JOC The Journal of Organic Chemistry
Article
Cite This: J. Org. Chem. XXXX, XXX, XXX−XXX
pubs.acs.org/joc

Gold-Catalyzed Selective 6-*exo-dig* and 7-*endo-dig* Cyclizations of Alkyn-Tethered Indoles To Prepare Rutaecarpine Derivatives

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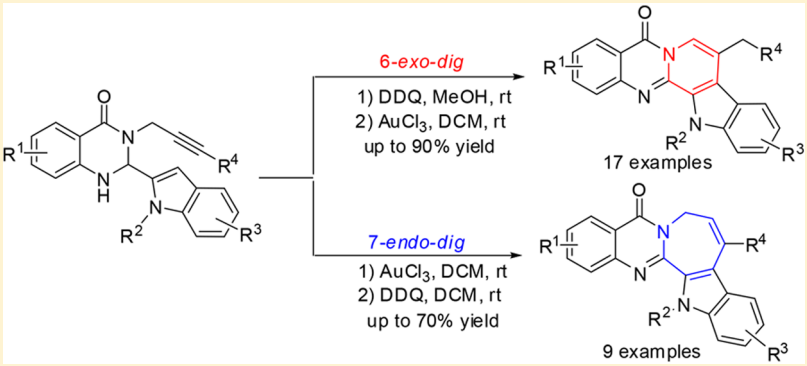
Supporting Information



ABSTRACT: An efficient method to synthesize rutaecarpine derivatives via the gold-catalyzed selective cyclization of alkyn-tethered indoles under mild conditions is described. The alkyn-tethered indole can undergo 6-*exo-dig* cyclization by oxidation and sequential gold catalysis, while it goes through 7-*endo-dig* cyclization by gold catalysis and sequential oxidation. Substrate scope studies reveal that the selectivity of cyclization was controlled by the substrates with sp^3 and sp^2 hybridization of carbon at the 2 position in quinazolinone. Furthermore, the rutaecarpine scaffold was prepared in 67% yield at gram scale easily in four steps from isatoic anhydride.

INTRODUCTION

Rutaecarpine and its derivatives are one important family of quinazolinone alkaloids (Figure 1)[1] and exhibit a wide range of interesting biological activities, such as vasorelaxing, cytotoxity, antiobesity, antiplatelet aggregation, and cyclooxygenase-2 inhibitory activity.[2]

From the structure of rutaecarpine and its derivatives, it shows that the core scaffolds are constituted of A, B, C, D, and E rings. A variety of synthetic endeavors have been devoted to synthesize these natural or unnatural products.[3,4] Among them, the construction of a C ring is important for the synthesis of rutaecarpine because it connects two important pharmacophores of quinazolinone and indole. Many synthetic routes to the construction of a C ring have been developed to prepare rutaecarpine in the past decade. In 2007, Bowman and Weaver group reported a radical cyclization of 2-bromoindole precursor to afford rutaecarpine in 15% yield (Scheme 1A).[5] In 2015, Bannister and co-worker developed a general strategy of sequential Sonagashira reaction and Larock indole synthesis reaction to provide 2-quinazoline-substituted indole precursor, which then underwent intramolecular substitution to give rutaecarpine in 81% yield in 7 days (Scheme 1B).[6] In 2015, an efficient cascade strategy to construct rutacarpine derivatives

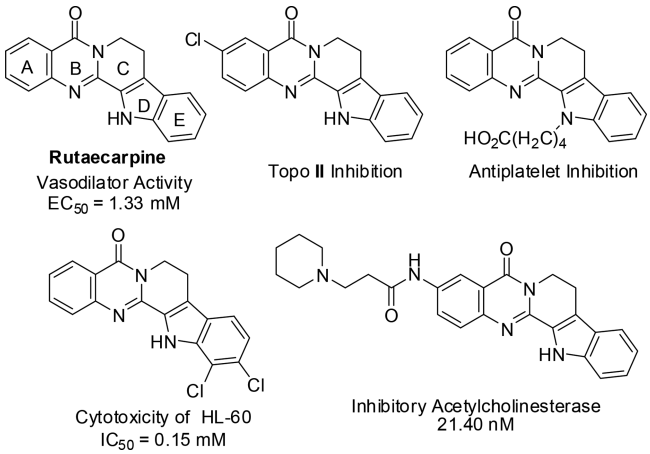


Figure 1. Rutaecarpine and its derivatives.

was developed by the Pan and Liu group, which featured an elegant construction of the characteristic B/C rings in a one-pot

Received: November 21, 2017

DOI: 10.1021/acs.joc.7b02956
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 1. Strategies for the Construction of the C Ring of Rutaecarpine

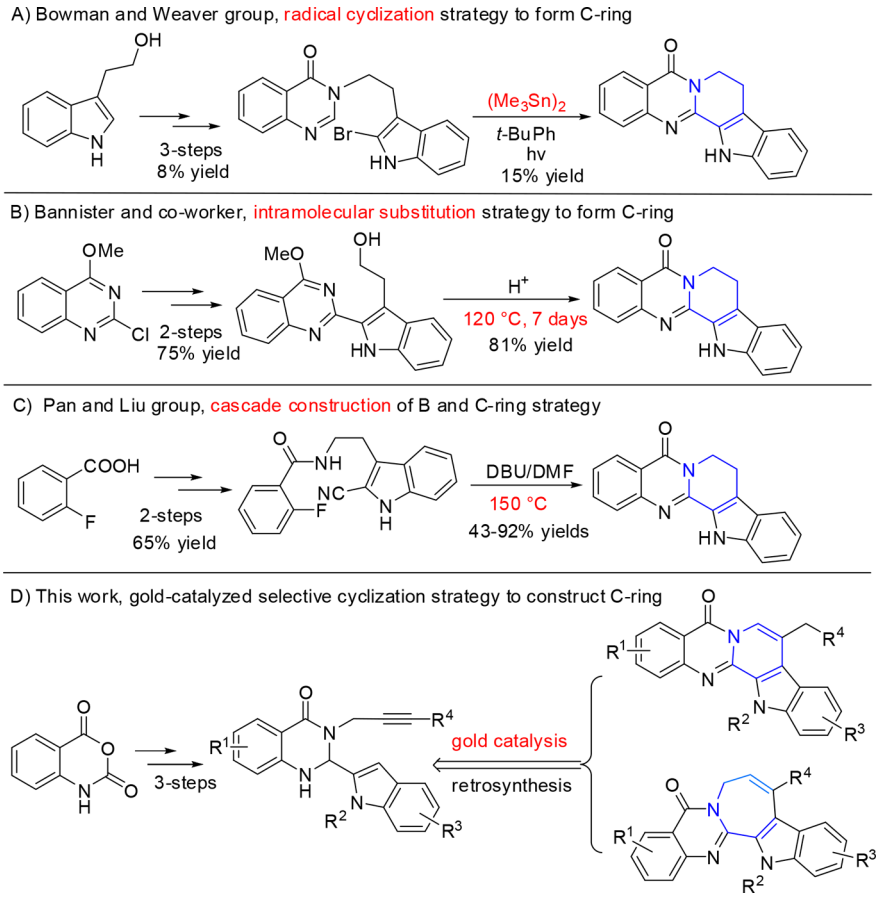
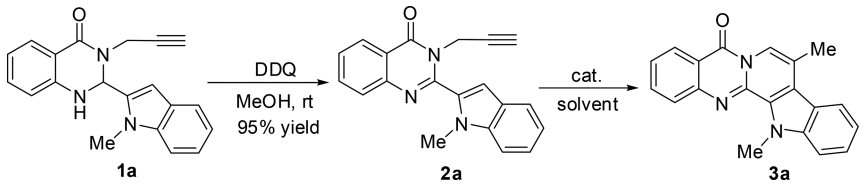


Table 1. Optimization of 6-*exo*-*dig* Cylization Conditions[a]



entry	cat.	amount (% mol)	solvent	**3a** (%)[b]
1	$AuCl_3$	5	MeOH	38
2	$AuCl_3$	5	DMSO	55
3	$AuCl_3$	5	THF	38
4	$AuCl_3$	5	MeCN	85
5	$AuCl_3$	5	toluene	89
6	$AuCl_3$	5	DCM	90
7	AuCl	5	DCM	85
8	$AuPPh_3Cl$	5	DCM	10
9	$AuPPh_3Cl/AgOTf$	5	DCM	70
10	$Pd(OAc)_2$	5	DCM	22
11	CuI	5	DCM	0
12	$AgNO_3$	5	DCM	0
13	$AuCl_3$	1	DCM	87
14	$AuCl_3$	0.1	DCM	44

[a]Reaction conditions: **2a** (0.2 mmol), solvent (2 mL), 25 °C, 0.5 h. [b]Isolated yield.

reaction (Scheme 1C).[7] Although most of these methods were accomplished to access rutaecarpines, they suffered from some drawbacks, such as using toxic tin reagents, long reaction time, high temperature, lack of gram-scale preparation, and use of unavailable starting materials, which limited the further modification and application of rutaecarpines. Therefore, a green, efficient, and simple strategy to prepare rutaecarpine derivatives from readily available materials is desirable.

