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Au(I)-Catalyzed Cascade Reaction Involving Formal Double Hydroamination of Alkynes Bearing Tethered Carboxylic Groups: An Easy Access to Fused Dihydrobenzimidazoles and Tetrahydroquinazolines

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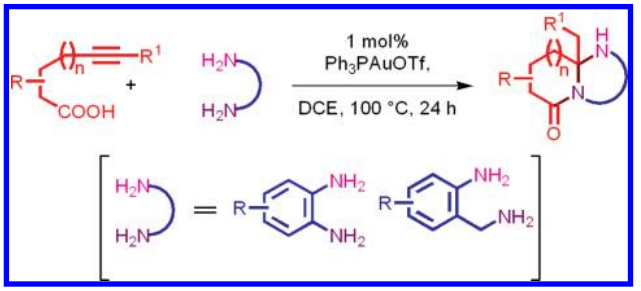

A process involving gold(I)-catalyzed formal double hydroamination of alkynes, bearing a tethered carboxylic group, for the synthesis of fused dihydrobenzimidazoles and tetrahydroquinazolines has been developed. A series of transition metal catalysts have been screened for this transformation, and a catalyst system consisting of Ph_3PAuCl (1 mol %) and AgOTf (1 mol %) was found to be the best. The procedure entails the reaction of easily accessible starting materials such as alkynoic acids and 1,2-diaminobenzenes/2-aminobenzylamines in the presence of the catalyst in 1,2-dichloroethane at 100 °C. In the case of α-substituted alkynoic acids, the corresponding products were obtained in high diastereoselectivities; the structure of the diastereomers has been unambiguously characterized by NMR techniques. The mechanism of the reaction is discussed, and the origin of the diastereoselectivities is addressed. It was observed that under the microwave irradiation conditions, the reaction time is significantly shortened (0.5 h).

Introduction

As a result of the rigid conformation of nitrogen-containing polycyclic compounds, the three-dimensional relationship of the molecule is restricted and therefore a specific biological activity would be expected. Such compounds are characterized by their ability to bind to a multitude of receptors through a variety of favorable interactions. Therefore, the nitrogen-containing compounds are considered as attractive templates for drug discovery. Among various N-containing heterocycles, fused dihydrobenzimidazoles[1] and tetrahydroquinazolines[2] are important structural motifs found in numerous natural products and/or pharmaceutically important compounds. General and convenient methods for the construction of these compounds bearing multiple reactive sites for further functionalization would be of great interest to the synthetic organic chemists. The ideal way to access these molecules would be to implement metal-catalyzed reaction cascade[3] using easily available starting materials in one-pot fashion without isolating any intermediates.[4]

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The catalytic hydroamination of alkynes[5] has emerged as a highly atom-economical[6] and broadly applicable transformation.[7] In general, primary or secondary amines can undergo addition reactions with alkynes to give imines or enamines. Very recently, we expanded the alkyne hydroamination strategy beyond the example of imines/enamines formation and further developed cascade reactions involving formal double hydroamination of alkynes (Figure 1, path a).[8] In this case, a proximal hydroxyl group was proved to be necessary for the reaction to occur. Interestingly, when $PtCl_2$ was used as a catalyst, double hydroamination product **A** was obtained; on the other hand, using $PtCl_4$ as a catalyst, cyclic fused compound **A′** was obtained. Later, we reported Au(I)-catalyzed direct double hydroamination of terminal alkynes having no hydroxyl group in the proximity.[9] Dixon and co-workers reported conceptually different Au(I)-catalyzed formal hydroamination-hydroarylation of alkynes bearing tethered carboxylic group.[10] They utilized alkyonic acids and amino-aromatics as starting materials, and the process led to the efficient synthesis of complex multiring heterocyclic compounds. Recently, Liu and co-workers broadened the scope of the reaction to a formal double hydroamination process for the synthesis of pyrrolo/pyrido[2,1-*a*]quinazolinones and pyrrolo/pyrido[2,1-*a*][1,3]benzoxazinones.[11] It should be further emphasized that although formal or direct hydroalkoxylation-hydroarylation,[12] double hydroalkoxylation,[13] hydroamination-hydroarylation,[10] double hydroarylation,[14] and hydroamination-hydroalkoxylation[15] of alkynes have recently been reported, only few reports exist on double hydroamination.[8a,11a]

In this context, we assumed that a π-acid catalyzed[16] intramolecular hydrocarboxylation reaction of alkynoic acid would form corresponding cyclic lactone,[17] which would then react with diamines to form either **B** or **B′** (Figure 1, path b). Such a gold-catalyzed cascade process would be synthetically valuable, as it would correspond to an overall

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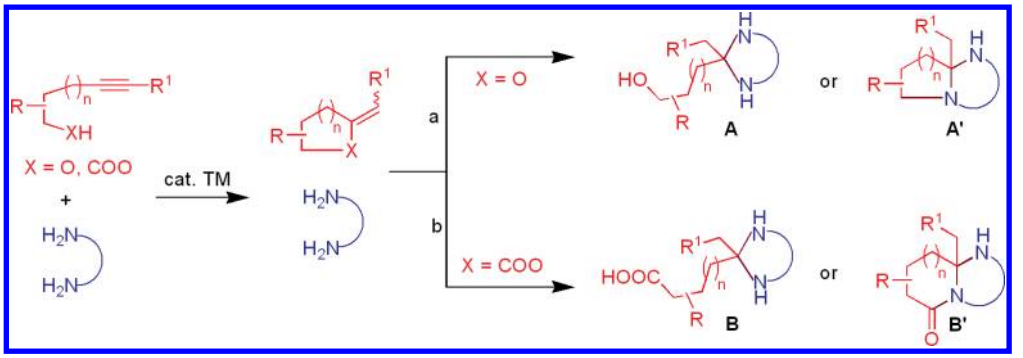


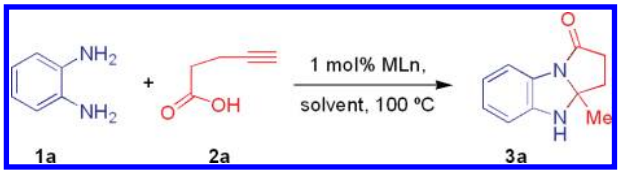
FIGURE 1. Concept of the double hydroamination of alkynes.

double hydroamination process of the starting alkynoic acids and would provide an easy access to pharmaceutically important molecules such as pyrrolo/pyrido[1,2-*a*]benzimidazol-1-ones and pyrrolo/pyrido[2,1-*b*]quinazolin-1-ones in an apparently very simple way.

