JOC The Journal of Organic Chemistry

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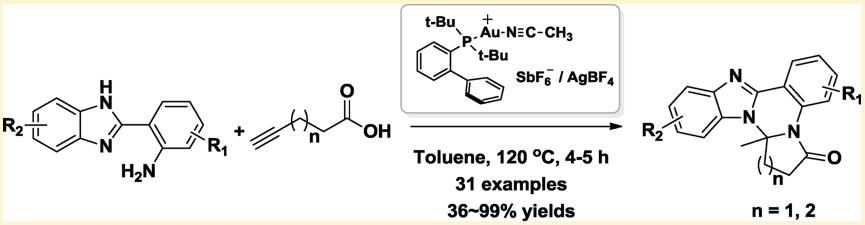
Au(I)/Ag(I)-Catalyzed Cascade Approach for the Synthesis of Benzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolinones

Xun Ji,[†,‡] Yu Zhou,*[,†] Jinfang Wang,[†] Linxiang Zhao,[‡] Hualiang Jiang,[†,‡] and Hong Liu*[,†]

[†]State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China

[‡]School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, Liaoning 110016, China

Supporting Information



ABSTRACT: An efficient and facile Au(I)/Ag(I)-catalyzed cascade method has been developed for one-pot synthesis of the complex polycyclic heterocycles benzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolinone derivatives through treatment of the substituted 2-(1*H*-benzo[*d*]imidazol-2-yl)anilines with 4-pentynoic acid or 5-hexynoic acid. The strategy features a Au(I)/Ag(I)-catalyzed one-pot cascade process involving the formation of three new C−N bonds in high yields, and with broad a substrate scope.

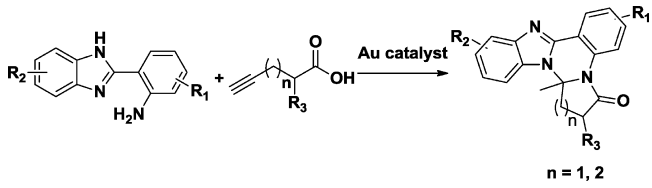
INTRODUCTION

Nitrogenous heterocyclic compounds are widely distributed in alkaloids and biologically active synthetic substances.[1−9] For example, compounds containing benzimidazole fragments are usually used as enzyme inhibitors.[10−12] Compounds that contain quinazoline moieties have various biological and medicinal properties, such as potent tyrosine kinase inhibitors,[13−16] DNA-binding agents,[17] α_{1A} adrenoceptor antagonists,[18] and β-catenin/Tcf4 inhibitors.[19] Furthermore, combinations of benzimidazole and quinazoline moieties have been utilized as anticancer,[20] antimicrobial,[21] and anti-inflammatory agents.[22,23] Nevertheless, there are few methods available for the synthesis of benzimidazoquinazoline derivatives.[21,24,25] Recently, gold-catalyzed cascade reactions for the synthesis of polycyclic heterocycles have received significant attention, with many efficient strategies from various research groups reported.[26−31] As part of our ongoing efforts to construct potential bioactive polycyclic compounds through new transition-metal-catalyzed cascade strategies,[32−37] we present an efficient and facile gold-catalyzed cascade reaction for the synthesis of highly substituted benzo[4,5]imidazo[1,2-*c*]-pyrrolo[1,2-*a*]quinazolinones (Scheme 1).

RESULTS AND DISCUSSION

As shown in Table 1, 2-(1*H*-benzo[*d*]imidazol-2-yl)aniline (**1A**) and 4-pentynoic acid (**2a**) were chosen as model substrates to optimize reaction conditions, including catalysts and solvents. First, different gold (Au) and silver (Ag) catalysts, namely, [Au{P(*t*-Bu)$_2$(*o*-biphenyl)}{CH$_3$CN}]SbF$_6$ (Au catalyst I), AuCl(PPh$_3$) (Au catalyst II), AgSbF$_6$, AgBF$_4$, and their

Scheme 1. Synthesis of Benzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]quinoxalin-3(2*H*)-one

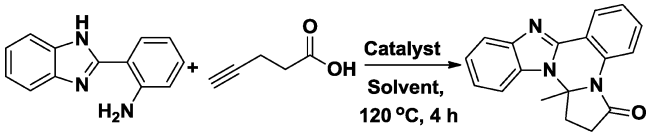


mixtures, were tested at 120 °C for 4 h in a sealed tube, using toluene as the solvent. Among the catalysts examined, Au catalyst I and II were found to be the more effective than others (Table 1, entries 1−5). Silver catalysts such as AgBF$_4$ and AgSbF$_6$ were also found to be effective for the transformation[38] (Table 1, entries 6 and 7). Improving the amounts of Au catalyst I and AgBF$_4$ to 30 mol % increased the yields to 88% and 81% (Table 1, entries 8 and 9), respectively. In the absence of either gold or silver catalysts, only 10% of the desired product could be detected, even after the reaction time was prolonged to 12 h (Table 1, entry 10). We examined the possible additive effects from the combination of different catalysts, AgSbF$_6$, AgBF$_4$, AgO$_2$CCF$_3$, AgOTf, and TFA as a cocatalyst of gold (Table 1, entries 11−17). Excellent yields, 95% and 92%, were obtained for Au catalyst I/AgBF$_4$ and Au catalyst II/AgSbF$_6$, respectively (Table 1, entries 12 and 13). Subsequently, we screened different organic solvents and

Received: February 8, 2013
Published: April 4, 2013

dx.doi.org/10.1021/jo400228g | *J. Org. Chem.* 2013, 78, 4312−4318

Table 1. Optimization of the Reaction Conditions of Tandem Synthesis of 3Aa[a]