DOI: 10.1021/acs.joc.7b02956
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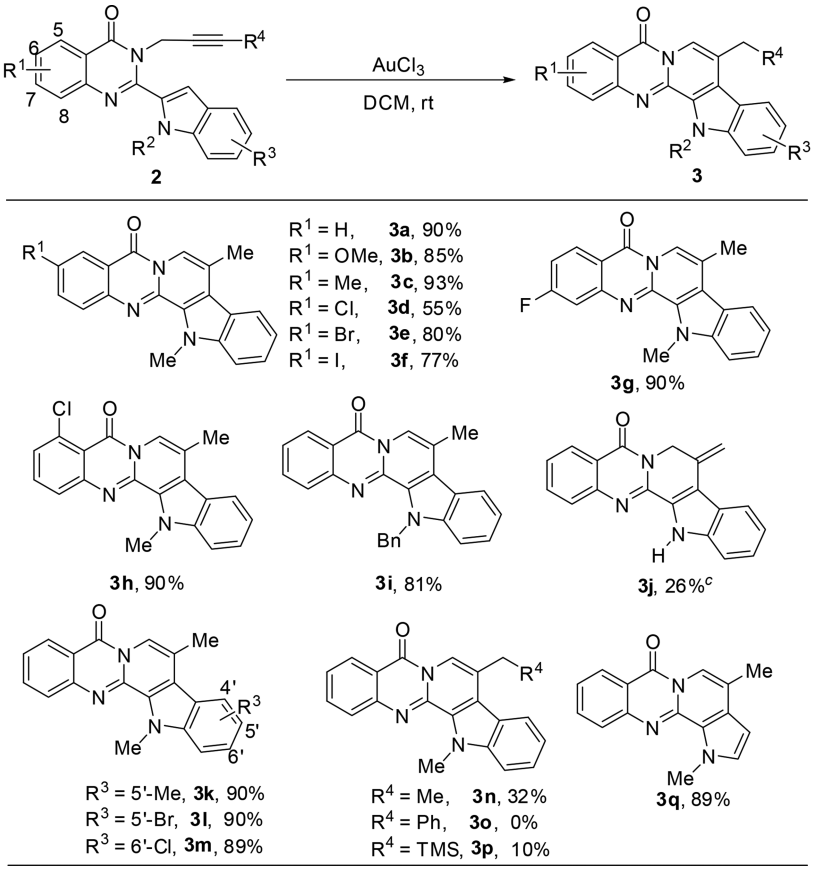
Table 2. Scope of Forming 6-*exo-dig* Product 3[a,b,c]



[a]Reaction conditions: **2** (0.2 mmol), $AuCl_3$ (0.01 mmol, 5 mol %), DCM (2 mL), 25 °C, 0.5 h. [b]Isolated yield. [c]Thirty-three percent of **2j** was recovered.

Transition-metal-catalyzed cyclization has served as an efficient strategy to construct cyclic compounds in recent years, especially using gold catalysts.[8] Various gold catalysts have been considered to activate C−C triple bonds and undergo cyclization reactions smoothly with diverse nucleophiles under mild reaction conditions, such as the O atom,[9] N atom,[10] or C atom[11] served as a nucleophile. Gold-catalyzed 6-*exo-dig*, 6-*endo-dig*, or 7-*endo-dig* cyclization of indole substrates has been reported previously,[12] but few reports have showed that 6-*exo-dig* and 7-*endo-dig* cyclizations could be selectively achieved in one reaction. Our current research efforts are focusing on the synthesis of quinazolinone and the studies of its bioactivity.[13] It was envisioned that selective cyclization of alkyn-tethered indoles would be a direct strategy to access rutaecarpine derivatives through retro-synthetic analysis (Scheme 1D). Herein, we reported gold-catalyzed selective 6-*exo-dig* and 7-*endo-dig* cyclizations of alkyn-tethered indoles to afford two types of rutaecarpine derivatives from readily available materials.

RESULTS AND DISCUSSION

Initially, to probe the possible cyclization strategy alkyn-tethered indole **2a** was prepared in 95% yield by oxidation of **1a** in methanol with DDQ. When **2a** was treated with 5 mol % of $AuCl_3$ in MeOH at room temperature, the desired 6-*exo-dig* cyclization product **3a** was afforded in 38% yield. However, 7-*endo-dig* cyclization product was not observed under this condition (Table 1, entry 1). Solvent screening showed that DCM was the best solvent, providing product **3a** in 90% yield compared to MeOH, DMSO, THF, MeCN, and toluene (Table 1, entries 1−6). Other Au (I) catalysts were also tested. AuCl could give product **3a** in 85% yield, while $AuPPh_3Cl$ afforded product **3a** in only 10% yield (Table 1, entries 7 and 8). Adding AgOTf to $AuPPh_3Cl$ improved the yield of **3a** to 70% (Table 1, entry 9). Using $Pd(OAc)_2$ as catalyst resulted in product **3a** in 22% yield (Table 1, entry 10). Product **3a** was not observed when CuI or $AgNO_3$ was used as catalyst (Table 1, entries 11 and 12). Product **3a** was also obtained in 87% yield though reducing the amount of $AuCl_3$ to 1 mol % (Table 1, entry 13). However, further lowering the amount of $AuCl_3$ to 0.1 mol %, the yield of **3a** was sharply dropped to 44% (Table 1, entry 14). Addition of DDQ with $AuCl_3$ in a one-pot reaction from substrate **1a** gave a lower yield of **3a** accompanied by other complex mixtures. Therefore, the optimal conditions for preparing 6-*exo-dig* cyclization product **3a** were initially oxidation of **1a** by DDQ in methanol and sequential 5 mol % of $AuCl_3$ in DCM at room temperature (Table 1, entry 6).

Next, we set out to explore the generality of this catalytic system for 6-*exo-dig* cyclization. The scope with respect to various alkyn-tethered indole **2** was examined (Table 2). A variety of substituents (R^1, R^2, R^3, R^4) in compound **2** were well tolerated and delivered to product **3** in uniformly high efficiency. The R^1 group at the 5, 6, or 7 position of the aryl ring in quinazolinone bearing electron-donating groups or electron-withdrawing groups furnished product **3** from moderate to excellent yields (**3a**−**h**). Product **3i** could be

DOI: 10.1021/acs.joc.7b02956
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 2. Observation of Forming 7-*endo-dig* Product 5a

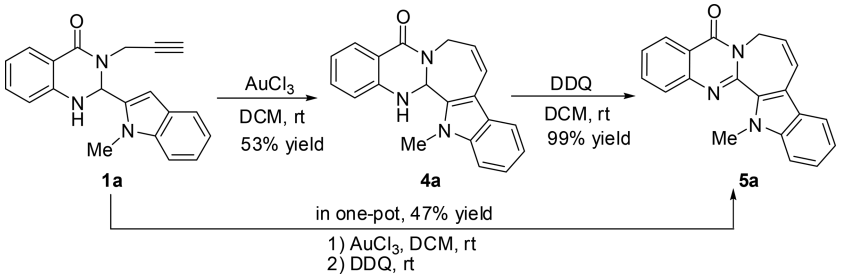
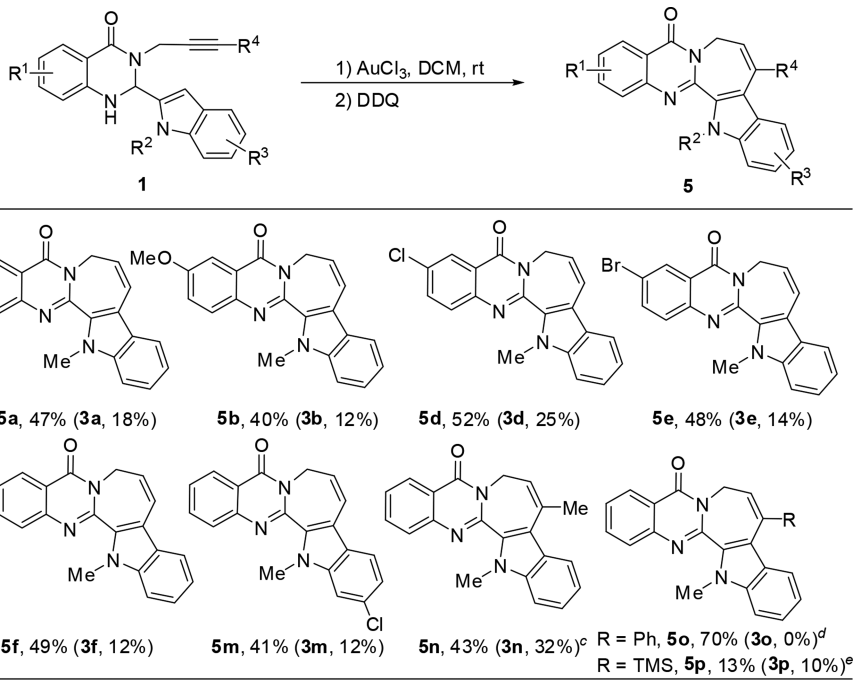


Table 3. Scope of Forming 7-*endo-dig* Product 5[a,b,c,d,e]



[a]Reaction conditions: **1** (0.3 mmol), $AuCl_3$ (5 mol %), DCM (3 mL), 25 °C, 1.5−3 h. [b]Isolated yield. [c]$AuCl_3$ (15 mol %). [d]$AuCl_3$ (15 mol %), ran with **2o**. [e]Ran with **2p**.

afforded in 81% yield when an *N*-protecting group (R^2) was presented with a Bn group, which will facilitate more applications by a deprotection procedure. However, substrate **2j** with an N−H group only provided product **3j** without isomerization in 26% yield, and substrate **2j** was recovered in 33% yield. When the R^3 group in the indole moiety was a methyl, bromo, or chloro group, the corresponding products were afforded in excellent yields (**3k−m**). The structure of compound **3** was confirmed by X-ray diffraction analysis of product **3k**.[14] The alkynyl moiety was also evaluated. When R^4 was a methyl or TMS substituent, desired product **3n** or **3p** was obtained in 32% and 10% yield, respectively. A lower yield of product **3p** was obtained because product **3a** was also observed by deprotection of the TMS group. However, product **3o** was not observed when the R^4 group is a phenyl group. When the indole moiety was replaced by an *N*-methyl pyrrole, the desired product **3q** was obtained in 89% yield.

Although the 7-*endo-dig* cyclization product was not observed during optimization for substrate **2a**, when compound **1a** was treated with $AuCl_3$ in DCM at room temperature, a 7-*endo-dig* cyclization product **4a** was obtained in 53% yield as a major isomer accompanied by 6-*exo-dig* cyclization product **3a** in 18% yield as a minor isomer (Scheme 2). Due to the stability and purification of compound **4a**, compound **4a** was finally oxidized with DDQ, and product **5a**, which was purified easily by flash chromatography, was obtained in 99% yield. Treatment of substrate **1a** with $AuCl_3$ until the reaction was completed and then adding DQQ directly in one flask provided product **5a** in 47% yield.