Results and Discussion

At the outset of this study, our efforts were directed to find an appropriate catalyst and reaction conditions to perform the proposed reaction. We commenced our study of the metal-catalyzed reaction with readily accessible benzene-1,2-diamine (**1a**) and pent-4-ynoic acid (**2a**). The results of this study are summarized in Table 1. We focused our attention on the use of platinum salts as they have proved to be efficient catalysts in related reactions.[8] The substrate **1a** was treated with 1 equiv of pent-4-ynoic acid (**2a**) in the presence of 1 mol % $PtCl_2$ in DCE at 100 °C for 24 h. Indeed, the desired product **3a** was obtained in 91% yield (entry 1). The use of $PtCl_4$ as a catalyst gave **3a** in 90% yield (entry 2). Although we had satisfactory results in hand, we were curious to know the activity of other metal catalysts for the present transformation. When AgOTf and $Cu(OTf)_2$ catalysts were employed independently, **3a** was obtained in 40% and 45% yields, respectively (entries 3 and 4). Among the gold catalysts examined (AuCl, Ph_3PAuCl, $Ph_3PAuOTf$, and $Ph_3PAuNTf_2$) (entries 5−8), $Ph_3PAuOTf$ afforded the highest yield of **3a** (entry 7). Interestingly, even copper(I) catalysts such as CuBr and CuI provided **3a** in moderate yields (entry 9 and 10). Since the catalyst $Ph_3PAuOTf$ was found to be superior (entry 7), we next examined the effect of various solvents and quickly came to the conclusion that the reaction is sensitive to the solvents employed. The yield dropped significantly when toluene, THF and 1,4-dioxane were used (entries 11−13). On the other hand, solvents such as nitromethane and *N*,*N*′-dimethylformamide were completely ineffective and did not lead to the formation of **3a** (entries 14 and 15). It is interesting to note that when TfOH was used as catalyst, **3a** was obtained only in 51% yields (entry 16).

TABLE 1. Optimization Studies



entry	catalyst[a]	solvent	yield (%)[b]
1	$PtCl_2$	DCE	91
2	$PtCl_4$	DCE	90
3	AgOTf	DCE	40
4	$Cu(OTf)_2$	DCE	45
5	AuCl	DCE	50
6	Ph_3PAuCl	DCE	60
7	**Ph_3PAuCl/AgOTf**	**DCE**	**95**
8	$Ph_3PAuNTf_2$	DCE	92
9	CuBr	DCE	65
10	CuI	DCE	70
11	Ph_3PAuCl/AgOTf	toluene	30[c]
12	Ph_3PAuCl/AgOTf	THF	40
13	Ph_3PAuCl/AgOTf	1,4-dioxane	30
14	Ph_3PAuCl/AgOTf	$MeNO_2$	trace
15	Ph_3PAuCl/AgOTf	DMF	trace
16	TfOH	DCE	51

[a]All reactions were carried out using 1 mol % metal catalysts (MLn), 0.46 mmol of **1a**, and 0.46 mmol of **2a** in 2 mL of DCE at 100 °C for 24 h. [b]Isolated yields. [c]The starting material **1a** was partly soluble in toluene at 100 °C.

The substrate scope toward this cascade reaction was further investigated, and the results are summarized in Table 2. Gratifyingly, the reaction was proved to be very general under the optimized conditions, performing well in most of the cases examined. At first, the scope of the reaction with various alkynoic acids was studied using **1a** as a model substrate. The alkynoic acids bearing sterically demanding substituents in the tether such as **2b**, **2c**, and **2d** reacted well, giving corresponding products **3b**, **3c**, and **3d** in 92%, 84%, and 91% yields, respectively (entries 1−3). As can be judged from entries 4 and 5, hexynoic acids **2e** and **2f** on reaction with **1a** gave products **3e**[18] and **3f** in 79% and 96% yields,

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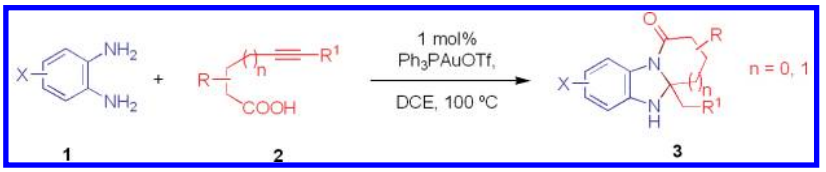
(18) X-ray crystallographic data of **3e** is given in Supporting Information

TABLE 2. $Ph_3PAuOTf$ -Catalyzed Reactions of Alkynoic Acids with Benzene-1,2-diamines[a]



