (m, 9H), 7.15 (d, J = 7.8 Hz, 2H), 7.09−6.96 (m, 6H), 3.73 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 140.7, 138.7, 137.1, 136.7, 132.1, 131.1, 131.0, 130.6, 129.2, 128.9, 128.0, 127.7, 127.5, 127.4, 126.7, 124.9, 124.2, 121.9, 121.5, 119.3, 118.7, 114.8, 29.1, 21.3; HRMS (ESI) calcd for $C_{31}H_{25}N_2O$ [M + H]$^+$ 441.1961, found 441.1959.

General Procedure for Synthesis of Chromeno[3,4-*b*]pyrrol-4(3*H*)-ones 8. To a mixture of 3-bromo-4-(phenylethynyl)-2*H*-chromen-2-one (**3a′**) (49 mg, 0.15 mmol), $Pd(OAc)_2$ (1.7 mg, 0.0075 mmol), (*R*)-BINAP (9.4 mg, 0.015 mmol), and K_3PO_4 (95 mg, 0.45 mmol) in a Schlenk flask under argon atmosphere were added an amine (0.18 mmol) and dimethylacetamide (1 mL). The reaction mixture was heated to 130 °C for 8 h. After being quenched with water, the reaction mixture was extracted with ethyl acetate and the organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 4:1 to 3:1) to afford products **8a−c**.

*2,3-Diphenylchromeno[3,4-b]pyrrol-4(3H)-one (**8a**):* brown solid (17 mg, 34% yield); mp 215−216 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.7 Hz, 1H), 7.41−7.20 (m, 13H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 151.5, 145.2, 137.3, 130.9, 130.6, 129.1, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 124.0, 123.0, 118.0, 117.5, 117.1, 103.3; HRMS (ESI) calcd for $C_{23}H_{16}NO_2$ [M + H]$^+$ 338.1176, found 338.1171.

*3-(4-Methoxyphenyl)-2-phenylchromeno[3,4-b]pyrrol-4(3H)-one (**8b**):* white solid (29 mg, 53% yield); mp 182−183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.5 Hz, 1H), 7.42−7.37 (m, 2H), 7.34−7.17 (m, 8H), 6.91−6.88 (m, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 154.0, 151.4, 145.3, 131.0, 130.4, 130.1, 129.4, 129.1, 128.3, 128.0, 124.0, 123.0, 118.1, 117.6, 117.1, 113.8, 103.1, 55.4; HRMS (ESI) calcd for $C_{24}H_{18}NO_3$[M + H]$^+$ 368.1281, found 368.1298.

*3-(4-Fluorophenyl)-2-phenylchromeno[3,4-b]pyrrol-4(3H)-one (**8c**):* pale yellow solid (19 mg, 36% yield); mp 227−228 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.7 Hz, 1H), 7.41 (d, J = 3.7 Hz, 2H), 7.36−7.20 (m, 8H), 7.07 (t, J = 8.5 Hz, 2H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 (d, J = 247.3 Hz), 154.0, 151.4, 145.3, 133.3, 130.7 (d, J = 3.7 Hz), 130.2 (d, J = 8.7 Hz), 129.1, 128.6, 128.4, 128.3, 124.1, 123.0, 118.0, 117.4, 117.1, 115.6 (d, J = 22.9 Hz), 103.4; HRMS (ESI) calcd for $C_{23}H_{15}FNO_2$[M + H]$^+$ 356.1081, found 356.1072.

General Procedure for Synthesis of Thieno[2,3-*c*]quinolin-4(5*H*)-one 5. To a suspension of sodium sulfide nonahydrate (72 mg, 0.3 mmol) in NMP (1 mL) was added 4-alkynyl-3-bromoquinolin-2(1*H*)-one **3** (0.15 mmol), and then the mixture was heated at 80 °C for 6 h. After being poured into saturated aqueous ammonium chloride solution, the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. After evaporation of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 3:1 to 2:1) to give thieno[2,3-*c*]quinolin-4(5*H*)-one **5a−m**.

*5-Methyl-2-phenylthieno[2,3-c]quinolin-4(5H)-one (**5a**):* yellow solid (37 mg, 85% yield); mp 218−219 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.8 Hz, 1H), 7.84 (s, 1H), 7.73 (d, J = 7.5 Hz, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.47−7.37 (m, 4H), 7.31 (t, J = 7.5 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 151.7, 142.6, 138.7, 133.4, 129.6, 129.1, 129.0, 126.5, 124.3, 122.4, 118.4, 117.5, 115.2, 29.5; HRMS (ESI) calcd for $C_{18}H_{14}NOS$ [M + H]$^+$ 292.0791, found 292.0793.