After a variety of conditions were tested, we investigated the scope for the formation of 7-*endo-dig* product **5**. As shown in Table 3, various alkyn-tethered indole **1** could convert to 7-*endo-dig* product **5** in moderate yields accompanied by minor 6-*exo-dig* product **3** by gold catalysis and sequential oxidation with DDQ in a one-pot reaction. When the R^4 group was presented with a phenyl group, the desired product **5o** was obtained in 70% yield and 6-*exo-dig* cyclization product **3o** was not observed. The reversed selectivity for **5o** might be caused by the conjugated effect of the phenyl group to the alkynyl group. Although there were two products **3** and **5** obtained under these conditions, the two products could be separated easily by flash column chromatography. This also provided a new entry to access the 7-*endo-dig* cyclization products for further studies in pharmaceuticals.

During identification of the structure for compound **5**, we found that the protons of the methylene group adjacent to

DOI: 10.1021/acs.joc.7b02956
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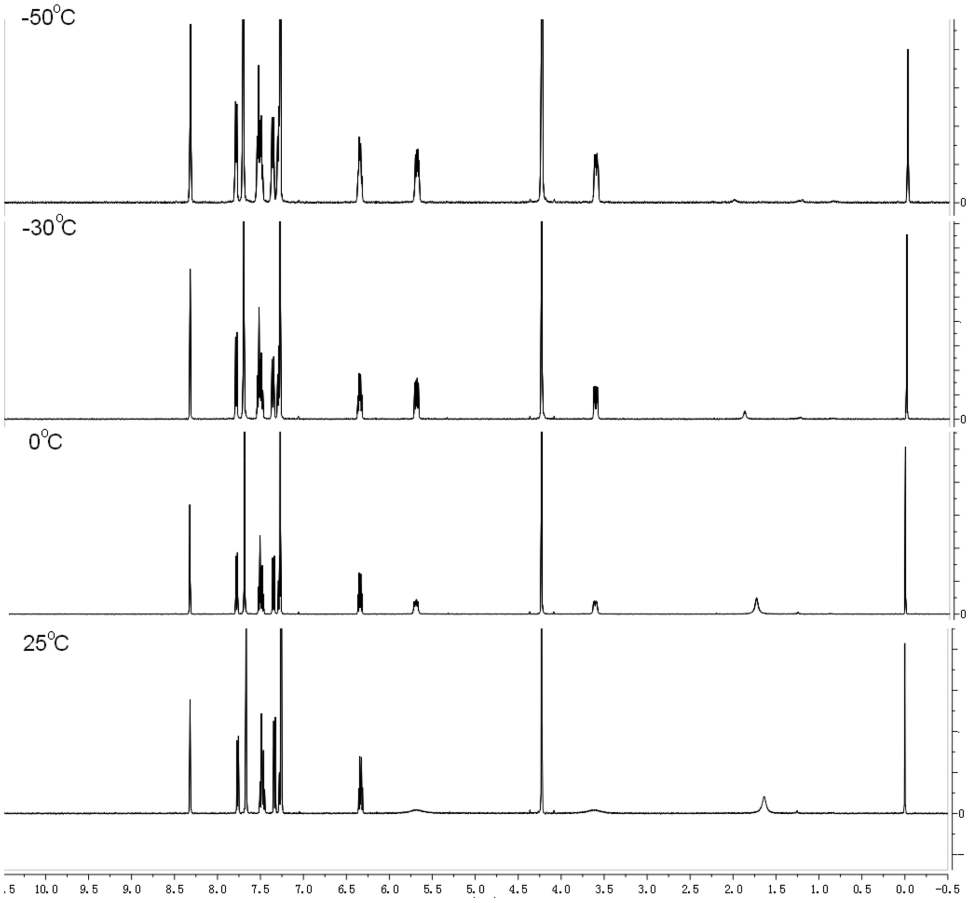
Scheme 3. Studies of Variable-Temperature ^{1}H NMR for Compound 5d in $CDCl_3$



nitrogen in compound **5** appeared as broad resonances while compounds **5n** and **5o** showed sharp multiplets. To understand better the structure of the seven-membered ring in compound **5**, a variable-temperature NMR study of compound **5d** in $CDCl_3$ was further studied (Scheme 3). The variable-temperature ^{1}H NMR experiment for **5d** revealed that the protons of the methylene group adjacent to nitrogen in compound **5** appear as 2 resonances separated by 2 ppm (5.689 and 3.617 ppm). The two protons are broad single peaks at 25 °C, while they appear as sharp multiplets below 25 °C. It suggests that the 7-membered ring is in two slowly interconverting conformers, which was further confirmed by the X-ray structure of compound **5d** (Figure 2).[15] The X-ray structure of **5d** shows that the 7-membered ring is a twist ring so that the two conformers might be interconverted as the temperature.

On the basis of the experimental results and the literature,[11f,12c] a plausible reaction mechanism was proposed for the formation of the selective cyclized products **3a** and **5a** from alkyn-tethered indoles (Scheme 4).

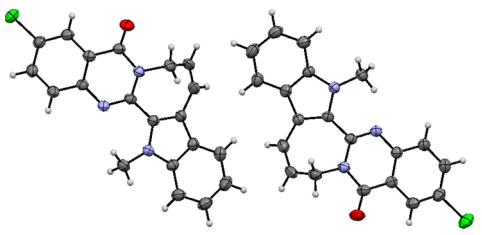


Figure 2. X-ray structure of compound **5d**.

In the presence of the gold catalyst, substrate **2a** would give intermediate **A**. This intermediate **A** would further undergo 6-*exo-dig* cyclization to give intermediate **B** and finally afforded product **3a** via protodeauration and isomerization which could be supported by isolation of product **3j** in Table 2 (Scheme 4A). In the same manner, substrate **1** would give intermediate **E** by activation of gold catalyst and subsequent 7-*endo-dig* cyclization. Then intermediate **E** undergoes protodeauration to provide intermediate **4a**. Compound **4a** was oxidized by DDQ to give product **5a** (Scheme 4B). The selectivity of 6-*exo-dig* and 7-*endo-dig* cyclization perhaps correlates with the hybridization of the carbon at the 2 position in quinazolinone. The planarity of sp^2 hybridization is favorable to undergo 6-*exo-dig* cyclization, while sp^3 hybridization is favorable to undergo 7-*endo-dig* cyclization.

To illustrate this new protocol for rapid synthesis of rutaecarpine scaffolds, a gram-scale preparation of **3a** from the commercial material isatoic anhydride was performed (Scheme 5). When 1.3 g of isatoic anhydride was used as starting material, followed with aminolysis, condensation, oxidation, and gold-catalyzed 6-*exo-dig* cyclization procedure, the desired product **3a** was obtained in 67% yield (0.9 g) in four steps. This efficient gram-scale preparation of a rutaecarpine derivative will enable more potent application of these compounds in pharmaceuticals.

DOI: 10.1021/acs.joc.7b02956
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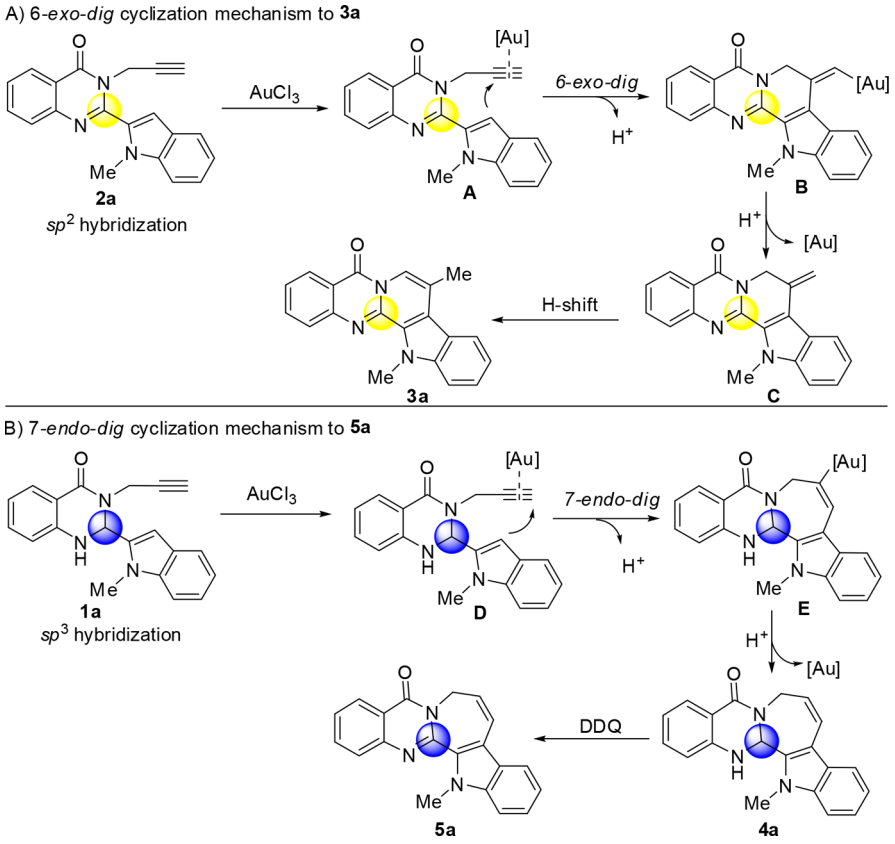
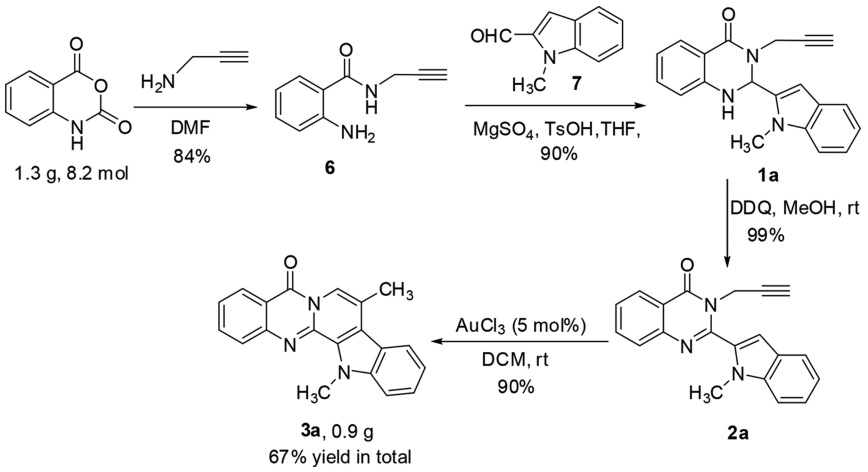
Scheme 4. Plausible Mechanisms for the Formation of 3a and 5a



Scheme 5. Gram-Scale Preparation of Compound 3a



CONCLUSIONS

In summary, we developed an efficient and practical synthetic method for the formation of two types of rutaecarpine scaffolds in moderate to excellent yields from alkyn-tethered indoles. The alkyn-tethered indole can undergo *6-exo-dig* cyclization by oxidation and sequential gold catalysis, while it goes through 7-*endo-dig* cyclization under gold catalysis and sequential oxidation. The rutaecarpine derivative could be prepared in gram scale easily in good yield in four steps from isatoic anhydride.