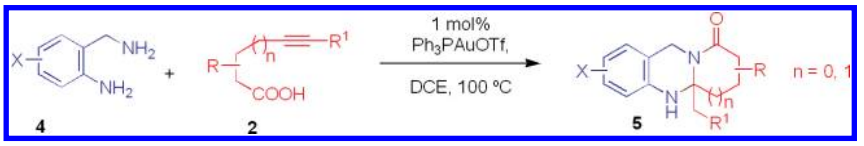
entry	1	2	3, yield[b]	entry	1	2	3, yield[b]
1	1a	2b	3b, 92%	9	1b	2a	3i, 73%[c]
2	1a	2c	3c, 84%	10	1b	2f	3j, 78%[c]
3	1a	2d	3d, 91%	11	1c	2a	3k, 86%[c]
4	1a	2e	3e, 79%	12	1d	2a	3l, 78%[d]
5	1a	2f	3f, 96%	13	1e	2a	3m, 68%[e]
6	1a	2g	3g, 73%	14	1f	2a	3n, 76%[f]
7	1a	2h	3h, 85%	15	1g	2a	3o, 85%[d]
8	1a	2i	3e, 81%[c]	16	1a	2j	3p, 00%[g]

[a]Reactions were performed in DCE (2 mL) employing **1** (0.46 mmol), **2** (0.46 mmol) and 1 mol % $Ph_3PAuOTf$ at 100 °C for 24 h. [b]Isolated yields. [c]Obtained as a single regioisomer. [d]Inseperable mixture (70:30) of regioisomers. [e]Inseperable mixture (90:10) of regioisomers. [f]Inseperable mixture (80:20) of regioisomers. [g]Starting material **1a** was recovered in quantitiative yields.

respectively. Interestingly, 2-ethynylbenzoic acid (**2g**) also reacted well, giving fused polycyclic compound **3g** in 73% yield (entry 6). Even internal alkynes such as **2h** and **2i** were found to be useful substrates, giving the corresponding products **3h** and **3e** in 85% and 81% yields, respectively (entries 7 and 8). Particularly noteworthy is the fact that in the latter case only one regioisomer **3e** was obtained, indicating that **2i** cyclized in 6-*endo*-*dig* fashion (entry 8). Next, the scope of the reaction with differentially substituted benzene-1,2-diamines was studied. When 3-methylbenzene-1,2-diamine (**1b**) was treated with **2a** and **2f**, the products **3i** and **3j** were obtained as single regioisomers in 73% and 78% yields (entries 9 and 10).[19] The reason for excellent regioselectivity might be attributed to the steric hindrance created by the methyl group. The amine group, located ortho to methyl group, should be less nucleophilic than the one at meta position. As shown in

(19) See Supporting Information for NOE details.

TABLE 3. $Ph_3PAuOTf$-Catalyzed Reactions of Alkynoic Acids with 2-(Aminomethyl)benzenamines[a]



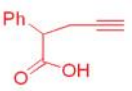
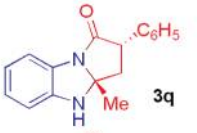
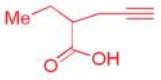
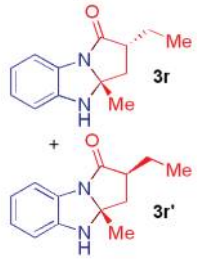
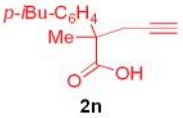
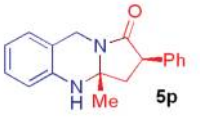
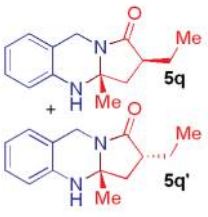
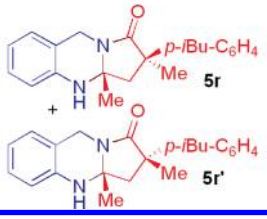
entry	4	2	5, yield[b]	entry	4	2	5, yield[b]
1	4a	2a	5a, 96%	8	4b	2a	5h, 95%
2	4a	2b	5b, 82%	9	4c	2a	5i, 81%
3	4a	2d	5c, 75%	10	4d	2a	5j, 86%
4	4a	2g	5d, 96%	11	4e	2a	5k, 80%
5	4a	2h	5e, 82%	12	4f	2a	5l, 78%
6	4a	2k	5f, 74%	13	4g	2a	5m, 71%
7[c]	4a	2i	5e, 83% 5g, 8%	14	4h	2f	5n, 73%
				15	4a	2j	5o, 00%[d]

[a]Reactions were performed in DCE (2 mL) employing **1** (0.46 mmol), **2** (0.46 mmol), and 1 mol % $Ph_3PAuOTf$ at 100 °C for 24 h. [b]Isolated yields. [c]A mixture of regioisomers **5e** and **5g** in a ratio of 90:10 was obtained as judged by ^1H NMR spectra of crude product. [d]Starting material **1a** was recovered in quantitiative yield.

entry 11, the reaction of 4-ethoxybenzene-1,2-diamine (**1c**) with **2a** gave **3k** in 86% yield as single regioisomer. The observed regioselectivity could be due to the resonance effect of the -OEt group, which make the amine located at the para position more nucleophilic than the one at meta position. However, in the case of **1d**, **1e**, **1f**, and **1g** the desired products **3l**, **3m**, **3n** and **3o** were obtained as inseparable mixtures of regioisomers in variable ratios (entries 12−15). It should be noted that heptynoic acids are not viable substrates for this transformation; for instance, the reaction between **1a** and **2j** did not give **3p** under the optimized reaction conditions (entries 16).