*2-(4-Methoxyphenyl)-5-methylthieno[2,3-c]quinolin-4(5H)-one (**5b**):* pale yellow solid (48 mg, 99% yield); mp 193−194 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00−7.98 (m, 1H), 7.75 (s, 1H), 7.69−7.66 (m, 2H), 7.57−7.53 (m, 1H), 7.44 (d, J = 8.2 Hz, 1H), 7.34−7.31 (m, 1H), 6.99−6.96 (m, 2H), 3.87 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 157.9, 151.6, 142.7, 138.6, 128.9, 128.6, 127.7, 126.0, 124.3, 122.2, 118.3, 116.2, 115.1, 114.4, 55.3, 29.4; HRMS (ESI) calcd for $C_{19}H_{16}NO_2S$ [M + H]$^+$ 322.0896, found 322.0905.

*5-Methyl-2-(p-tolyl)thieno[2,3-c]quinolin-4(5H)-one (**5c**):* pale yellow solid (36 mg, 79% yield); mp 224−225 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00−7.98 (m, 1H), 7.81 (s, 1H), 7.63 (d, J = 8.1 Hz, 2H), 7.56−7.52 (m, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.33−7.30 (m, 1H), 7.25 (d, J = 7.9 Hz, 2H), 3.81 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 151.9, 142.6, 139.3, 138.7, 130.6, 129.8, 129.1, 129.0, 126.4, 124.3, 122.3, 118.4, 116.9, 115.1, 29.5, 21.3; HRMS (ESI) calcd for $C_{19}H_{16}NOS$ [M + H]$^+$ 306.0947, found 306.0962.

*2-(4-Chlorophenyl)-5-methylthieno[2,3-c]quinolin-4(5H)-one (**5d**):* white solid (46 mg, 94% yield); mp 244−245 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01−7.99 (m, 1H), 7.84 (s, 1H), 7.68−7.65 (m, 2H), 7.59−7.56 (m, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.43−7.41 (m, 2H), 7.36−7.33 (m, 1H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 150.2, 142.6, 138.7, 135.1, 131.9, 129.3, 127.7, 124.3, 122.4, 118.3, 117.9, 115.3, 29.5; HRMS (ESI) calcd for $C_{18}H_{13}ClNOS$ [M + H]$^+$ 326.0401, found 326.0409.

*5-Methyl-2-(thiophene-2-yl)thieno[2,3-c]quinolin-4(5H)-one (**5e**):* pale yellow solid (37 mg, 83% yield); mp 221−222 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98−7.96 (m, 1H), 7.71 (s, 1H), 7.57−7.54 (m, 1H), 7.44 (d, J = 8.5 Hz, 1H), 7.39 (d, J = 3.6 Hz, 1H), 7.37 (d, J = 5.1 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.10−7.09 (m, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 144.6, 142.5, 138.7, 136.3, 129.2, 128.9, 128.2, 126.5, 126.0, 124.4, 122.3, 118.1, 117.7, 115.2, 29.5; HRMS (ESI) calcd for $C_{16}H_{12}NOS_2$ [M + H]$^+$ 298.0355, found 298.0358.

*2-Butyl-5-methylthieno[2,3-c]quinolin-4(5H)-one (**5f**):* yellow solid (24 mg, 59% yield); mp 51−52 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93−7.91 (m, 1H), 7.54−7.50 (m, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.39 (s, 1H), 7.30−7.27 (m, 1H), 3.80 (s, 3H), 2.96 (t, J = 7.6 Hz, 2H), 1.80−1.74 (m, 2H), 1.48−1.41 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 154.7, 142.1, 138.6, 128.8, 128.7, 124.3, 122.1, 119.1, 118.4, 115.1, 33.4, 30.6, 29.4, 22.1, 13.7; HRMS (ESI) calcd for $C_{16}H_{18}NOS$ [M + H]$^+$ 272.1104, found 272.1108.

*2-tert-Butyl-5-methylthieno[2,3-c]quinolin-4(5H)-one (**5g**):* pale yellow solid (35 mg, 86% yield); mp 121−122 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97−7.95 (m, 1H), 7.54−7.51 (m, 1H), 7.45−7.43 (m, 2H), 7.32−7.28 (m, 1H), 3.81 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 158.1, 141.8, 138.6, 128.7, 128.2, 124.2, 122.1, 118.5, 116.4, 115.0, 35.3, 32.2, 29.4; HRMS (ESI) calcd for $C_{16}H_{18}NOS$ [M + H]$^+$ 272.1104, found 272.1117.