EXPERIMENTAL SECTION

General Methods. All reactions were carried out at room temperature. All commercially available reagents and solvents were used as received without further purification. Analytical thin layer chromatography (TLC) was performed on silica gel plates (GF_{254}) and was visualized with a UV lamp (254 nm). Flash column chromatography was performed on silica gel (200−400 mesh). Melting points were recorded on a digital microscopic melting apparatus and uncorrected. Infrared (IR) spectra were recorded on a PerkinElmer spectrometer (FTIR-Spectrum TWO) with KBr pellet, and only major peaks are reported in cm^{-1}. High-resolution mass spectra (HRMS) were performed using ESI (electrospray ionization) mode and a TOF (time-of-flight) mass analyzer. ^1H NMR spectra were recorded in $CDCl_3$ or a mixture of chloroform-*d* and methanol-d_4

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(v/v = 10/1) on a 400, 500, or 600 MHz NMR spectrometer (Bruker). ^{13}C NMR spectra were proton decoupled and recorded in $CDCl_3$ or a mixture of chloroform-*d* and methanol-d_4 (v/v = 10/1) on a 100, 125, or 150 MHz NMR spectrometer. The ^1H and ^{13}C chemical shifts are referenced to signals at δ 0.00 (TMS). ^1H NMR coupling constants (J) are reported in Hertz (Hz), and multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), and m (multiplet).

General Procedure for the Synthesis of Products 3a−3n, 3p−3q, and 5n−5p. To a stirred solution of compound **2** (0.2 mmol) in dichloromethane (2 mL) was added $AuCl_3$ (0.003 g, 0.01 mmol) under an atmosphere of air, and then the reaction mixture was stirred at room temperature for 0.5 h. After completion of the reaction as monitored by TLC, the solvent was removed under vacuum. The residue was purified by flash column chromatography (silica gel, dichloromethane) to give product **3** or **5**.

*8,13-Dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3a**).* Pale yellow crystalline; 0.056 g, 90% yield. Mp: 239−240 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35−8.33 (m, 1H), 8.30 (d, J = 0.8 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.72−7.65 (m, 2H), 7.47−7.40 (m, 2H), 7.33 (t, J = 8.0 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 4.62 (s, 3H), 2.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 147.1, 141.5, 140.4, 133.9, 127.9, 127.2, 126.7, 126.3, 124.3, 122.2, 121.5, 121.3, 120.8, 119.3, 115.9, 115.7, 110.1, 32.9, 17.9. IR (KBr) 3057, 2917, 1684, 1450, 1251, 1113, 759, 724 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{16}N_3O$ $[M + H]^+$ 314.1293, found 314.1288.

*3-Methoxy-8,13-dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3b**).* Pale yellow crystalline; 0.059 g, 85% yield. Mp: 255−256 °C. ^1H NMR (500 MHz, $CDCl_3$ + CD_3OD) δ 8.43 (s, 1H), 8.13 (d, J = 6.5 Hz, 1H), 7.74−7.69 (m, 2H), 7.55 (s, 2H), 7.43 (d, J = 6.5 Hz, 1H), 7.32 (s, 1H), 4.64 (s, 3H), 3.95 (s, 3H), 2.79 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$ + CD_3OD) δ 158.9, 156.8, 142.3, 141.4, 138.8, 128.5, 128.2, 126.1, 125.9, 122.0, 121.6, 120.8, 120.5, 119.9, 116.1, 115.4, 110.2, 104.8, 55.6, 32.8, 17.9. IR (KBr) 3102, 2939, 1671, 1496, 1329, 1160, 1032, 743 cm^{-1}. HRMS (ESI) m/z for $C_{21}H_{18}N_3O_2$ $[M + H]^+$ 344.1399, found 344.1406.

*3,8,13-Trimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3c**).* Pale yellow crystalline; 0.061 g, 93% yield. Mp: 258−259 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 1.2 Hz, 1H), 8.07 (s, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.50−7.44 (m, 3H), 7.26−7.22 (m, 1H), 4.53 (s, 3H), 2.66 (d, J = 0.8 Hz, 3H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 145.1, 141.4, 139.8, 135.7, 134.3, 128.0, 126.5, 126.1, 122.1, 121.5, 121.0, 120.6, 119.2, 115.7, 115.6, 110.1, 32.8, 21.3, 17.9. IR (KBr) 3047, 2917, 1673, 1537, 1480, 1328, 1250, 818, 732 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O$ $[M + H]^+$ 328.1450, found 328.1455.

*3-Chloro-8,13-dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3d**).* Pale yellow crystalline; 0.038 g, 55% yield. Mp: 269−270 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.32 (d, J = 8.0 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.5 Hz, 1H), 7.65−7.63 (m, 1H), 7.55−7.52 (m, 2H), 7.32 (t, J = 7.1 Hz, 1H), 4.62 (s, 3H), 2.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 158.4, 145.8, 141.9, 140.6, 134.8, 129.9, 128.7, 128.1, 126.8, 126.1, 122.5, 121.9, 121.6, 121.2, 120.4, 116.5, 115.7, 110.4, 33.1, 18.1. IR (KBr) 3100, 2930, 1676, 1536, 1472, 1328, 1132, 729 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}ClN_3O$ $[M + H]^+$ 348.0904, found 348.0890.

*3-Bromo-8,13-dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3e**).* Pale yellow crystalline; 0.063 g, 80% yield. Mp: 268−269 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, J = 2.0 Hz, 1H), 8.42 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.79−7.77 (m, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 2H), 7.33 (t, J = 8.0 Hz, 1H), 4.62 (s, 3H), 2.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 158.2, 146.0, 141.0, 140.7, 137.4, 129.5, 128.7, 128.1, 126.9, 122.5, 122.0, 121.6, 121.2, 120.5, 117.5, 116.9, 115.8, 110.5, 33.1, 18.0. IR (KBr) 3068, 2928, 1691, 1531, 1471, 1325, 1134, 821, 732 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}BrN_3O$ $[M + H]^+$ 392.0393, found 392.0388.

*3-Iodo-8,13-dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3f**).* Pale yellow crystalline; 0.068 g, 77% yield. Mp: 279−280 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.43 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.58−7.53 (m, 2H), 7.47 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 4.62 (s, 3H), 2.76 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$ + CD_3OD) δ 157.9, 146.4, 142.6, 141.8, 140.8, 135.9, 128.7, 128.1, 126.8, 122.4, 122.0, 121.5, 121.1, 120.3, 117.4, 115.8, 110.4, 87.8, 33.0, 18.0. IR (KBr) 3056, 2915, 1686, 1570, 1470, 1326, 1280, 1137, 817, 729 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}IN_3O$ $[M + H]^+$ 440.0260, found 440.0253.

*2-Fluoro-8,13-dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3g**).* Pale yellow crystalline; 0.060 g, 90% yield. Mp: 262−263 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.41−8.36 (m, 2H), 8.10 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 6.0 Hz, 2H), 7.34−7.32 (m, 2H), 7.07 (d, J = 8.0 Hz, 1H), 4.60 (s, 3H), 2.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6 (J = 252.0 Hz), 158.4, 149.0, 141.9, 141.3, 130.2 (d, J = 11.0 Hz), 127.8, 126.8, 122.5, 121.5, 121.0, 119.8, 115.9, 113.9 (d, J = 24.0 Hz), 112.7, 111.0 (d, J = 21.0 Hz), 110.4, 33.1, 18.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ − 103.6. IR (KBr) 3100, 2923, 1680, 1542, 1455, 1327, 1275, 1149, 726 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}FN_3O$ $[M + H]^+$ 332.1199, found 332.1172.

*4-Chloro-8,13-dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3h**).* Pale yellow crystalline; 0.063 g, 90% yield. Mp: 293−294 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.64−7.59 (m, 3H), 7.41 (d, J = 8.0 Hz, 1H), 7.37−7.34 (m, 1H), 4.68 (s, 3H), 2.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 149.6, 142.0, 141.0, 134.4, 133.1, 128.1, 126.9, 126.8, 126.2, 122.5, 122.4, 121.6, 121.0, 119.9, 116.0, 113.1, 110.4, 33.0, 18.1. IR (KBr) 3057, 2922, 1684, 1527, 1470, 1325, 1281, 1164, 803, 727 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}ClN_3O$ $[M + H]^+$ 348.0904, found 348.0908.

*13-Benzyl-8-methylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5-(13H)-one (**3i**).* Pale yellow crystalline; 0.063 g, 81% yield. Mp: 284−285 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.46 (d, J = 8.0 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.77−7.70 (m, 2H), 7.58 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.24−7.21 (m, 4H), 7.19−7.17 (m, 1H), 6.62 (s, 2H), 2.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 159.7, 147.5, 141.7, 140.4, 138.7, 134.5, 128.7, 128.0, 127.3, 127.2, 127.1, 126.9, 124.8, 122.6, 122.3, 122.2, 121.4, 121.2, 120.1, 116.3, 116.1, 111.3, 49.0, 18.2. IR (KBr) 3059, 1673, 1539, 1458, 1326, 1253, 1149, 729 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{20}N_3O$ $[M + H]^+$ 390.1606, found 390.1616.