The applicability of benzene-1,2-diamines as a bisnucleophile having been established, for a formal double hydroamination cascade, the scope of the reaction has been extended to 2-aminobenzylamines. The results are summarized in Table 3. Treatment of **4a** with pent-4-ynoic acid (**2a**) in the presence of 1 mol % $Ph_3PAuOTf$ in DCE at 100 °C gave fused tetrahydroquinazolines **5a**, as a single regioisomer, in 96% yield (entry 1). The observed regioselectivity could be due to the higher nucleophilicity of $-CH_2NH_2$ compared to that of $Ar-NH_2$ (see Mechanistic Studies). The alkynoic acids **2b** and **2d** on reaction with **4a** gave the expected products **5b** and **5c** in 82% and 75% yields, respectively (entries 2 and 3). 2-Ethynylbenzoic acid (**2g**) also reacted well with **4a**, for this cascade transformation, to give **5d** in 96% yield (entry 4). Internal alkynes such as hex-3-ynoic acid (**2h**) and dodec-3-ynoic acid (**2k**) on reaction with **4a** gave **5e** and **5f** in 82% and 74% yields, respectively (entries 5 and 6). However, in the case of hex-4-ynoic acid (**2i**) a mixture of regioisomers **5e** and **5g** in the ratio of 90:10 was obtained; each of the regioisomers was separated by column chromatography (entry 7). As can be judged from entries 8−13, various substituents such as -Me, -OMe, -Cl, and -F in

TABLE 4. Diastereoselectivity Studies[a]

entry	1/4	2	3/5	yield[b,c]
1	1a	 2l	 3q	78%
2[d]	1a	 2m	 3r + 3r'	81% + 10%
3	1a	 2n	 3s	92%
4	4a	2l	 5p	74%
5[d]	4a	2m	 5q + 5q'	86% + 11%
6[e]	4a	2n	 5r + 5r'	78% + 4%

[a]Reactions were performed in DCE (2 mL) employing **1/4** (0.46 mmol), **2** (0.46 mmol), and 1 mol % $Ph_3PAuOTf$ at 100 °C for 24 h. [b]Isolated yields. [c]Structures of diastereomers were unambigiously determined by NOE studies (Figure 2) except **3s**, whose structure was confirmed by X-ray crystallography. [d]The ^1H NMR of crude product showed 90:10 mixture of diastereomers. [e]The ^1H NMR of crude product showed 95:05 mixture of diastereomers.

2-aminobenzylamines were well tolerated in the reaction (**4b**−**g** → **5h**−**m**).[20] The reaction of **4h** with **2f** afforded **5n** in 73% yield (entry 14). As anticipated, the reaction between **4a** and **2j** did not give **5o** under the optimized reaction conditions (entry 15).

As a part of continuing work, we next planned to investigate the diastereoselectivity of the reaction, and therefore α-substituted alkynoic acids such as **2l**, **2m**, and **2n** were prepared.[21] The reaction between 2-phenyl-pent-4-ynoic acid (**2l**) and **1a** was conducted under earlier optimized reaction conditions. Pleasingly, the reaction was found to be very diastereoselective and **3q** was obtained as a single 1,3-*trans* diastereomer in 78% yield (Table 4, entry 1). In the case of 2-ethyl-pent-4-ynoic acid (**2m**), a mixture of diastereomers **3r** and **3r′** was obtained favoring more of 1,3-*trans* isomer (**3r**:**3r′** = 90:10). This observation suggests that the steric bulk of the α-substituent plays an important role in deciding the diastereoselectivity (vide infra). Interestingly, in the case of disubstituted alkynoic acid **2n** only a single diastereomer **3s** was obtained in 92% yield (entry 3). An X-ray crystal structure analysis of **3s** unambiguously allowed the determination of relative stereochemistry.[22] When 2-(aminomethyl)-benzenamine (**4a**) was treated with **2l**, the product **5p** was obtained as a single 1,3-*cis* diastereomer in 74% yield (entry 4). As anticipated, a mixture of diastereomers **5q** and **5q′** in the ratio of 90:10 was obtained when **2m** was treated with **4a** (entry 5). Similar observation was noticed in the case of **2n**; a mixture of diastereomers was obtained (**5r**:**5r′** = 95:05) in 82% yield (entry 6). The relative stereochemistries of the diastereomers **3q**, **3q′** (vide infra), **3r**, **3r′**, **5p**, **5p′** (vide infra), **5q**, **5q′**, **5r**, and **5r′** were unambiguously determined by examining the nuclear Overhauser effect (NOE) enhancements (Figure 2).

Mechanistic Studies

A mechanism involving multiple catalytic cycles[23] for the gold-catalyzed formal double hydroamination of alkynes, which is presumably analogous to that reported by Dixon[10] and Liu,[11] is outlined in Figure 3. The first step would be the complexation of Au(I) catalyst to the alkyne function in **2e**, which leads to an intermediate **6** (Figure 3, cycle **A**). The cyclization may then occur directly by the attack of proximal hydroxyl group to form the vinylgold intermediate **7**.[24] The next step would be the proto-demetalation to generate exocyclic enol lactone **8** with the release of catalyst.[25] Once **8** is formed, it enters another catalytic cycle **B** where $Ph_3PAuOTf$ acts as a Lewis acid. Thus, the Lewis acidic Au(I) complex catalyzes the formation of oxonium ion **9** from **8**. Intermolecular nucleophilic addition of the benzene-1,2-diamine (**1a**) to **9** (cf. **10**) followed by proto-demetalation would lead to the keto amide **11** with the liberation of the catalyst. The keto amide **11** would then be poised to undergo *N*-acyl iminium ion[26] formation **12b**, which could be derived from **12a**, in the presence of Au(I) catalyst.[27] The

(20) X-ray crystallographic data of **5m** is given in Supporting Information

(21) See Supporting Information for the preparation of **2l**, **2m** and **2n**.

(22) X-ray crystallographic data of **3s** is given in Supporting Information

(23) (a) Shindoh, N.; Takemoto, Y.; Takasu, K. *Chem.*−*Eur. J.* **2009**, *15*, 12168–12179. (b) Wasilke, J.-C.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005**, *105*, 1001–1020.