1A 2a 3Aa

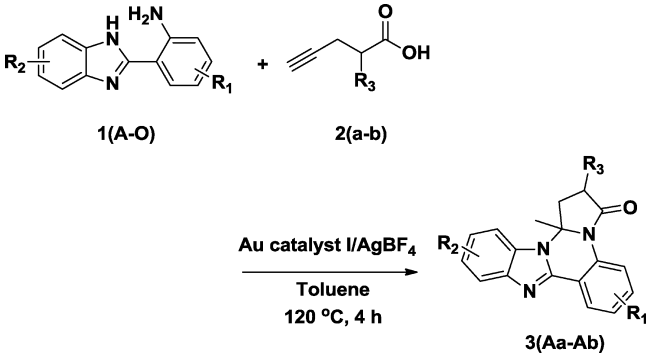
entry	catalytic conditions[b]	solvent	yield (%)
1	Au catalyst I	toluene	82
2	Au catalyst II	toluene	80
3	Au catalyst III	toluene	50[c]
4	Au catalyst IV	toluene	75[c]
5	Au catalyst V	toluene	43[d]
6	$AgSbF_6$	toluene	50[d]
7	$AgBF_4$	toluene	75
8	Au catalyst I	toluene	88[e]
9	$AgBF_4$	toluene	81[e]
10	none	toluene	10[d]
11	Au catalyst I/$AgSbF_6$	toluene	88
12	**Au catalyst I/$AgBF_4$**	**toluene**	**95**
13	**Au catalyst II/$AgSbF_6$**	**toluene**	**92**
14	Au catalyst II/$AgBF_4$	toluene	80
15	Au catalyst I/$AgOCOCF_3$	toluene	57
16	Au catalyst I/AgOTf	toluene	64
17	Au catalyst I/TFA	toluene	42
18	Au catalyst I/$AgBF_4$	$ClCH_2CH_2Cl$	84
19	Au catalyst I/$AgBF_4$	THF	15
20	Au catalyst I/$AgBF_4$	CH_3OH	10
21	Au catalyst I/$AgBF_4$	dioxane	80
22	Au catalyst I/$AgBF_4$	$CHCl_3$	83
23	Au catalyst I/$AgBF_4$	H_2O	55

[a]**1A** (0.1 mmol), **2a** (0.2 mmol), Au catalyst (10 mol %), Ag(I) (20 mol %), 120 °C, 4 h. [b]Au catalyst I = [Au{P(*t*-Bu)$_2$(*o*-biphenyl)}-{CH_3CN}]SbF_6; Au catalyst II = $AuCl(PPh_3)$; Au catalyst III = AuCl[P(*t*-Bu)$_2$(*o*-biphenyl)]; Au catalyst IV = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidenegold(I) chloride; Au catalyst V = [tris(2,4-di-*tert*-butylphenyl)phosphite]gold chloride. [c]The reaction time was prolonged to 6 h. [d]The reaction time was prolonged to 12 h. [e]The amount of catalyst was improved to 30 mol %.

identified toluene as the most effective solvent for this cascade transformation (Table 1, entries 12 and 18−23). Therefore, the optimized reaction conditions were demonstrated as 2-(1*H*-benzo[*d*]imidazol-2-yl)aniline (0.1 mmol, **1A**) and 4-pentynoic acid (0.2 mmol, **2a**) mediated with 10 mol % Au catalyst I and 20 mol % $AgBF_4$ in toluene at 120 °C for 4 h.

On the basis of the aforementioned optimal conditions, we extended the substrate scopes of this cascade transformation. As indicated in Table 2, a variety of substituted 2-(1*H*-benzo[*d*]-imidazol-2-yl)anilines efficiently produced moderate to excellent yields (60−99%) of the desirable benzimidazoquinazoline products **3Aa-Ab**. The position and molecular property of substituents on 2-(1*H*-benzo[*d*]imidazol-2-yl)aniline were important factors in influencing the yields of the corresponding products (Table 2, entries 1−15). When an electron-donating group was introduced to position R_1, such as methyl and methoxyl at *meta* and *para* positions of the aniline, respectively, a lower product yield was observed (Table 2, entries 2−5). Furthermore, when the methyl group was at the *ortho* position of the aniline (Table 2, entry 2), the product yield was significantly decreased, which was most likely due to steric hindrance from the methyl group. However, when certain

Table 2. Au(I)/Ag(I)-Catalyzed One-Pot Tandem Synthesis of 3[a]



1(A-O) 2(a-b) 3(Aa-Ab)

entry	product		yield (%)	entry	product		yield (%)
1		3Aa	95	9		3Ja	90
2		3Ba	60	10		3La	80
3		3Da	75	11		3Ma	99
4		3Ea	81	12		3Na	84[b]
5		3Fa	88	13		3Oa	75
6		3Ga	81	14		3Pa	82
7		3Ha	92	15		3Qa	92
8		3Ia	98	16		3Ab	79 (1:1.2, *dr*)[c]

[a]**1** (0.1 mmol), **2** (0.2 mmol), Au catalyst I (10 mol %), $AgBF_4$ (20 mol %), toluene (2−3 mL). [b]The ratio of isomers was 1:1, determined by ^1H nuclear magnetic resonance (NMR). [c]The reaction time was prolonged to 12 h.