*8-Methylene-8,13-dihydroindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(7H)-one (**3j**).* Pale yellow crystalline; 0.016 g, 26% yield. Mp: 230−231 °C. ^1H NMR (400 MHz, CD_3OD) δ 8.25−8.23 (m, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.84−7.80 (m, 1H), 7.78−7.76 (m, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.52−7.48 (m, 1H), 7.38−7.34 (m, 1H), 7.24−7.20 (m, 1H), 5.76 (t, J = 1.6 Hz, 1H), 5.43 (t, J = 1.6 Hz, 1H), 5.11 (t, J = 1.6 Hz, 2H) (the resonance of N−H was not observed in CD_3OD). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 147.3, 143.8, 138.6, 134.4, 131.6, 127.8, 127.1, 126.7, 126.6, 125.9, 123.8, 121.8, 121.5, 120.8, 117.5, 112.3, 110.1, 48.2. IR (KBr) 3062, 1640, 1588, 1472, 1324, 1246, 870, 732 cm^{-1}. HRMS (ESI) m/z calcd for $C_{19}H_{14}N_3O$ $[M + H]^+$ 300.1137, found 300.1133.

*8,10,13-Trimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5-(13H)-one (**3k**).* Pale yellow crystalline; 0.059 g, 90% yield. Mp: 287−288 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.45−8.44 (m, 2H), 7.88 (s, 1H), 7.83−7.77 (m, 2H), 7.45−7.40 (m, 2H), 7.36 (d, J = 8.0 Hz, 1H), 4.65 (s, 3H), 2.78 (s, 3H), 2.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$+ CD_3OD) δ 159.2, 147.0, 140.4, 140.2, 134.1, 130.3, 128.2, 128.0, 127.0, 126.6, 124.3, 121.62, 121.57, 121.1, 119.9, 115.7, 115.3, 109.9, 32.9, 21.4, 17.9. IR (KBr) 3095, 2916, 1676, 1540, 1459, 1308, 1251, 1101, 763 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O$ $[M + H]^+$ 328.1450, found 328.1452.

*10-Bromo-8,13-dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3l**).* Pale yellow crystalline; 0.071 g, 90% yield. Mp: 313−314 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.46 (d, J = 8.0 Hz, 1H), 8.26 (d, J = 1.6 Hz, 1H), 7.83−7.82 (m, 2H), 7.64−7.62 (m, 1H), 7.47−7.44 (m, 2H), 4.69 (s, 3H), 2.78 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$ + CD_3OD) δ 159.3, 147.1, 140.5, 140.2, 134.4, 129.3, 128.8, 127.1, 127.0, 124.9, 124.6, 123.0, 120.6, 119.4, 116.1, 116.0, 113.9, 111.8, 33.2, 17.8. IR (KBr) 3099, 2913, 1675, 1637, 1540, 1455,

DOI: 10.1021/acs.joc.7b02956
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1304, 1226, 1106, 858, 761 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}BrN_3O$ $[M + H]^+$ 392.0393, found 392.0389.

*11-Chloro-8,13-dimethylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3m**).* Pale yellow crystalline; 0.061 g, 89% yield. Mp: 315−316 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.47 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 1.6 Hz, 1H), 7.83−7.80 (m, 2H), 7.64−7.62 (m, 1H), 7.47−7.44 (m, 2H), 4.68 (s, 3H), 2.83 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$ + CD_3OD) δ 159.3, 147.2, 140.5, 140.2, 134.4, 129.3, 128.8, 127.1, 126.9, 124.9, 124.6, 123.0, 120.6, 119.4, 116.1, 116.0, 113.9, 111.8, 33.2, 17.8. IR (KBr) 3078, 2928, 1693, 1539, 1454, 1325, 1251, 1111, 837, 763 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}ClN_3O$ $[M + H]^+$ 348.0904, found 348.0894.

*8-Ethyl-13-methylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5-(13H)-one (**3n**).* Pale yellow crystalline; 0.021 g, 32% yield. Mp: 171−172 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.44 (d, J = 8.0 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.78−7.77 (m, 2H), 7.55−7.53 (m, 2H), 7.43−7.40 (m, 1H), 7.34−7.31 (m, 1H), 4.66 (s, 3H), 3.20−3.15 (m, 2H), 1.49 (t, J = 8.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 147.2, 141.7, 140.7, 134.1, 128.5, 127.3, 126.8, 126.3, 125.4, 124.4, 122.6, 121.0, 120.9, 120.8, 116.0, 114.8, 110.3, 33.1, 24.8, 13.5. IR (KBr) 3053, 2926, 1673, 1543, 1459, 1328, 1250, 1149, 733 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O$ $[M + H]^+$ 328.1450, found 328.1442.

*8-(Trimethylsilyl)methyl-13-methylindolo[2′,3′:3,4]pyrido[2,1-b]quinazolin-5(13H)-one (**3p**).* Pale yellow crystalline; 0.008 g, 10% yield. Mp: 238−239 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.46−8.44 (m, 1H), 8.37 (s, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.79−7.76 (m, 1H), 7.57−7.52 (m, 2H), 7.42−7.40 (m, 1H), 7.33−7.30 (m, 1H), 4.69 (s, 3H), 2.66 (s, 2H), 0.06 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.9, 147.1, 141.8, 140.2, 134.0, 128.5, 127.2, 126.7, 126.3, 124.3, 122.7, 121.7, 121.4, 120.6, 115.9, 114.2, 110.4, 33.2, 21.3, − 1.4. IR (KBr) 3051, 2930, 1673, 1459, 1321, 1251, 1149, 845, 733 cm^{-1}. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3OSi$ $[M + H]^+$ 386.1683, found 386.1688.

*1,4-Dimethylpyrrolo[2″,3′:3,4]pyrido[2,1-b]quinazolin-7(1H)-one (**3q**).* Pale yellow crystalline; 0.047 g, 89% yield. Mp: 187−188 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 8.0 Hz, 1H), 8.34 (s, 1H), 7.75−7.67 (m, 2H), 7.38−7.32 (m, 1H), 7.10 (d, J = 2.8 Hz, 1H), 6.40 (d, J = 2.8 Hz, 1H), 4.44 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 147.7, 140.8, 133.9, 132.3, 129.6, 127.3, 126.5, 123.7, 123.0, 118.4, 115.93, 115.91, 101.2, 37.9, 15.9. IR (KBr) 3056, 2920, 1674, 1544, 1461, 1309, 722 cm^{-1}. HRMS (ESI) m/z calcd for $C_{16}H_{14}N_3O$ $[M + H]^+$ 264.1137, found 264.1135.

*9,14-Dimethyl-7,14-dihydro-5H-indolo[2′,3′:3,4]azepino[2,1-b]quinazolin-5-one (**5n**).* White crystalline; 0.028 g, 43% yield. Mp: 163−164 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.77−7.73 (m, 2H), 7.52−7.44 (m, 3H), 7.24 (t, J = 8.0 Hz, 1H), 6.05 (t, J = 8.0 Hz, 1H), 5.61−5.56 (m, 1H), 4.18 (s, 3H), 3.57−3.52 (m, 1H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 147.4, 147.0, 139.3, 138.1, 134.1, 132.0, 127.3, 127.0, 126.4, 125.0, 124.7, 122.2, 121.0, 120.8, 120.7, 120.6, 110.4, 40.3, 32.8, 21.7. IR (KBr) 3065, 2921, 1685, 1554, 1470, 1371, 1243, 767, 723 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O$ $[M + H]^+$ 328.1450, found 328.1444.

*14-Methyl-9-phenyl-7,14-dihydro-5H-indolo[2′,3′:3,4]azepino-[2,1-b]quinazolin-5-one (**5o**).* White crystalline; 0.060 g, 70% yield. Mp: 290−291 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 8.0 Hz, 1H), 7.80−7.76 (m, 2H), 7.50−7.48 (m, 2H), 7.39−7.33 (m, 6H), 6.95 (t, J = 8.0 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 6.36 (t, J = 8.0 Hz, 1H), 5.79−5.75 (m, 1H), 4.24 (s, 3H), 3.73−3.69 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 147.3, 147.2, 143.0, 139.7, 139.2, 134.3, 133.4, 128.44, 128.41, 128.3, 127.3, 127.1, 126.6, 125.0, 124.9, 122.7, 121.4, 121.0, 120.5, 118.7, 110.2, 40.4, 32.8. IR (KBr) 3060, 2930, 1673, 1557, 1471, 1336, 1237, 1171, 754, 695 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{20}N_3O$ $[M + H]^+$ 390.1606, found 390.1600.

*14-Methyl-9-trimethylsilyl-7,14-dihydro-5H-indolo[2′,3′:3,4]-azepino[2,1-b]quinazolin-5-one (**5p**).* Pale yellow crystalline; 0.010 g, yield 13%. Mp: 233−235 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.40−8.38 (m, 1H), 7.84−7.76 (m, 3H), 7.51−7.41 (m, 3H), 7.25−7.21 (m, 1H), 6.63−6.58 (m, 1H), 5.70−5.65 (m, 1H), 4.17 (s, 3H), 3.57−3.52 (m, 1H), 0.26 (t, J = 3.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 147.2, 147.0, 142.7, 139.1, 134.3, 133.5, 131.4, 127.09, 127.07 126.5, 125.1, 125.0, 122.5, 122.2, 120.7, 120.3, 110.4, 40.6, 32.8, 0.5. IR (KBr) 3078, 2930, 1683, 1554, 1470, 1371, 1241, 1146, 843, 760 cm^{-1}. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3OSi$ $[M + H]^+$ 386.1683, found 386.1689.

General Procedure for the Synthesis of Compounds 5a, 5b, 5d−5f, and 5m. To a stirred solution of compound **1** (0.3 mmol) in dichloromethane (3 mL) was added $AuCl_3$ (14 mg, 0.045 mmol) under an atmosphere of air, and then the reaction mixture was stirred at room temperature for 1.5−3 h. When completion of the reaction was noted by TLC, 2,3-dicyano-5,6-dichlorobenzoquinone (DDQ, 68 mg, 0.3 mmol) was added. The resultant reaction mixture was stirred at room temperature for an additional 0.5 h (monitored by TLC). Evaporation of solvent and purification of the residue on a silica gel column using dichloromethane/petroleum ether (from 1/1 to 2/1) as eluent afforded product **5**.