(24) For reports on vinyl gold intermediates, see: (a) Hashmi, A. S. K.; Döpp, R.; Lothschütz, C.; Rudolph, M.; Riedel, D.; Rominger, F. *Adv. Synth. Catal.* **2010**, *352*, 1307–1314. (b) Hashmi, A. S. K.; Schuster, A. M.; Rominger, F. *Angew. Chem., Int. Ed.* **2009**, *48*, 8247–8249. (c) Seidel, G.; Mynott, R.; Fürstner, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 2510–2513. (d) Liu, L.-P.; Xu, B.; Mashuta, M. S.; Hammond, G. B. *J. Am. Chem. Soc.* **2008**, *130*, 17642–17643.

(25) The reaction between **1a** and **4a** with **2a**; independently, were carried out in the absence and presence of $Ph_3PAuOTf$ at 50 °C for 24 h. In the absence of catalyst, both the starting materials remained intact; while, in the presence of catalyst, formation of small amounts of **3a/5a**, corresponding ketoamides and unreacted **1a/4a** were obtained as judged by ^1H NMR spectra of crude product.

(26) For an excellent review on iminium ion catalysis, see: Erkkilä, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416–5470.

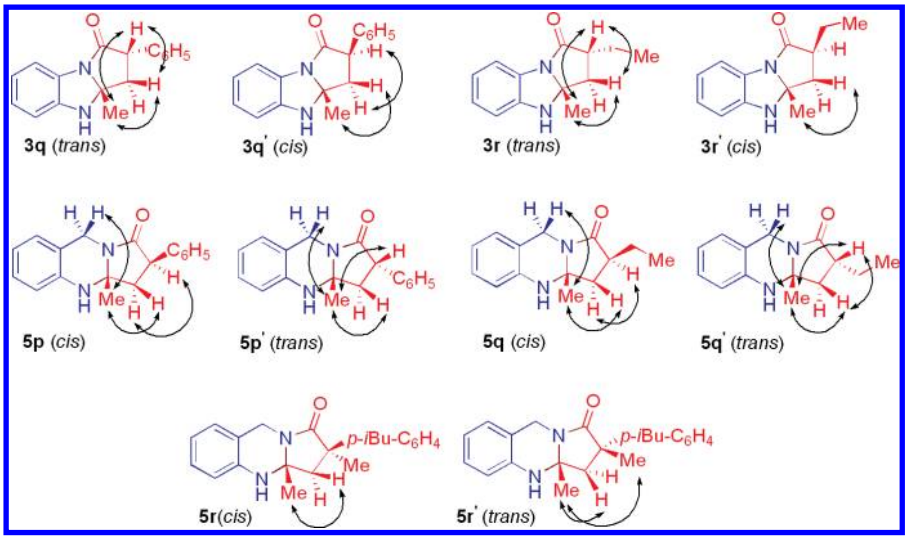


FIGURE 2. Structure elucidation of diastereomers by NOE studies.

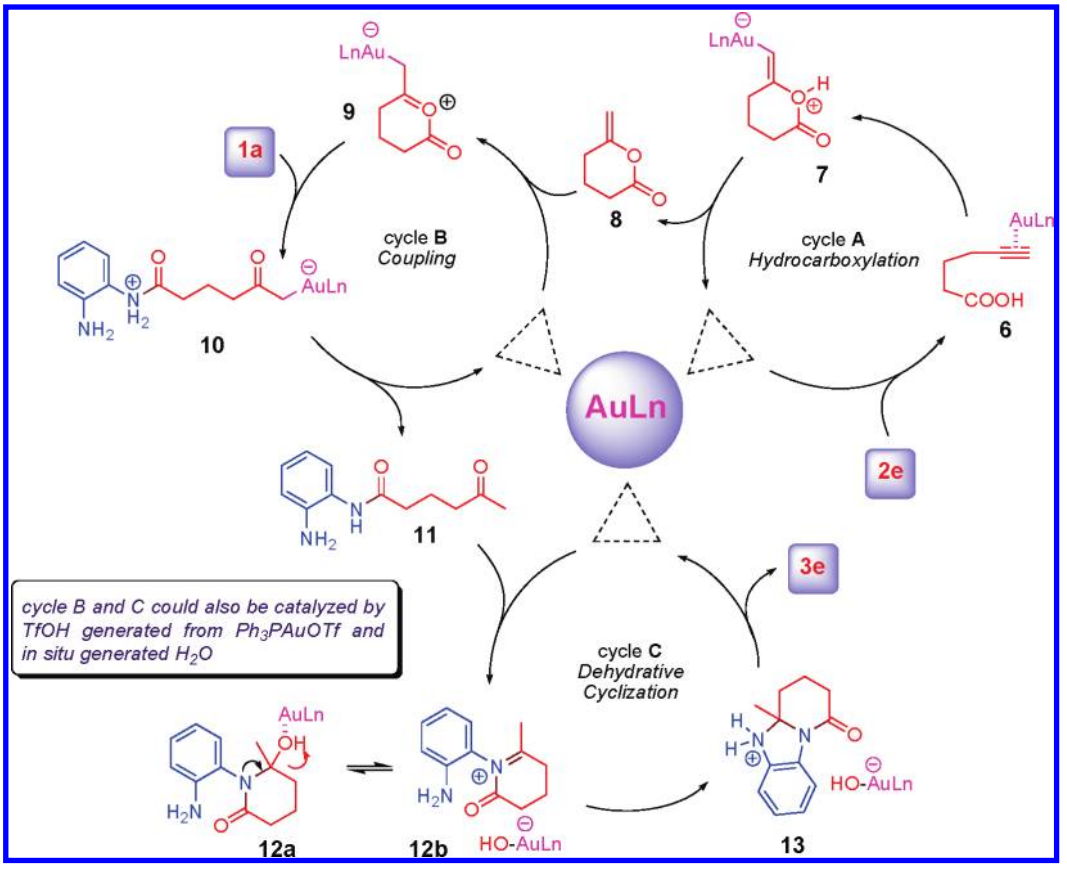


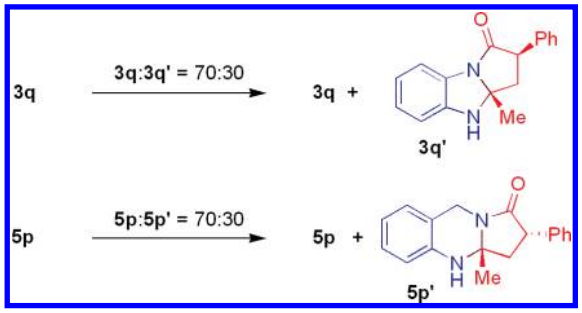
FIGURE 3. Mechanistic proposal for the formation of **3e** from **1a** and **2e**.

intramolecular trapping of *N*-acyl iminium ion in **12b** by tethered amine would produce final product **3e** (cf. **13**) with the regeneration of catalyst.