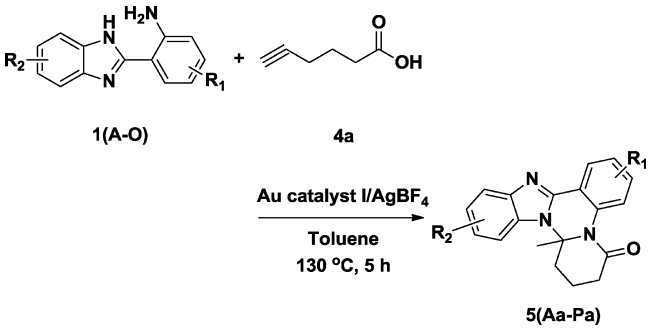
halogen atoms were introduced to the R_1 position, good to excellent yields of the products were obtained (Table 2, entries 6−11). Excitingly, excellent yields were achieved on addition of a chlorine atom at the *para* position of aniline (Table 2, entry 8), and two fluorine atoms at the *meta* and *para* positions of aniline (Table 2, entry 11), at 98% and 99%, respectively. These results indicated that the property of R_1 played an important role in determining the yield of the substituted aniline. We then explored the influence of introducing methyl groups or halogens to the R_2 group (Table 2, entries 12−15). The results indicated that the introduction of either a methyl group or a chlorine atom led to a decrease in the yield of the corresponding product (Table 2, entries 12−14). However, an excellent yield was produced when the 1*H*-benzo[*d*]imidazole moiety was replaced with 1*H*-naphtho[2,3-*d*]imidazole (Table 2, entry 15, 92%), which was likely to be a result of the electron effects of the naphthaline ring. In addition, a substitution of an alkynoic acid group at position R_3 was also explored but produced a relatively lower product yield (79%), despite the

dx.doi.org/10.1021/jo400228g | J. Org. Chem. 2013, 78, 4312−4318

prolonged reaction time (12 h). One possible explanation could be the steric effect of the long chain alkyl group (*n*-hexyl group).

We then chose substituted 2-(1*H*-benzo[*d*]imidazol-2-yl)-aniline (**1A-O**) and 5-hexynoic acid (**4a**) as model substrates to investigate whether this protocol could be applied to produce benzo[4,5]imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-ones that included a six-membered lactam fragment (**5Aa-Pa**). As demonstrated in Table 3, the yields for the six-membered

Table 3. Scopes of Au(I)/Ag(I)-Catalyzed Tandem Synthesis of 5[a]



entry	product		yield (%)	entry	product		yield (%)
1		5Aa	87	9		5Ia	71
2		5Ba	65	10		5Ja	90
3		5Ca	70	11		5Ka	92
4		5Da	60	12		5La	75
5		5Ea	80	13		5Ma	73
6		5Fa	74	14		5Oa	45
7		5Ga	67	15		5Pa	36
8		5Ha	85				

[a]**1** (0.1 mmol), **2** (0.2 mmol), Au catalyst I (10 mol %), $AgBF_4$ (20 mol %), toluene (2−3 mL); the reaction was performed at 130 °C for 5 h.

lactam products, with 5-hexynoic acid (**4a**) as the starting material, were relatively low compared to the yields obtained from 4-pentynoic acid (**2a**) as the starting material, even after temperatures were elevated to 130 °C (data not shown). Overall, the influences of the molecular property and positioning of the substituents (**1A-O**) on the yields listed in Table 3 were similar to those listed in Table 2. Namely, an electron-donating group at position R_1 resulted in decreased yields, whereas increased yields were observed only when a single fluorine atom was introduced to the same position (Table 3, entries 1−13). Introducing an electron-donating group or a halogen group to position R_2 resulted in significantly decreased yields (Table 3, entries 14 and 15). In view of these findings, this cascade strategy could serve as a general approach for the preparation of fused benzimidazoquinazoline molecular scaffolds, which have potential biological activities that could be applied to the screening of lead compounds.

On the basis of these results and our previous findings,[32,33] we have postulated a plausible mechanism for this cascade transformation. As shown in Scheme 2, the gold catalyst activated the unactivated alkynoic acid **2** to generate activated enol-lactone intermediate **A**.[39−41] This intermediate was then attracted by an aromatic primary amino group, 2-(1*H*-benzo[*d*]imidazol-2-yl)aniline **1**, to form an ammonolysis product **B**. Then *N*-acyl iminium ion was formed and converted to the transition state **C** in the presence of gold or silver catalyst. Finally, the target product **3** was produced through a nucleophilic addition of the amine group. Furthermore, we have also treated the enol-lactone intermediate **A** with the amino compound **1** under the optimized conditions, and the target product **3** was obtained with high yield (91%).[42] The product **3Aa** was recrystallized from dichloromethane, and the structure was characterized using X-ray crystallography (Figure S1, see the Supporting Information for details).[43]

CONCLUSIONS

In summary, we have developed an efficient and facile method for one-pot synthesis of polycyclic heterocycles benzo[4,5]-imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolinones from two simple starting materials via an Au(I)/Ag(I)-catalyzed domino coupling/cyclization reaction. We present a straightforward approach in constructing novel polycyclic molecular architectures that form three C−N bonds *via* a one-pot procedure with moderate to excellent product yields. On the basis of a large assortment of bioactive benzimidazoquinazolines, we believe that this new synthetic method will serve as a valuable tool to efficiently construct new members of fused isoquinoline derivatives in drug discovery, with potential for biological applications.