*14-Methyl-7,14-dihydro-5H-indolo[2′,3′:3,4]azepino[2,1-b]-quinazolin-5-one (**5a**).* White crystalline; 0.044 g, 47% yield. Mp: 184−185 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 8.0 Hz, 1H), 7.78−7.72 (m, 3H), 7.51−7.44 (m, 3H), 7.33 (d, J = 9.5 Hz, 1H), 7.28−7.24 (m, 1H), 6.37−6.31 (m, 1H), 5.71 (s, 1H), 4.28 (s, 3H), 3.62 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 147.1, 139.5, 134.3, 131.9, 127.4, 127.1, 127.0, 126.4, 125.7, 124.8, 123.9, 121.0, 120.98, 120.0, 119.5, 110.4, 41.0, 33.2. IR (KBr) 3057, 2927, 1674, 1556, 1472, 1344, 1243, 1024, 745, 729 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{16}N_3O$ $[M + H]^+$ 314.1293, found 314.1303.

*3-Methoxy-14-methyl-7,14-dihydro-5H-indolo[2′,3′:3,4]azepino-[2,1-b]quinazolin-5-one (**5b**).* White crystalline; 0.041 g, 40% yield. Mp: 166−167 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 2.8 Hz, 1H), 7.67 (d, J = 8.9 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.45−7.41 (m, 1H), 7.36−7.33 (m, 1H), 7.31 (d, J = 9.5 Hz, 1H), 7.26−7.22 (m, 1H), 6.35−6.29 (m, 1H), 5.71 (s, 1H), 4.22 (s, 3H), 3.94 (s, 3H), 3.63 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 158.1, 145.2, 142.1, 139.3, 132.3, 128.9, 127.4, 125.4, 124.84, 124.82, 123.5, 121.8, 120.8, 119.8, 118.6, 110.2, 106.0, 55.9, 41.0, 33.0. IR (KBr) 3046, 2925, 1683, 1556, 1489, 1365, 1256, 1030, 829, 723 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O_2$ $[M + H]^+$ 344.1399, found 344.1396.

*3-Chloro-14-methyl-7,14-dihydro-5H-indolo[2′,3′:3,4]azepino-[2,1-b]quinazolin-5-one (**5d**).* White crystalline; 0.054 g, 52% yield. Mp: 232−233 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.35−8.34 (m, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 2.0 Hz, 2H), 7.53−7.48 (m, 2H), 7.37 (d, J = 9.5 Hz, 1H), 7.31−7.28 (m, 1H), 6.38−6.34 (m, 1H), 5.72 (s, 1H), 4.25 (s, 3H), 3.63 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 147.3, 145.8, 139.5, 134.7, 131.9, 131.7, 128.9, 127.5, 126.4, 125.9, 124.8, 123.7, 122.0, 121.1, 120.1, 119.6, 110.4, 41.2, 33.2. IR (KBr) 3045, 2945, 1677, 1553, 1471, 1336, 1230, 825, 730 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}ClN_3O$ $[M + H]^+$ 348.0904, found 348.0896.

*3-Bromo-14-methyl-7,14-dihydro-5H-indolo[2′,3′:3,4]azepino-[2,1-b]quinazolin-5-one (**5e**).* White crystalline; 0.056 g, 48% yield. Mp: 236−237 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 2.3 Hz, 1H), 7.85−7.72 (m, 2H), 7.59 (d, J = 8.7 Hz, 1H), 7.52−7.41 (m, 2H), 7.33 (d, J = 9.5 Hz, 1H), 7.28−7.24 (m, 1H), 6.36−6.30 (m, 1H), 5.68 (s, 1H), 4.22 (s, 3H), 3.61 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 147.4, 146.2, 139.4, 137.4, 131.8, 129.5, 129.1, 127.4, 125.8, 124.7, 123.7, 122.4, 121.0, 120.0, 119.5, 110.3, 41.1, 33.1. IR (KBr) 3062, 2942, 1669, 1552, 1468, 1340, 1150, 828, 730 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}BrN_3O$ $[M + H]^+$ 392.0393, found 392.0388.

*3-Iodo-14-methyl-7,14-dihydro-5H-indolo[2′,3′:3,4]azepino[2,1-b]quinazolin-5-one (**5f**).* White crystalline; 0.065 g, 49% yield. Mp: 160−161 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, J = 2.0 Hz, 1H), 8.01−7.98 (m, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.51−7.45 (m, 3H), 7.34 (d, J = 8.0 Hz, 1H), 7.30−7.25 (m, 1H), 6.36−6.31 (m, 1H), 5.68 (s, 1H), 4.23 (s, 3H), 3.63 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 147.6, 146.7, 142.9, 139.5, 135.9, 131.9, 129.1, 127.4, 125.9, 124.8, 123.7, 122.7, 121.1, 120.0, 119.6, 110.3, 90.2, 41.2, 33.1. IR (KBr) 3056, 2922, 2852, 1678, 1589, 1468, 1338, 958, 780, 730 cm^{-1}.

DOI: 10.1021/acs.joc.7b02956
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HRMS (ESI) m/z calcd for $C_{20}H_{15}IN_3O$ $[M + H]^+$ 440.0254, found 440.0249.

*12-Chloro-14-methyl-7,14-dihydro-5H-indolo[2′,3′:3,4]azepino-[2,1-b]quinazolin-5-one (**5m**).* White crystalline; 0.043 g, 41% yield. Mp: 246−247 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37−8.35 (m, 1H), 7.78−7.72 (m, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.48−7.44 (m, 2H), 7.27 (d, J = 9.5 Hz, 1H), 7.23−7.20 (m, 1H), 6.38−6.32 (m, 1H), 5.68 (s, 1H), 4.20 (s, 3H), 3.64 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 147.2, 146.8, 139.7, 134.3, 132.7, 131.7, 127.3, 127.1, 126.9, 126.5, 124.5, 123.3, 121.8, 121.1, 121.0, 119.1, 110.3, 40.8, 33.3. IR (KBr) 3076, 2939, 1691, 1556, 1467, 1329, 1236, 1067, 803, 770 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}ClN_3O$ $[M + H]^+$ 348.0904, found 348.0903.

Synthesis of Alkyn-Tethered Indole 1. The solution of 2-aminobenzoic acid derivatives (5 mmol), triphosgene (0.50 g, 1.7 mmol) in THF (9 mL) was stirred at room temperature under an atmosphere of air until 2-aminobenzoic acid derivative was consumed completely (8−16 h, monitored by TLC). Then, water (90 mL) was added to the mixture giving a white or gray precipitate. Filtration, the solid was washed with ether, and then dried to give substituted isatoic anhydride as solid. It was used directly for the next step.

To a stirred solution of substituted isatoic anhydride (2.5 mmol) in DMF (4 mL) was added propynylamine derivative (3.77 mmol) at room temperature under an atmosphere of air. The reaction was completed over a period of 2−6 h. Then, the reaction mixture was poured into water (40 mL). The aqueous layer was extracted with dichloromethane (4 × 15 mL). After removal of the solvent under vacuum, water (10 mL) was then added to give a white or gray precipitate. Filtration, the solid was washed with petroleum ether, and then dried to give alkynyl anilines as solid.

To a stirred mixture of alkynyl anilines (1.5 mmol), indole-2-carboxaldehyde (1.65 mmol) and anhydrous magnesium sulfate (0.6 g, 5 mmol) in THF (5 mL) was added p-toluene sulfonic acid (0.077 g, 0.45 mmol) at 25 °C under an atmosphere of nitrogen. The resulting mixture was allowed to stir at 25 °C for 8−12 h. After completion of the reaction, as indicated by TLC, the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica gel, gradient eluent: dichloromethane/petroleum ether = 3/1 to 6/1) to afford compound **1**.

*2-(1-Methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1H)-one (**1a**).* White crystalline; 0.460 g, 90% yield. Mp: 186−187 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00−7.97 (m, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.36−7.28 (m, 3H), 7.15−7.11 (m, 1H), 6.90−6.86 (m, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.61 (s, 1H), 6.34 (s, 1H), 4.88−4.83 (m, 1H), 4.64 (s, 1H), 3.90 (s, 3H), 3.40−3.35 (m, 1H), 2.15 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 145.5, 138.8, 134.0, 133.6, 129.0, 126.6, 123.0, 121.3, 120.1, 119.9, 115.8, 114.9, 109.4, 105.0, 78.3, 71.8, 66.7, 32.7, 31.1. IR (KBr) 3291, 3056, 2935, 2122, 1634, 1508, 1236, 1174, 755 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{17}N_3NaO$ $[M + Na]^+$ 338.1269, found 338.1280.

*6-Methoxy-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1H)-one (**1b**).* White crystalline; 0.440 g, 84% yield. Mp: 192−193 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 2.4 Hz, 1H), 7.35−7.33 (m, 1H), 7.29−7.25 (m, 1H), 7.14−7.10 (m, 1H), 6.95−6.92 (m, 1H), 6.64 (d, J = 8.0 Hz, 1H), 6.54 (s, 1H), 6.29 (s, 1H), 4.96−4.91 (m, 1H), 4.33 (s, 1H), 3.92 (s, 3H), 3.80 (s, 3H), 3.47−3.42 (m, 1H), 2.19 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 154.1, 139.1, 138.7, 133.9, 126.6, 122.9, 122.5, 121.2, 120.0, 117.8, 110.8, 109.4, 104.6, 78.4, 72.0, 66.6, 55.8, 32.9, 31.0. IR (KBr) 3224, 3062, 2942, 2837, 2116, 1640, 1504, 1285, 1139, 794, 734 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{20}N_3O_2$ $[M + H]^+$ 346.1556, found 346.1566.

*6-Chloro-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1H)-one (**1d**).* White crystalline; 0.370 g, 71% yield. Mp: 219−220 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 2.4 Hz, 1H), 7.62−7.58 (m, 1H), 7.37−7.34 (m, 0.8 Hz, 1H), 7.31−2.29 (m, 1H), 7.27−7.25 (m, 1H), 7.16−7.12 (m, 1H), 6.62−6.58 (m, 2H), 6.36 (s, 1H), 4.92−4.87 (m, 1H), 4.57 (s, 1H), 3.91 (s, 3H), 3.44−3.39 (m, 1H), 2.18 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 143.7, 138.8, 133.9, 133.2, 128.5, 126.5, 125.3, 123.2, 121.3, 120.2, 117.1, 116.5, 109.4, 105.1, 77.9, 72.1, 66.4, 32.8, 31.0. IR (KBr) 3235, 3078, 2909, 2123, 1635, 1496, 1230, 1143, 791, 733 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{17}ClN_3O$ $[M + H]^+$ 350.1060, found 350.1061.