To determine the role of TfOH, which could be generated from $Ph_3PAuOTf$ in the presence of in situ generated water, in catalytic cycles **B** and **C**, the reaction was conducted between **1a** and **8** in the presence of 1 mol % TfOH in DCE at 100 °C (eq 1). The product **3e** was obtained in 93% yield. This suggests that residual TfOH may be responsible for cycles **B** and **C**. Interestingly, the same transformation was also catalyzed by $Ph_3PAuOTf$, leading to the formation of **3e** in 91% yield. It should be noted that in the absence of

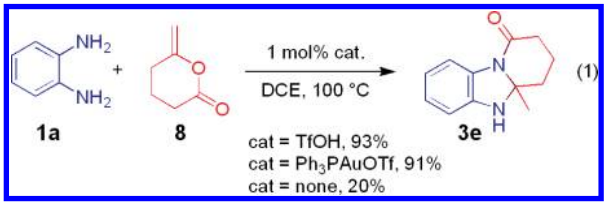
(27) The possibility of Brønsted acid catalysis assisted by a Lewis acid, which results from the use of Au catalysts in the presence of water, cannot be ruled out completely. An example of this type of catalysis, see: (a) Ishihara, K.; Ishibashi, H.; Yamamoto, H. *J. Am. Chem. Soc.* **2002**, *124*, 3647–3655. Such type of activation has been envisaged for other reactions, see: (b) Barluenga, J.; Fernández, A.; Diéguez, A.; Rodríguez, F.; Fañanás, F. J. *Chem.—Eur. J.* **2009**, *15*, 11660–11667. (c) ref 8b (d) ref 10b.

SCHEME 1. Diastereomerization of 3q/5p under Brönsted Acid Catalysis[a]



[a]Reaction conditions: 5 mol % *p*TSA·H_2O, DCE, rt, 12 h.

any catalyst the reaction of **1a** with **8** is sluggish and the desired product **3e** was formed only in 20% yield (eq 1).

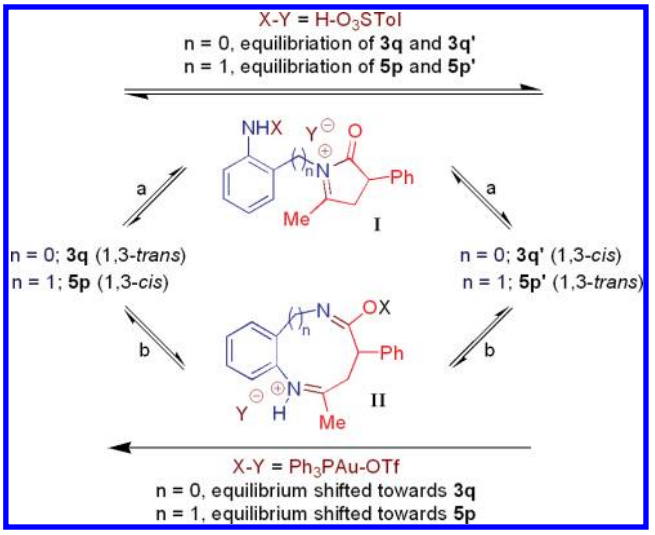


Kinetic versus Thermodynamic Control and Origin of Diastereoselectivity

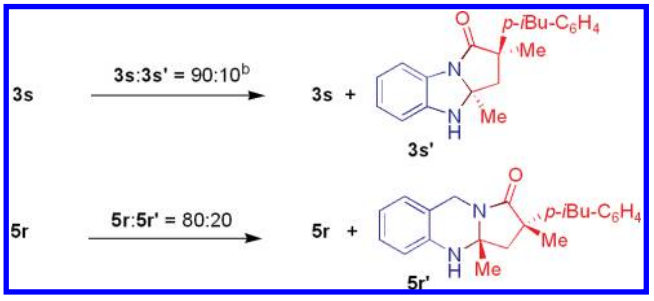
It is evident that only a single diastereomer (**3q** and **5p**) was obtained when 2-phenyl-pent-4-ynoic acid (**2l**) was reacted with **1a** and **4a**, independently (Table 4, entry 1 and 4). At this stage, we were intrigued to study the effect of Brönsted acid on diastereomerization of **3q** and **5p**. Accordingly, **3q** was treated with 5 mol % *p*TSA·H_2O in DCE at rt for 12 h. The reaction furnished a mixture of diastereomers **3q** and **3q′** in the ratio of 70:30 (Scheme 1). In an analogous manner, diastereomerization of **5p** occurred (**5p**:**5p′** = 70:30). This clearly establishes the mildness of gold-mediated reactions as compared to Brönsted acid mediated reactions. The plausible mechanism for the diastereomerization of **3q**/**3q′** and **5p**/**5p′** is given in Scheme 2. In path a, the intermediacy of *N*-acyl iminium ion **I** was proposed, which after trapping with proximal amine would give the products. On the other hand, path b explains the intermediacy of the amidoenolate **II**, which on transannular cyclization would furnish products **3q′**/**5p′**. At present, we do not have any conclusive evidence to prove which pathway is operating. The other possibility, that the stereogenic center α to the amide group undergoes epimerization by the Lewis acidic Au catalyst, can be ruled out completely. The treatment of **3s**/**5r**, which do not possess hydrogen at the α position of the carbonyl group, with 5 mol % *p*TSA·H_2O in DCE at rt afforded a mixture of regioisomer **3s**/**3s′** and **5r**/**5r′** (Scheme 3).