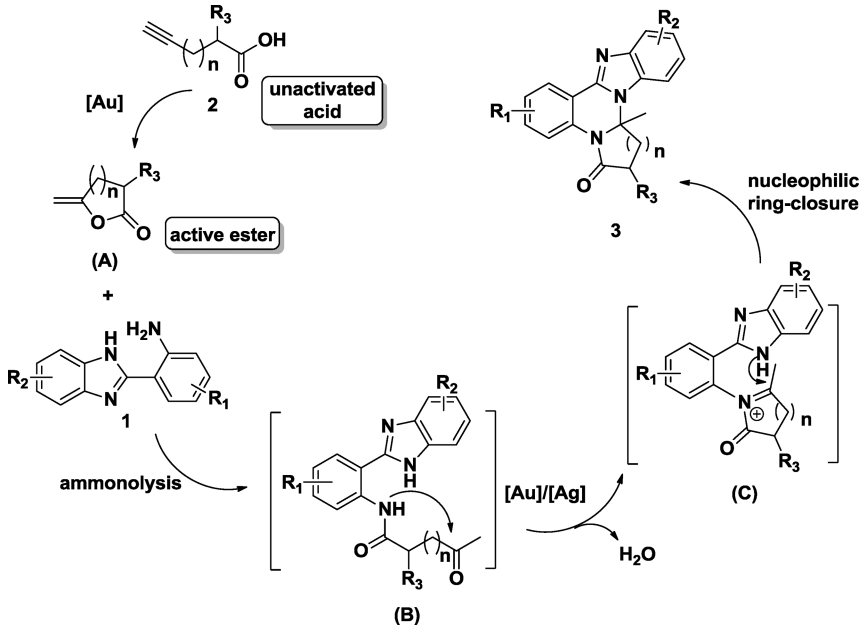
EXPERIMENTAL SECTION

Chemistry. The reagents (chemicals) were purchased and used without further purification. Nuclear magnetic resonance (NMR) spectroscopy was performed on a Bruker AMX-400 NMR instrument (IS as TMS). Chemical shifts were reported in parts per million (δ) downfield from tetramethylsilane. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Low- and high-resolution mass spectra (Micromass Ultra Q-TOF) were obtained with electrospray and matrix-assisted laser desorption ionization (ESI).

General Procedure for Synthesis of Benzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Aa as an example). To a solution of 4-pentynoic acids (98 mg, 1.0 mmol) in toluene (2−3 mL) were added Au catalyst I ([Au{P(*t*-Bu)$_2$(*o*-biphenyl)}{CH_3CN}]-SbF_6, 39 mg, 10 mol %) and $AgBF_4$ (20 mg, 20 mol %). After the mixture had been stirred for 10 min at room temperature, 2-(1*H*-benzo[*d*]imidazol-2-yl)aniline (105 mg, 0.5 mmol) was added. Subsequently, the reaction vial was sealed, and the mixture was heated to 120 °C for 4 h. Then the cold mixture was concentrated under reduced pressure, and the resulting reside was purified by flash column chromatography (petroleum ether/ethyl acetate = 2/1) to afford the expected product **3Aa** in 95% yield (138 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.33 (d, J = 8.0 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.51−7.55 (t, J = 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.34−7.38 (t, J = 8.0 Hz, 1H), 7.27−7.33 (m, 2H), 2.96−3.04 (m, 2H), 2.84−2.94 (m, 1H), 2.72−2.80 (m, 1H), 1.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.2, 145.7, 144.1, 132.2, 131.8, 131.2, 125.9, 125.6, 123.3, 123.0, 121.6, 120.3, 117.8, 110.1, 78.2, 32.7, 30.0, 24.8. LRMS (ESI): m/z 290 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{18}H_{15}N_3ONa$ $[M + Na]^+$ 312.1113, found 312.1127.

dx.doi.org/10.1021/jo400228g | J. Org. Chem. 2013, 78, 4312−4318

Scheme 2. A Plausible Mechanism



5,14a-Dimethyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]-pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Ba, 60%, 86 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.28−7.43 (m, 4H), 3.41−3.46 (m, 1H), 2.82−2.89 (m, 2H), 2.58−2.65 (m, 1H), 2.39 (s, 3H), 1.68 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.1, 148.4, 144.4, 137.0, 135.8, 133.4, 132.9, 129.7, 125.7, 125.5, 122.0, 112.5, 80.8, 33.0, 31.0, 28.0, 20.7. LRMS (ESI): m/z 304 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{17}N_3ONa$ $[M + Na]^+$ 326.1269, found 326.1283.

7,14a-Dimethyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]-pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Da, 75%, 107 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.34−7.25 (m, 3H), 2.97−3.03 (m, 2H), 2.82−2.91 (m, 1H), 2.71−2.78 (m, 1H), 2.42 (s, 3H), 1.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.0, 147.9, 146.1, 137.8, 134.0, 133.8, 131.8, 127.7, 125.2, 124.9, 123.5, 122.3, 119.5, 112.1, 80.2, 34.6, 31.9, 26.6, 22.9. LRMS (ESI): m/z 304 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{17}N_3ONa$ $[M + Na]^+$ 326.1269, found 326.1269.

7-Methoxy-14a-methyl-1,14a-dihydrobenzo[4,5]imidazo-[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Ea, 81%, 114 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.13 (d, J = 12.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.80 (s, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.25−7.34 (m, 2H), 7.08 (d, J = 8.0 Hz, 1H), 3.91 (s, 3H), 2.95−3.03 (m, 2H), 2.82−2.91 (m, 1H), 2.64−2.77 (m, 1H), 1.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.9, 159.4, 147.7, 145.8, 133.8, 127.6, 125.4, 125.2, 125.0, 122.3, 120.9, 120.8, 112.2, 110.3, 80.3, 57.7, 34.6, 31.9, 26.6. LRMS (ESI): m/z 320 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{18}N_3O_2$ $[M + H]^+$ 320.1399, found 320.1384.

6,7-Dimethoxy-14a-methyl-1,14a-dihydrobenzo[4,5]-imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Fa, 88%, 120 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (s, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.76 (s, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.28−7.31 (m, 2H), 4.01 (s, 3H), 3.99 (s, 3H), 2.73−3.04 (m, 4H), 1.64 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.0, 153.3, 149.1, 148.1, 146.0, 133.8, 128.8, 124.9, 124.8, 121.9, 112.1, 111.9, 108.9, 106.7, 80.5, 58.3, 58.2, 34.5, 32.0, 26.3. LRMS (ESI): m/z 350 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{20}H_{20}N_3O_3$ $[M + H]^+$ 350.1505, found 350.1490.