*6-Bromo-2-(1-methy-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1H)-one (**1e**).* White crystalline; 0.420 g, 68% yield. Mp: 223−224 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 2.4 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.41−7.39 (m, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.31−7.28 (m, 1H), 7.17−7.13 (m, 1H), 6.61 (s, 1H), 6.55 (d, J = 8.0 Hz, 1H), 6.36 (s, 1H), 4.91−4.87 (m, 1H), 4.60 (s, 1H), 3.91 (s, 3H), 3.44−3.39 (m, 1H), 2.18 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 144.1, 138.8, 136.6, 133.2, 131.5, 126.5, 123.2, 121.3, 120.2, 117.4, 116.7, 112.1, 109.4, 105.1, 77.9, 72.1, 66.4, 32.8, 31.0. IR (KBr) 3234, 3061, 2907, 2115, 1634, 1495, 1231, 733 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{16}BrN_3NaO$ $[M + Na]^+$ 416.0374, found 416.0393.

*6-Iodo-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1H)-one (**1f**).* White crystalline; 0.260 g, 40% yield. Mp: 208−209 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 2.4 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.57−7.55 (m, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.31−7.27 (m, 1H), 7.16−7.12 (m, 1H), 6.61 (s, 1H), 6.43 (d, J = 8.0 Hz, 1H), 6.35 (s, 1H), 4.90−4.61 (m, 1H), 4.61 (s, 1H), 3.89 (s, 3H), 3.41−3.36 (m, 1H), 2.17 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 144.7, 142.3, 138.8, 137.4, 133.2, 126.5, 123.2, 121.3, 120.2, 117.7, 117.0, 109.4, 105.1, 81.1, 77.9, 72.1, 66.3, 32.8, 31.0. IR (KBr) 3241, 3057, 2931, 2116, 1633, 1494, 1142, 735 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{17}IN_3O$ $[M + H]^+$ 442.0416, found 442.0408.

*2-(6-Chloro-1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1H)-one (**1m**).* White crystalline; 0.400 g, 77% yield. Mp: 202−203 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−8.00 (m, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.34−7.31 (m, 2H), 7.11−7.09 (m, 1H), 6.94−6.90 (m, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.59 (s, 1H), 6.35 (s, 1H), 4.92−4.85 (m, 1H), 4.56 (s, 1H), 3.89 (s, 3H), 3.44−3.39 (m, 1H), 2.30 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 168.4, 149.7, 143.0, 139.0, 138.2, 132.6, 132.4, 129.0, 125.9, 124.6, 123.3, 119.0, 113.3, 108.2, 81.7, 76.1, 69.9, 36.8, 34.8. IR (KBr) 3289, 3064, 2935, 2125, 1634, 1513, 1341, 1158, 813, 757 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{17}ClN_3O$ $[M + H]^+$ 350.1060, found 350.1064.

Synthesis of Compound 2. To a stirred solution of compound **1** (0.5 mmol) in methanol (5 mL) was added DDQ (0.125 g, 0.55 mmol) in portions at room temperature in air. The reaction mixture was stirred for 0.5 h before the methanol was removed under reduced pressure. The crude product was purified by flash column chromatography (silica gel, gradient eluent: dichloromethane/petroleum ether = 1/1 to 3/1) to afford the corresponding products **2**.

*2-(1-Methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (**2a**).* White crystalline; 0.140 g, 87% yield. Mp: 194−195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.0 Hz, 1H), 7.81−7.78 (m, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.58−7.54 (m, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.21 (t, J = 8.0 Hz, 1H), 7.14 (s, 1H), 4.94 (d, J = 2.4 Hz, 2H), 3.89 (s, 3H), 2.34 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 148.0, 146.8, 138.2, 134.8, 131.0, 127.7, 127.1, 126.9, 123.9, 121.9, 120.8, 120.7, 110.1, 105.4, 78.4, 72.7, 36.2, 31.5. IR (KBr) 3059, 2947, 2126, 1692, 1515, 1242, 1170, 780, 721 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{16}N_3O$ $[M + H]^+$ 314.1293, found 314.1291.

*6-Methoxy-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-quinazolin-4(3H)-one (**2b**).* White crystalline; 0.160 g, 93% yield. Mp: 176−177 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 3.0 Hz, 1H), 7.75−7.73 (m, 2H), 7.47 (d, J = 8.0 Hz, 1H), 7.44−7.42 (m, 1H), 7.40−7.37 (m, 1H), 7.25−7.22 (m, 1H), 7.12 (s, 1H), 4.95 (d, J = 2.5 Hz, 2H), 3.99 (s, 3H), 3.89 (s, 3H), 2.36 (t, J = 2.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 159.2, 145.7, 141.4, 138.0, 131.1, 129.4, 127.0, 125.1, 123.7, 121.8, 121.6, 120.6, 110.1, 106.3, 105.1, 78.4, 72.6, 56.0, 36.3, 31.4. IR (KBr) 3057, 2926, 2246, 1673, 1555, 1470, 1242, 746 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O_2$ $[M + H]^+$ 344.1399, found 344.1413.

DOI: 10.1021/acs.joc.7b02956
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*6-Methyl-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-quinazolin-4(3H)-one (**2c**).* White crystalline; 0.150 g, 92% yield. Mp: 176−177 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.20 (m, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.65−7.63 (m, 1H), 7.46−7.44 (m, 1H), 7.40−7.36 (m, 1H), 7.25−7.21 (m, 1H), 7.13 (d, J = 0.8 Hz, 1H), 4.95 (d, J = 2.4 Hz, 2H), 3.89 (s, 3H), 2.56 (s, 3H), 2.35 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 147.2, 144.9, 138.2, 138.1, 136.3, 131.3, 127.6, 127.0, 126.5, 123.8, 121.8, 120.7, 120.6, 110.1, 105.2, 78.5, 72.6, 36.2, 31.5, 21.5. IR (KBr) 3054, 2930, 2120, 1698, 1576, 1199, 798, 727 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O$ $[M + H]^+$ 328.1450, found 328.1464.

*6-Chloro-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-quinazolin-4(3H)-one (**2d**).* White crystalline; 0.140 g, 83% yield. Mp: 204−205 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33−8.32 (m, 1H), 7.73−7.68 (m, 3H), 7.43 (d, J = 8.0 Hz, 1H), 7.38−7.35 (m, 1H), 7.21 (t, J = 8.0 Hz, 1H), 7.15 (s, 1H), 4.93 (d, J = 2.5 Hz, 2H), 3.88 (s, 3H), 2.36 (t, J = 2.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 148.2, 145.3, 138.2, 135.2, 133.5, 130.7, 129.3, 126.8, 126.4, 124.0, 121.9, 121.7, 120.7, 110.1, 105.6, 78.1, 72.9, 36.4, 31.5. IR (KBr) 3100, 2931, 2119, 1680, 1580, 1469, 1335, 1210, 831, 743 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}ClN_3O$ $[M + H]^+$ 348.0904, found 348.0898.

*6-Bromo-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-quinazolin-4(3H)-one (**2e**).* White crystalline; 0.160 g, 80% yield. Mp: 207−208 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 2.0 Hz, 1H), 7.88−7.85 (m, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.44−7.42 (m, 1H), 7.39−7.35 (m, 1H), 7.23−7.19 (m, 1H), 7.16 (s, 1H), 4.94 (d, J = 2.4 Hz, 2H), 3.88 (s, 3H), 2.36 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 148.4, 145.6, 138.3, 138.0, 130.7, 129.6, 129.5, 126.8, 124.0, 122.0, 121.9, 121.3, 120.8, 110.1, 105.7, 78.1, 73.0, 36.5, 31.5. IR (KBr) 3056, 2963, 2124, 1680, 1586, 1465, 1326, 1156, 753 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}BrN_3O$ $[M + H]^+$ 392.0398, found 392.0387.

*6-Iodo-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (**2f**).* White crystalline; 0.190 g, 88% yield. Mp: 205−206 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, J = 2.0 Hz, 1H), 8.06−8.04 (m, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.21 (t, J = 8.0 Hz, 1H), 7.16 (s, 1H), 4.93 (d, J = 2.0 Hz, 2H), 3.88 (s, 3H), 2.36 (t, J = 2.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 148.5, 146.0, 143.6, 138.3, 135.9, 130.6, 129.4, 126.8, 124.1, 122.2, 121.9, 120.7, 110.1, 105.7, 92.2, 78.1, 72.9, 36.5, 31.5. IR (KBr) 3060, 2937, 2128, 1692, 1568, 1465, 1342, 827, 732 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}IN_3O$ $[M + H]^+$ 440.0260, found 440.0250.

*7-Fluoro-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-quinazolin-4(3H)-one (**2g**).* White crystalline; 0.150 g, 90% yield. Mp: 186−187 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40−8.37 (m, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.45−7.36 (m, 3H), 7.28−7.24 (m, 1H), 7.21 (t, J = 8.0 Hz, 1H), 7.17 (s, 1H), 4.94 (d, J = 2.5 Hz, 2H), 3.90 (s, 3H), 2.37 (t, J = 2.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7 (J = 253.6 Hz), 160.8, 149.3, 148.9, 138.3, 130.6, 129.8 (d, J = 10.6 Hz), 126.8, 124.1, 121.9, 120.7, 117.4, 116.5 (d, J = 23.5 Hz), 113.0 (d, J = 21.8 Hz), 110.1, 105.7, 78.2, 72.9, 36.4, 31.5. IR (KBr) 3046, 2941, 2126, 1693, 1568, 1471, 1339, 1272, 1146, 860, 721 cm^{-1}. HRMS (ESI) m/z for $C_{20}H_{15}FN_3O$ $[M + H]^+$ 332.1199, found 332.1194.