In order to shed some light on the kinetic and thermodynamic aspects of the gold-catalyzed reactions, the following experiments were conducted. When **3q** and **3q′** were independently subjected to gold catalysis, **3q** remained unchanged, whereas **3q′** was converted completely into **3q** (Scheme 4). A controlled experiment was conducted between **1a** and **2l** under standard gold-catalyzed conditions (Scheme 5, eq 2) and the progress of the reaction was followed by

SCHEME 2. Diastereomerization of 3q and 5p

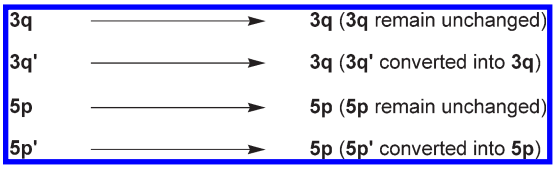


SCHEME 3. Diastereomerization of 3s/5r under Brönsted Acid Catalysis[a]



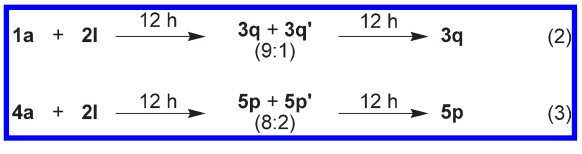
[a]Reaction conditions: 5 mol % *p*TSA·H_2O, DCE, rt, 12 h.[b]Inseperable mixture of diastereomers.

SCHEME 4. Diastereomerization of 3/5 under $Ph_3PAuOTf$ Catalysis[a]



[a]Reaction conditions: 1 mol % $Ph_3PAuOTf$, DCE, 100 °C

SCHEME 5. Controlled Experiments



analyzing the samples at end of 12 h intervals by ^1H NMR. The analysis of the sample after 12 h showed the presence of **1a**, **3q**, and **3q′**, while the sample after 24 h showed the presence of **3q** alone. This establishes that **3q′** is kinetically controlled product, while **3q** is a thermodynamically controlled product. In the case of **5p** and **5p′**, the former remain unchanged while the latter converted into **5p** when

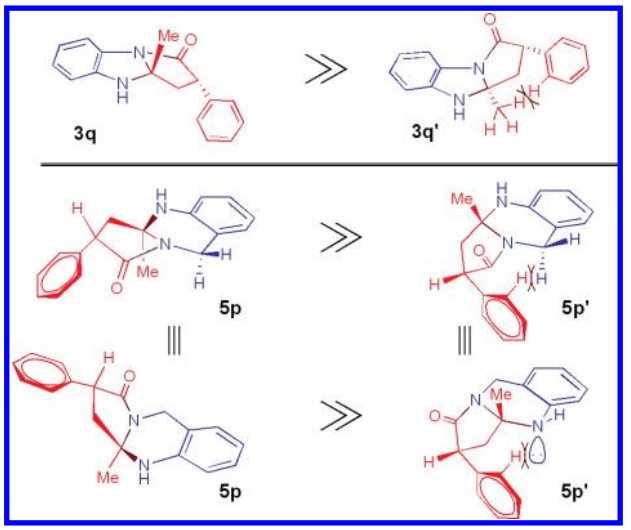


FIGURE 4. Proposed model for observed diastereoselectivity of **3q**/**3q**′ and **5p**/**5p**′.

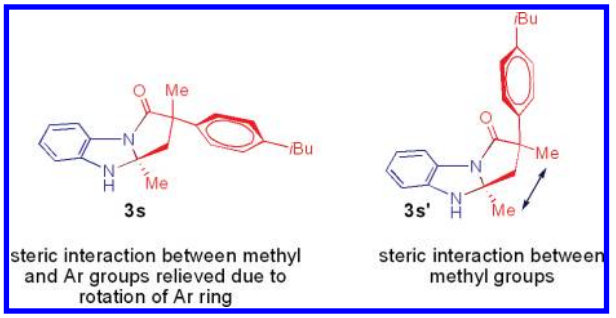


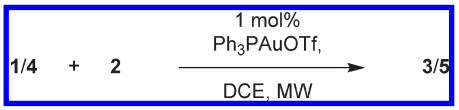
FIGURE 5. Plausible reason for the stability of **3s** over **3s**′.

treated under standard $Ph_3PAuOTf$ catalyzed conditions (Scheme 4). Next, we carefully monitored the progress of the reaction between **4a** and **2l**, and the results are presented in Scheme 5 (eq 3). This suggests that **5p**′ is akinetically controlled product, whereas **5p** is a thermodynamically controlled product.

Our proposed model for explaining the stability of diastereomers is shown in Figure 4 and is based on the steric hindrance created by the substituents present at the position α to the carbonyl groups. In the case of **3q** and **3q**′, we suggest that the latter one is highly disfavored because of severe steric interactions between the methyl and phenyl groups. Similarly, in the case of **5p** and **5p**′, the latter one is disfavored because of possible steric interactions of the phenyl group with either hydrogen (of hexahydropyrimidine ring) or nitrogen lone pair (Figure 4). The stability of **3s** over **3s**′ can be attributed to the possible preference of the -Ar ring to rotate in order to relieve the steric interaction with methyl group (Figure 5), which is further evidenced by the examination of the X-ray crystal structure of **3s**.[22]

(28) Selected reviews on microwave assisted reactions in organic synthesis see: (a) Appukkuttan, P.; Mehta, V. P.; Van der Eycken, E. *Chem. Soc. Rev.* **2010**, *39*, 1467–1477. (b) Kappe, C. O.; Dallinger, D. *Mol. Divers.* **2009**, *13*, 71–193. (c) Appukkuttan, P.; Van der Eycken, E. *Eur. J. Org. Chem.* **2008**, 1133–1155. (d) Kappe, C. O. *Chem. Soc. Rev.* **2008**, *37*, 1127–1139. (e) Das, S. K. *Synlett* **2004**, 915–932. (f) de la Hoz, A.; Díaz-Ortiz, Á.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164–178. (g) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225–9283.