5-Chloro-14a-methyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Ga, 81%, 113 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.25 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.58−7.61 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.51−7.54 (m, 1H), 7.43 (t, J = 8.0 Hz, 1H), 7.33−7.36 (m, 2H), 3.39−3.48 (m, 1H), 2.85−2.97 (m, 2H), 2.56−2.68 (m, 1H), 1.71 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.5, 147.6, 146.0, 134.1, 133.9, 133.0, 131.9, 130.5, 126.1, 125.6, 125.5, 125.2, 122.7, 112.4, 80.7, 33.1, 30.9, 28.2. LRMS (ESI): m/z 324 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{18}H_{14}N_3ONaCl$ $[M + Na]^+$ 346.0723, found 346.0729.

6-Chloro-14a-methyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Ha, 92%, 128 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.32 (d, J = 4.0 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.29−7.35 (m, 3H), 2.80−3.03 (m, 4H), 1.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 147.0, 145.8, 139.2, 135.0, 133.6, 128.7, 128.3, 125.6, 125.3, 123.7, 122.3, 118.0, 112.1, 80.3, 34.6, 31.9, 26.8. LRMS (ESI): m/z 324 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{18}H_{15}N_3OCl$ $[M + H]^+$ 324.0904, found 324.0904.

7-Chloro-14a-methyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Ia, 98%, 138 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.31 (d, J = 4.0 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 2H), 7.29−7.35 (m, 2H), 3.00−3.05 (m, 2H), 2.74−2.94 (m, 2H), 1.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 146.5, 146.1, 133.9, 133.5, 133.0, 132.6, 127.3, 125.7, 125.2, 125.0, 122.6, 121.3, 112.2, 80.3, 34.7, 31.9, 26.8. LRMS (ESI): m/z 324 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{18}H_{15}N_3OCl$ $[M + H]^+$ 324.0904, found 324.0899.

6-Fluoro-14a-methyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Ja, 90%, 128 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.28−8.31 (dd, J_1 = 4.0 Hz, J_2 = 4.0 Hz, 1H), 8.04−8.08 (dd, J_1 = 12.0 Hz, J_2 = 4.0 Hz, 1H), 7.80−7.82 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.25−7.31 (m, 2H), 7.05 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 2.98−3.01 (m, 2H), 2.79−2.88 (m, 2H), 1.64 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 166.1 (d, J = 200.0 Hz), 147.2, 146.1, 135.7 (d, J = 9.0 Hz), 133.7, 129.4 (d, J = 8.0 Hz), 125.3, 125.1, 122.2, 116.0, 115.4 (d, J = 18.0 Hz), 112.0, 111.1 (d, J = 21.0 Hz), 80.3, 34.6, 31.9, 26.8. LRMS (ESI): m/z 308 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{18}H_{15}N_3OF$ $[M + H]^+$ 308.1199, found 308.1207.

6-Bromo-14a-methyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3La, 80%, 107 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.48 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.30−7.35 (m, 2H), 3.00−3.03 (m, 2H), 2.76−2.94 (m, 2H), 1.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.0, 147.0, 146.0, 135.0, 133.8, 131.2, 128.7, 127.2, 126.5, 125.6, 125.2, 122.4, 118.6, 112.1, 80.3, 34.6, 31.9, 26.9. LRMS (ESI): m/z 368 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{18}H_{15}N_3OBr$ $[M + H]^+$ 368.0398, found 368.0403.

dx.doi.org/10.1021/jo400228g | J. Org. Chem. 2013, 78, 4312−4318

6,7-Difluoro-14a-methyl-1,14a-dihydrobenzo[4,5]imidazo-[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Ma, 99%, 138 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16−8.21 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 8.11 (t, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.28−7.34 (m, 2H), 2.99−3.04 (m, 2H), 2.75−2.93 (m, 2H), 1.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.0, 153.5 (dd, J_1 = 201.0 Hz, J_2 = 11.0 Hz), 150.2 (dd, J_1 = 198.0 Hz, J_2 = 11.0 Hz), 146.2, 146.0, 133.7, 130.8 (d, J = 6.0 Hz), 125.7, 125.3, 122.5, 116.7, 116.0 (d, J = 16.0 Hz), 113.4 (d, J = 18.0 Hz), 112.1, 80.4, 34.6, 31.8, 26.7. LRMS (ESI): m/z 326 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{18}H_{14}N_3OF_2$ $[M + H]^+$ 326.1105, found 326.1104.

11,14a-Dimethyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]-pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Na, 84%, 120 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.29−8.33 (br, 2H), 8.24 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 8.0 Hz, 1H), 7.62 (s, 1H), 7.51 (t, J = 8.0 Hz, 2H), 7.30−7.37 (q, J = 8.0 Hz, 3H), 7.23 (s, 1H), 7.09−7.15 (q, J = 8.0 Hz, 2H), 2.97−3.02 (m, 4H), 2.83−2.93 (m, 2H), 2.73−2.80 (m, 2H), 2.50 (s, 3H), 2.48 (s, 3H), 1.65 (s, 3H), 1.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.2, 147.7, 147.3, 146.5, 144.2, 134.1, 133.0, 132.9, 127.8, 127.5, 127.4, 126.7, 126.5, 123.6, 122.1, 121.8, 112.1, 111.6, 80.2, 80.1, 34.7, 34.6, 32.0, 26.7, 26.6, 23.9, 23.4. LRMS (ESI): m/z 304 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{17}N_3ONa$ $[M + Na]^+$ 326.1269, found 326.1267.