*5-Chloro-2-(1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-quinazolin-4(3H)-one (**2h**).* White crystalline; 0.140 g, 80% yield. Mp: 175−176 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 1H), 7.68−7.62 (m, 2H), 7.54−7.58 (m, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.38−7.36 (m, 1H), 7.23−7.20 (m, 1H), 7.18 (s, 1H), 4.91 (d, J = 2.5 Hz, 2H), 3.98 (s, 3H), 2.37 (t, J = 2.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 149.1, 148.8, 138.3, 134.6, 134.1, 130.6, 130.3, 126.9, 126.8, 124.1, 121.9, 120.7, 117.9, 110.1, 105.8, 78.3, 72.9, 36.5, 31.6. IR (KBr) 3062, 2953, 2123, 1681, 1586, 1460, 1344, 1224, 810, 735 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}ClN_3O$ $[M + H]^+$ 348.0904, found 348.0914.

*2-(1-Benzyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (**2i**).* White crystalline; 0.110 g, 58% yield. Mp: 124−125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (m, 1H), 7.81−7.70 (m, 3H), 7.55−7.48 (m, 2H), 7.37−7.33 (m, 1H), 7.25−7.22 (m, 2H), 7.15−7.09 (m, 3H), 6.89−6.88 (m, 2H), 5.59 (s, 2H), 4.43 (d, J = 2.4 Hz, 2H), 2.35 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 148.0, 146.7, 138.0, 137.8, 134.7, 130.5, 128.6, 127.7, 127.61, 127.60, 127.0, 126.9, 126.8, 124.2, 122.0, 120.8, 120.7, 110.4, 106.6, 78.5, 72.8, 47.9, 36.2. IR (KBr) 3058, 2907, 2123, 1672, 1576, 1470, 1334, 1173, 779, 722 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{20}N_3O$ $[M + H]^+$ 390.1606, found 390.1616.

*2-(1H-Indol-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (**2j**).* White crystalline; 0.110 g, 72% yield, mp: 210−211 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.36−8.32 (m, 1H), 7.82−7.73 (m, 3H), 7.61 (s, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.5 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 5.25 (d, J = 2.0 Hz, 2H), 2.54 (t, J = 2.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 147.3, 147.0, 136.3, 134.8, 128.8, 128.4, 127.1, 127.05, 127.0, 125.3, 122.2, 120.8, 119.9, 111.5, 107.5, 78.4, 73.7, 35.7. IR (KBr) 3296, 3058, 2124, 1678, 1552, 1474, 1396, 1230, 771 cm^{-1}. HRMS (ESI) m/z calcd for $C_{19}H_{14}N_3O$ $[M + H]^+$ 300.1137, found 300.1129.

*2-(1,5-Dimethyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (**2k**).* White crystalline; 0.140 g, 88% yield. Mp: 225−226 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40−8.37 (m, 1H), 7.83−7.77 (m, 2H), 7.57−7.53 (m, 1H), 7.50 (s, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.20−7.18 (m, 1H), 7.06 (s, 1H), 4.93 (d, J = 2.4 Hz, 2H), 3.86 (s, 3H), 2.48 (s, 3H), 2.34 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 148.1, 146.7, 136.8, 134.8, 130.9, 130.0, 127.7, 127.6, 127.1, 127.0, 125.7, 121.3, 120.7, 109.8, 105.0, 78.4, 72.6, 36.3, 31.5, 21.4. IR (KBr) 3061, 2915, 2127, 1697, 1582, 1471, 1340, 1170, 780, 728 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O$ $[M + H]^+$ 328.1450, found 328.1449.

*2-(5-Bromo-1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-quinazolin-4(3H)-one (**2l**).* White crystalline; 0.170 g, 87% yield. Mp: 255−256 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40−8.38 (m, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.84−7.80 (m, 1H), 7.78−7.76 (m, 1H), 7.59−7.55 (m, 1H), 7.45−7.43 (m, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.06 (d, J = 0.8 Hz, 1H), 4.91 (d, J = 2.4 Hz, 2H), 3.87 (s, 3H), 2.33 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 147.5, 146.6, 136.7, 134.9, 132.1, 128.4, 127.9, 127.7, 127.1, 126.8, 124.2, 120.8, 113.9, 111.6, 104.5, 78.2, 72.8, 36.1, 31.6. IR (KBr) 3071, 2962, 2124, 1694, 1584, 1468, 1170, 1100, 781, 722 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}BrN_3O$ $[M + H]^+$ 392.0398, found 392.0396.

*2-(6-Chloro-1-methyl-1H-indol-2-yl)-3-(prop-2-yn-1-yl)-quinazolin-4(3H)-one (**2m**).* White crystalline; 0.150 g, 91% yield. Mp: 225−226 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40−8.38 (m, 1H), 7.84−7.77 (m, 2H), 7.62 (d, J = 8.0 Hz, 1H), 7.59−7.55 (m, 1H), 7.43 (s, 1H), 7.19−7.16 (m, 1H), 7.11 (s, 1H), 4.93 (d, J = 2.4 Hz, 2H), 3.86 (s, 3H), 2.35 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 146.5, 145.6, 137.5, 133.9, 130.8, 128.9, 126.9, 126.6, 126.1, 124.4, 121.7, 120.5, 119.8, 109.1, 104.4, 77.2, 71.8, 35.1, 30.6. IR (KBr) 3058, 2959, 2125, 1690, 1582, 1470, 1283, 1065, 804, 771 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{15}ClN_3O$ $[M + H]^+$ 348.0904; found 348.0899.

*3-(But-2-yn-1-yl)-2-(1-methyl-1H-indol-2-yl)quinazolin-4(3H)-one (**2n**).* White crystalline; 0.150 g, 93% yield. Mp: 159−160 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, J = 8.0 Hz, 1H), 7.81−7.75 (m, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 7.13 (s, 1H), 4.88 (d, J = 2.0 Hz, 2H), 3.88 (s, 3H), 1.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 148.2, 146.8, 138.1, 134.6, 131.3, 127.6, 127.5, 127.0, 126.9, 123.7, 121.8, 120.9, 120.5, 110.0, 105.2, 80.5, 73.8, 36.6, 31.4, 3.6. IR (KBr) 3057, 2915, 2233, 1679, 1591, 1472, 1339, 1237, 781, 731 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O$ $[M + H]^+$ 328.1450, found 328.1441.

*2-(1-Methyl-1H-indol-2-yl)-3-(3-phenylprop-2-yn-1-yl)-quinazolin-4(3H)-one (**2o**).* White crystalline; 0.180 g, 93% yield. Mp: 152−153 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, J = 8.0 Hz, 1H), 7.82−7.78 (m, 2H), 7.73 (d, J = 8.0 Hz, 1H), 7.58−7.54 (m, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.33−7.25 (m, 5H), 7.21 (t, J = 8.0 Hz, 1H), 7.15 (s, 1H), 5.18 (s, 2H), 3.87 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 148.2, 146.7, 138.0, 134.7, 131.9, 131.3, 128.6, 128.3, 127.7, 127.1, 127.0, 123.7, 122.1, 121.8, 120.9, 120.6, 110.0, 105.1, 84.1, 83.7, 36.7, 31.4. IR (KBr) 3057, 2943, 2243, 1679,

DOI: 10.1021/acs.joc.7b02956
J. Org. Chem. XXXX, XXX, XXX−XXX

1570, 1470, 1238, 1170, 754, 690 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{26}H_{20}N_3O$ $[M + H]^+$ 390.1606, found 390.1618.

*2-(1-Methyl-1H-indol-2-yl)-3-(3-(trimethylsilyl)prop-2-ynyl)-quinazolin-4(3H)-one (**2p**).* White crystalline; 0.174 g, 90% yield. Mp: 136−137 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41−8.39 (m, 1H), 7.84−7.79 (m, 2H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.59−7.54 (m, 1H), 7.45−7.43 (m, 1H), 7.39−7.34 (m, 1H), 7.23−7.19 (m, 1H), 7.14 (d, *J* = 0.4 Hz, 1H), 4.96 (s, 2H), 3.89 (s, 3H), 0.13 (t, *J* = 3.6 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 148.2, 146.7, 138.0, 134.7, 127.6, 127.1, 127.0, 123.7, 121.7, 120.9, 120.5, 110.0, 105.3, 99.8, 89.5, 36.8, 31.4, − 0.3. IR (KBr) 3057, 2915, 2233, 1679, 1591, 1472, 1257, 841, 731 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{23}H_{24}N_3OSi$ $[M + H]^+$ 386.1683, found 386.1689.

*2-(1-Methyl-1H-pyrrol-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (**2q**).* White crystalline; 0.110 g, 83% yield, mp: 180−181 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.34−8.32 (m, 1H), 7.78−7.73 (m, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.50−7.46 (m, 1H), 6.94−6.93 (m, 1H), 6.85−6.83 (m, 1H), 6.26−6.25 (m, 1H), 4.96 (d, *J* = 2.4 Hz, 2H), 3.85 (s, 3H), 2.36 (t, *J* = 2.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 148.0, 147.0, 134.5, 127.2, 126.9, 126.8, 124.7, 120.2, 113.7, 108.2, 78.8, 72.4, 36.4, 35.8. IR (KBr) 3057, 2930, 2122, 1675, 1473, 1340, 1240, 958, 746 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{16}H_{14}N_3O$ $[M + H]^+$ 264.1137, found 264.1128.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b02956.

Spectra of compounds **3**, **5**, **2** and **1** (PDF)
X-ray structure of compound **3k** (CIF)
X-ray structure of compound **5d** (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the National Natural Science Foundation of China (21462008, 21562005), China Postdoctoral Science Foundation (2017M612869), Natural Science Foundation of Guangxi (2015GXNSFCA139001, 2016GXNSFFA380005, 2017GXNSFDA198045), State Key Laboratory for Chemistry and Molecular Engineering of Medicinal Resources, Ministry of Science and Technology of China (CMEMR2015-A05, CMEMR2014-A01), and "Overseas 100 Talents Program" of Guangxi Higher Education are greatly appreciated.

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(14) CCDC: 1568829 (compound **3k**) contains the supplementary crystallographic data for this paper. These data can be obtained free of

DOI: 10.1021/acs.joc.7b02956
J. Org. Chem. XXXX, XXX, XXX−XXX

charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(15) CCDC: 1568828 (compound **5d**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

DOI: 10.1021/acs.joc.7b02956
J. Org. Chem. XXXX, XXX, XXX−XXX