*2-Cyclopropyl-5-methylthieno[2,3-c]quinolin-4(5H)-one (**5h**):* pale yellow solid (38 mg, 99% yield); mp 105−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, J = 7.8, 1.2 Hz, 1H), 7.54−7.50 (m, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.35 (s, 1H), 7.30−7.26 (m, 1H), 3.79 (s, 3H), 2.27−2.21 (m, 1H), 1.20−1.15 (m, 2H), 0.94−0.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 157.7, 142.1, 138.6, 128.8, 127.4, 124.3, 122.1, 118.2, 117.2, 115.0, 29.4, 12.3, 11.2; HRMS (ESI) calcd for $C_{15}H_{14}NOS$ [M + H]$^+$ 256.0791, found 256.0795.

*5-Methylthieno[2,3-c]quinolin-4(5H)-one (**5i**):* pale yellow solid (12 mg, 36% yield); mp 128−129 °C; ^{1}H NMR (500 MHz, $CDCl_3$)

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δ 8.00−7.98 (m, 1H), 7.78 (d, J = 5.2 Hz, 1H), 7.72 (d, J = 5.3 Hz, 1H), 7.57−7.54 (m, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.34−7.31 (m, 1H), 3.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 141.9, 138.6, 133.2, 130.7, 129.0, 124.4, 122.4, 122.2, 118.5, 115.2, 29.5; HRMS (ESI) calcd for $C_{12}H_{10}NOS$ $[M + H]^+$ 216.0478, found 216.0485.

*5-Ethyl-2-phenylthieno[2,3-c]quinolin-4(5H)-one (**5j**):* pale yellow solid (45 mg, 98% yield); mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.8 Hz, 1H), 7.88 (s, 1H), 7.76 (d, J = 7.3 Hz, 2H), 7.56 (t, J = 7.8 Hz, 1H), 7.50−7.45 (m, 3H), 7.42−7.38 (m, 1H), 7.32 (t, J = 7.4 Hz, 1H), 4.49 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 151.6, 142.6, 137.6, 133.4, 129.6, 129.1, 129.0, 126.5, 124.6, 122.1, 118.6, 117.5, 115.1, 37.3, 13.0; HRMS (ESI) calcd for $C_{19}H_{16}NOS$ $[M + H]^+$ 306.0947, found 306.0951.

*2-(4-Methoxyphenyl)-5-phenylthieno[2,3-c]quinolin-4(5H)-one (**5k**):* yellow solid (47 mg, 82% yield); mp 245−246 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04−8.02 (m, 1H), 7.84 (s, 1H), 7.72 (d, J = 8.7 Hz, 2H), 7.61 (t, J = 7.5 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.36−7.25 (m, 4H), 6.99 (d, J = 8.7 Hz, 2H), 6.76−6.74 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 157.9, 152.4, 143.5, 140.1, 137.8, 130.1, 129.2, 128.9, 128.6, 127.9, 126.1, 124.0, 122.5, 118.1, 117.1, 116.5, 114.5, 55.4; HRMS (ESI) calcd for $C_{24}H_{18}NO_2S$ $[M + H]^+$ 384.1053, found 384.1063.

*5,8-Dimethyl-2-phenylthieno[2,3-c]quinolin-4(5H)-one (**5l**):* white solid (43 mg, 94% yield); mp 179−180 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.80 (s, 1H), 7.76 (d, J = 7.3 Hz, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.42−7.33 (m, 3H), 3.80 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 151.4, 142.4, 136.6, 133.4, 131.9, 130.1, 129.6, 129.1, 129.0, 126.4, 124.2, 118.2, 117.4, 115.0, 29.4, 20.8; HRMS (ESI) calcd for $C_{19}H_{16}NOS$ $[M + H]^+$ 306.0947, found 306.0956.

*8-Chloro-5-methyl-2-phenylthieno[2,3-c]quinolin-4(5H)-one (**5m**):* white solid (48 mg, 99% yield); mp 210−211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 2.3 Hz, 1H), 7.74−7.71 (m, 3H), 7.47−7.38 (m, 4H), 7.32 (d, J = 9.0 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 152.1, 141.3, 137.1, 133.0, 130.2, 129.3, 129.2, 128.9, 127.9, 126.5, 123.7, 119.3, 117.2, 116.6, 29.7; HRMS (ESI) calcd for $C_{18}H_{13}ClNOS$ $[M + H]^+$ 326.0401, found 326.0412.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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