11,12,14a-Trimethyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Oa, 75%, 105 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.29 (d, J = 8.0 Hz, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.48 (t, J = 4.0 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.20 (s, 1H), 2.98−3.02 (m, 2H), 2.83−2.92 (m, 1H), 2.72−2.79 (m, 1H), 2.39 (s, 3H), 2.37 (s, 3H), 1.62 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 145.1, 142.8, 132.7, 132.1, 130.9, 130.5, 125.9, 125.5, 121.7, 120.4, 118.2, 110.5, 78.3, 32.8, 30.1, 24.8, 20.8, 20.4. LRMS (ESI): m/z 318 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{20}H_{21}N_3O$ $[M + H]^+$ 318.1606, found 318.1596.

11,12-Dichloro-14a-methyl-1,14a-dihydrobenzo[4,5]-imidazo[1,2-*c*]pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Pa, 82%, 111 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24−8.30 (q, J = 8.0 Hz, 2H), 7.91 (s, 1H), 7.51−7.59 (m, 2H), 7.38 (t, J = 8.0 Hz, 1H), 2.77−3.01 (m, 4H), 1.66 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.1, 147.8, 143.6, 132.5, 132.1, 131.0, 127.4, 127.2, 126.2, 126.0, 121.9, 121.4, 117.2, 111.4, 78.4, 32.6, 30.0, 25.0. LRMS (ESI): m/z 358 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{18}H_{14}N_3OCl_2$ $[M + H]^+$ 358.0514, found 358.0521.

16a-Methyl-1,16a-dihydronaphtho[2′,3′:4,5]imidazo[1,2-*c*]-pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Qa, 92%, 126 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.39−8.41 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 8.28−8.30 (d, J = 8.0 Hz, 2H), 7.97 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.78 (s, 1H), 7.55−7.59 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.35−7.45 (m, 3H), 3.08−3.12 (m, 2H), 2.77−2.96 (m, 2H), 1.68 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.2, 151.3, 145.8, 134.9, 134.5, 134.0, 132.5, 132.4, 130.3, 129.3, 128.2, 127.8, 126.8, 125.9, 123.6, 119.3, 119.2, 108.0, 80.4, 34.5, 32.0, 26.2. LRMS (ESI): m/z 340 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{22}H_{18}N_3O$ $[M + H]^+$ 340.1450, found 340.1463.

2-Hexyl-14a-methyl-1,14a-dihydrobenzo[4,5]imidazo[1,2-*c*]-pyrrolo[1,2-*a*]quinazolin-3(2*H*)-one (3Ab, 79%, 148 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.32 (d, J = 8.0 Hz, 2H), 8.26 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.46−7.55 (m, 4H), 7.27−7.39 (m, 6H), 3.38 (t, J = 8.0 Hz, 1H), 3.16 (q, J = 8.0 Hz, 1H), 2.73−2.92 (m, 2H), 2.63 (t, J = 12.0 Hz, 2H), 2.05 (m, 2H), 1.55−1.69 (m, 8H), 1.24−1.50 (m, 16H), 0.85−0.95 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.7, 175.1, 147.9, 147.7, 146.0, 134.3, 134.2, 133.8, 133.2, 133.0, 127.6, 127.5, 125.2, 125.1, 125.0, 122.2, 112.3, 112.2, 79.6, 78.4, 43.2, 42.8, 41.6, 38.9, 34.9, 33.6, 33.5, 32.1, 31.0, 30.9, 29.9, 29.7, 28.9, 26.5, 24.5, 24.4, 16.0, 15.9. LRMS (ESI): m/z 374 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{24}H_{28}N_3O$ $[M + H]^+$ 374.2232, found 374.2236.

9a-Methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]imidazo[1,2-*c*]-pyrido[1,2-*a*]quinazolin-6-one (5Aa, 87%, 126 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27−8.30 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.64−7.67 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.50 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.40 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.24−7.33 (m, 2H), 3.07−3.14 (m, 1H), 2.78−2.91 (m, 2H), 2.56−2.64 (m, 1H), 2.04−2.18 (m, 2H), 1.60 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.3, 149.3, 146.0, 136.3, 134.0, 132.1, 129.3, 128.8, 127.4, 125.3, 124.7, 123.4, 122.4, 113.2, 78.8, 36.4, 35.5, 29.2, 18.9. LRMS (ESI): m/z 304 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{18}N_3O$ $[M + H]^+$ 304.1450, found 304.1463.

4,9a-Dimethyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]imidazo-[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ba, 65%, 92 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.13 (t, J = 4.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.28−7.30 (m, 2H), 3.23−3.29 (m, 1H), 2.67−2.79 (m, 2H), 2.54−2.61 (m, 1H), 2.25 (s, 3H), 2.06−2.10 (m, 2H), 1.53 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.5, 150.1, 145.7, 138.2, 135.9, 134.5, 133.7, 129.5, 125.5, 125.4, 124.7, 124.5, 122.4, 112.9, 79.0, 35.9, 35.4, 20.1, 19.1. LRMS (ESI): m/z 318 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{20}H_{20}N_{23}O$ $[M + H]^+$ 318.1606, found 318.1591.

3,9a-Dimethyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]imidazo-[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ca, 70%, 100 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 4.0 Hz, 1H), 7.47 (s, 1H), 7.21−7.30 (m, 3H), 3.07−3.13 (m, 1H), 2.77−2.90 (m, 2H), 2.58−2.64 (m, 1H), 2.45 (s, 3H), 2.04−2.19 (m, 2H), 1.59 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.4, 147.8, 144.2, 140.8, 134.3, 132.1, 128.0, 127.8, 125.4, 123.2, 122.7, 120.5, 119.0, 111.3, 76.9, 34.6, 33.7, 27.3, 31.9, 17.1. LRMS (ESI): m/z 318 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{20}H_{20}N_{23}O$ $[M + H]^+$ 318.1606, found 318.1619.

2,9a-Dimethyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]imidazo-[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Da, 60%, 85 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.09 (s, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 2H), 7.23−7.31 (m, 3H), 3.03−3.10 (m, 1H), 2.75−2.89 (m, 2H), 2.53−2.61 (m, 1H), 2.43 (s, 3H), 2.03−2.13 (m, 2H), 1.58 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.5, 149.4, 145.7, 138.8, 133.9, 133.7, 133.1, 129.0, 127.6, 125.3, 124.8, 122.9, 122.3, 113.2, 78.9, 36.4, 35.4, 29.1, 22.9, 18.9. LRMS (ESI): m/z 318 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{20}H_{19}N_3ONa$ $[M + Na]^+$ 340.1426, found 340.1422.

2-Methoxy-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ea, 80%, 111 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 4.0 Hz, 1H), 7.55 (t, J = 8.0 Hz, 2H), 7.23−7.31 (m, 2H), 7.03−7.06 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 3.91 (s, 3H), 3.06 (t, J = 12.0 Hz, 1H), 2.74−2.89 (m, 2H), 2.52−2.60 (m, 1H), 2.02−2.12 (m, 2H), 1.58 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 160.0, 149.4, 145.9, 134.0, 130.5, 129.4, 125.3, 124.8, 124.3, 122.4, 120.1, 113.2, 109.8, 79.1, 57.8, 36.4, 35.4, 29.0, 19.0. LRMS (ESI): m/z 334 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{20}H_{20}N_3O_2$ $[M + H]^+$ 334.1556, found 334.1548.

2,3-Dimethoxy-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo-[4,5]imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Fa, 74%, 100 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.51−7.59 (m, 1H), 7.44−7.48 (m, 1H), 7.34 (d, J = 4.0 Hz, 1H), 7.33 (s, 1H), 4.12 (s, 3H), 4.06 (s, 3H), 3.49 (t, J = 8.0 Hz, 2H), 2.81 (t, J = 8.0 Hz, 2H), 2.37 (m, 2H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 208.2, 149.9, 148.6, 145.4, 138.9, 138.1, 132.3, 128.8, 125.7, 123.5, 122.8, 56.6, 56.3, 42.5, 34.71, 31.5, 19.6. LRMS (ESI): m/z 364 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{21}H_{22}N_3O_3$ $[M + H]^+$ 364.1661, found 364.1660.

4-Chloro-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ga, 67%, 93 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.21 (d, J = 8.0 Hz, 1H), 7.86 (m, 1H), 7.55 (m, 2H), 7.41 (t, J = 8.0 Hz, 1H), 7.27−7.34 (m, 2H), 3.15−3.19 (m, 1H), 2.77−2.85 (m, 2H), 2.56−2.62 (m, 1H), 2.09−2.14 (m, 2H), 1.58 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.3, 146.9, 144.1, 132.9, 132.6, 132.0, 131.6, 128.5, 124.8, 124.2, 123.9, 123.0, 120.8, 111.2, 77.2, 34.1, 33.6, 27.4, 17.3. LRMS (ESI): m/z 338 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{16}N_3ONaCl$ $[M + Na]^+$ 360.0880, found 360.0876.

3-Chloro-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ha, 85%, 118 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.21 (d, J = 8.0 Hz, 1H), 7.85

dx.doi.org/10.1021/jo400228g | J. Org. Chem. 2013, 78, 4312−4318

(d, J = 8.0 Hz, 1H), 7.70 (d, J = 4.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.27−7.30 (m, 2H), 3.07−3.14 (m, 1H), 2.80−2.89 (m, 2H), 2.60−2.66 (m, 1H), 2.04−2.17 (m, 2H), 1.60 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.3, 146.7, 144.2, 136.0, 135.2, 132.1, 127.7, 127.4, 126.4, 123.6, 123.0, 120.7, 120.2, 111.4, 77.3, 34.5, 33.6, 27.4, 17.0. LRMS (ESI): m/z 338 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{17}N_3OCl$ $[M + H]^+$ 338.1060, found 338.1064.

2-Chloro-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ia, 71%, 98 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.28 (d, J = 4.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.42−7.45 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H) 7.27−7.33 (m, 2H), 3.05−3.11 (m, 1H), 2.77−2.91 (m, 2H), 2.54−2.62 (m, 1H), 2.03−2.15 (m, 2H), 1.59 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 148.0, 145.7, 141.1, 134.6, 134.5, 133.9, 132.1, 130.8, 127.1, 125.8, 125.1, 124.7, 122.6, 113.3, 79.0, 35.4, 34.9, 29.2, 18.9. LRMS (ESI): m/z 338 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{17}N_3OCl$ $[M + H]^+$ 338.1060, found 338.1045.

3-Fluoro-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ja, 90%, 127 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98 (dd, J_1 = 4.0 Hz, J_2 = 4.0 Hz, 1H), 7.87 (d, J = 4.0 Hz, 1H), 7.63 (q, J = 4.0 Hz, 1H), 7.58 (d, J = 4.0 Hz, 1H), 7.27−7.35 (m, 2H), 7.20 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 3.09−3.15 (m, 1H), 2.78−2.91 (m, 2H), 2.54−2.63 (m, 1H), 2.02−2.16 (m, 2H), 1.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 165.2 (d, J = 199.0 Hz), 148.8, 146.1, 137.8 (d, J = 9.0 Hz), 133.4, 129.0.4 (d, J = 8.0 Hz), 125.3, 124.7, 122.4, 119.9, 116.8 (d, J = 20.0 Hz), 116.5 (d, J = 17.0 Hz), 113.2, 79.0, 36.3, 35.4, 29.2, 18.9. LRMS (ESI): m/z 322 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{17}N_3OF$ $[M + H]^+$ 322.1356, found 322.1349.

2-Fluoro-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ka, 92%, 130 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98 (dd, J_1 = 4.0 Hz, J_2 = 4.0 Hz, 1H), 7.87 (d, J = 4.0 Hz, 1H), 7.63 (q, J = 4.0 Hz, 1H), 7.58 (d, J = 4.0 Hz, 1H), 7.27−7.35 (m, 2H), 7.20 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 3.09−3.15 (m, 1H), 2.78−2.91 (m, 2H), 2.54−2.63 (m, 1H), 2.02−2.16 (m, 2H), 1.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 162.6 (d, J = 196.0 Hz), 148.4, 146.1, 134.0, 132.1, 131.4 (d, J = 7.0 Hz), 125.6, 125.3 (d, J = 8.0 Hz), 124.9, 122.7, 119.2 (d, J = 18.0 Hz), 113.6 (d, J = 20.0 Hz), 113.3, 79.0, 36.3, 35.4, 29.2, 18.9. LRMS (ESI): m/z 322 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{17}N_3OF$ $[M + H]^+$ 322.1356, found 322.1349.

3-Bromo-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5La, 75%, 99 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15 (d, J = 12.0 Hz, 1H), 7.85−7.87 (m, 2H), 7.54−7.58 (m, 2H), 7.28−7.34 (m, 2H), 3.10 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 2.79−2.92 (m, 2H), 2.58−2.66 (m, 1H), 2.05−2.17 (m, 2H), 1.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.2, 148.5, 145.7, 137.1, 133.9, 132.4, 132.2, 128.6, 126.0, 125.6, 125.0, 122.4, 122.2, 113.3, 79.2, 36.3, 35.4, 29.2, 18.8. LRMS (ESI): m/z 382 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{17}N_3OBr$ $[M + H]^+$ 382.0555, found 382.0556.

2,3-Difluoro-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Ma, 73%, 101 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07−8.12 (t, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.27−7.35 (m, 2H), 3.12 (m, 1H), 2.79−2.91 (m, 2H), 2.58−2.66 (m, 1H), 2.09−2.16 (m, 2H), 1.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.2, 152.9 (dd, J_1 = 183.0 Hz, J_2 = 11.0 Hz), 150.9 (dd, J_1 = 180.0 Hz, J_2 = 11.0 Hz), 147.8, 146.0, 134.0, 132.6 (d, J = 8.0 Hz), 125.7, 125.0, 122.6, 120.5 (d, J = 6.0 Hz), 119.1 (d, J = 17.0 Hz), 115.4 (d, J = 16.0 Hz), 113.3, 79.1, 36.3, 35.4, 29.2, 18.8. LRMS (ESI): m/z 340 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{16}N_3OF_2$ $[M + H]^+$ 340.1261, found 340.1272.

9a,12,13-Trimethyl-7,8,9,9a-tetrahydro-6*H*-benzo[4,5]-imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Oa, 45%, 63 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.67 (d, J = 8.0 Hz, 1H), 7.92 (s, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.78 (s, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 3.47 (t, J = 4.0 Hz, 2H), 2.82 (t, J = 4.0 Hz, 2H), 2.51 (s, 3H), 2.46 (s, 3H), 2.37 (m, 2H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.4, 146.7, 145.4, 138.9, 134.1, 132.5, 129.8, 127.4, 126.8, 125.3, 120.5, 111.6, 34.6, 33.7, 27.2, 20.9, 20.2, 17.1. LRMS (ESI): m/z 332 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{21}H_{22}N_3O$ $[M + H]^+$ 332.1763, found 332.1768.

12,13-Dichloro-9a-methyl-7,8,9,9a-tetrahydro-6*H*-benzo-[4,5]imidazo[1,2-*c*]pyrido[1,2-*a*]quinazolin-6-one (5Pa, 36%, 48 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.23 (d, J = 8.0 Hz, 1H), 7.94 (s, 1H), 7.67 (s, 1H), 7.65 (s, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 2.82−2.97 (m, 2H), 2.64 (m, 1H), 2.54 (t, J = 4.0 Hz, 1H), 2.39 (t, J = 4.0 Hz, 1H), 1.90 (m, 1H), 1.60 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.1, 151.2, 145.6, 136.4, 133.1, 132.8, 129.4, 129.0, 128.9, 127.6, 123.3, 122.7, 114.5, 79.0, 36.4, 35.4, 29.0, 18.9. LRMS (ESI): m/z 372 $[M + H]^+$. HRMS (ESI): m/z calcd $C_{19}H_{16}N_3OCl_2$ $[M + H]^+$ 372.0670, found 372.0668.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Crystallographic data for compound **3Aa** and copies of ^{1}H NMR and ^{13}C NMR spectra of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*H.L.: phone, +86-21-50807042; fax, +86-21-50807042; e-mail, hliu@mail.shcnc.ac.cn. Y.Z.: e-mail, zhouyu@mail.shcnc.ac.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge financial support from the National Basic Research Program of China (Grants 2009CB940903, 2009CB918502, and 2012CB518005), National Natural Science Foundation of China (Grants 21021063, 91229204,81025017, and 81102307), National S&T Major Projects (2012ZX09103-101-072), China-EU Science and Technology Cooperation Project (1109), and Silver Project (260644).

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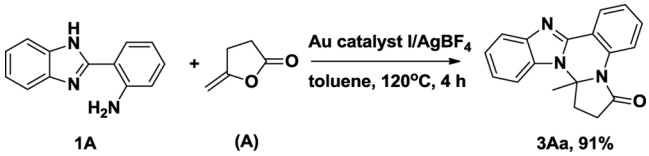
(42) To further explore the proposed mechanism, we have treated the tautomer of intermediate **A** (alphaangelica lactone, 17 μL, 2.0 mmol) with the amino compound **1A** (20 mg, 1.0 mmol) under the optimal reaction conditions, and the desirable product **3Aa** has been obtained in 91% yield.



(43) CCDC 911824 contains the supplementary crystallographic data for **3Aa**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_ request/cif.