TABLE 5. $Ph_3PAuOTf$-Catalyzed Reactions of Alkynoic Acids with Diamines under MW Conditions[a]



entry	1/4	2	3/5	yield (%)[b]
1	**1a**	**2a**	**3a**	75
2	**1a**	**2g**	**3g**	79
3	**1a**	**2d**	**3d**	76
4	**4a**	**2a**	**5a**	81
5	**4a**	**2d**	**5c**	85
6	**4a**	**2k**	**5f**	73
7	**1a**	**2l**	**3q** + **3q**′	70[c]
8	**4a**	**2l**	**5p** + **5p**′	73[d]

[a]A solution of the aminoaromatics **1/4** (0.46 mmol), alkynoic acids **2** (0.46 mmol), and $Ph_3PAuOTf$ (1 mol %) in DCE (0.8 mL) was subjected to microwave irradiation at 150 °C (P = 40−80 W) for 30 min (Biotage, Initiator Eight, single-mode reactor). [b]Isolated yield. [c]75:25 mixture of diastereomers favoring **3q**. [d]70:30 mixture of diastereomers favoring **5p**.

Effect of Microwave Irradiation

Considering the advantages of microwave-assisted reaction[28] over conventional heating in terms of efficiency, we became interested in testing the feasibility of the present reaction under MW irradiation. Indeed, a significant rate enhancement was observed when the reactions were conducted under microwave conditions (Table 5). Reactions of **1a** with **2a** in the presence of 1 mol % $Ph_3PAuOTf$ under microwave conditions for 30 min afforded **3a** in 75% yield (entry 1).[29] The reaction of **2g** and **2d** with **1a** furnished **3g** and **3d** in 79% and 76% yields, respectively (entries 2 and 3). Similarly, **4a** on reaction with **2a**, **2d**, and **2k** under the microwave-assisted conditions gave **5a**, **5c**, and **5f** in 81%, 85%, and 73% yields, respectively (entries 4−6). Unfortunately, α-substituted alkynoic acid **2l** afforded a mixture of diastereomers when reacted independently with **1a** and **4a** (entries 7 and 8).

Conclusion

In conclusion, we have developed a Au(I)-catalyzed cascade reaction involving formal double hydroamination of alkynes bearing tethered carboxylic groups. The method provides facile access to fused dihydrobenzimidazoles and tetrahydroquinazolines under very mild reaction conditions with high yields and excellent diastereo-/regioselectivities (wherever applicable). Furthermore, we have proven that this reaction could easily be performed in a microwave-assisted conditions, opening the way for the generation of number of these compounds in efficient manner.[30] Further investigation on the formal or direct double hydroamination reactions of alkynes, for the synthesis of structurally diverse biologically important scaffolds, is currently underway in our laboratory.

Experimental Section

$Ph_3PAuOTf$ Catalyzed Cascade Reactions Involving Formal Double Hydroamination of Alkynes (Tables 1−4). The preparation

(29) The reaction between **1a** and **2a** under gold catalysis in a preheated oil bath at 150 °C for 15 min gave **3a** only in 20% yield.

(30) (a) Schreiber, S. L. *Chem. Eng. News* **2003**, *81*, 51–61. (b) Schreiber, S. L. *Science* **2000**, *287*, 1964–1969.

of **3a** is representative. To a DCE (2 mL) solution of **1a** (0.050 g, 0.46 mmol) and **2a** (0.045 g, 0.46 mmol) in a screw cap vial were added Ph_3PAuCl (2.3 mg, 1 mol %) and AgOTf (1.2 mg, 1 mol %) under nitrogen atmosphere. The mixture was stirred at 100 °C for 24 h. Then, the reaction mixture was filtered through a pad of silica gel with ethyl acetate as an eluent, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel column chromatography using hexane/ethyl acetate (70/30) as eluent to obtain **3a** (0.082 g, 95%).

General Procedure for *p*TSA Catalyzed Diastereomerization of 3q/3s/5p/5r (Schemes 1 and 3). To a DCE (0.8 mL) solution of **3q/3s/5p/5r** (0.18 mmol) was added $pTSA \cdot H_2O$ (5 mol %) under nitrogen atmosphere. The mixture was stirred at rt for 12 h. Then, the reaction mixture was filtered through a pad of silica gel with ethyl acetate as an eluent, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel column chromatography using hexane/ethyl acetate (70/30) as eluent to obtain products as a mixture of diastereomers.

General Procedure for $Ph_3PAuOTf$ Catalyzed Cascade Reactions Involving Formal Double Hydroamination of Alkynes under Microwave-Assisted Conditions (Table 5). A solution of the aminoaromatic compound **1**/**4** (0.46 mmol), alkynoic acid **2** (0.46 mmol), Ph_3PAuCl (2.3 mg, 1 mol %), and AgOTf (1.2 mg, 1 mol %) in DCE (2 mL) was sealed under nitrogen in a reaction vial and irradiated in a microwave reactor (Biotage, initiator 8, single-mode reactor) for 30 min at 150 °C. On cooling of the reaction to ambient temperature, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel column chromatography using hexane/ethyl acetate (70/30) as eluent to afford **3**/**5**.

3a-Methyl-2,3,3a,4-tetrahydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazol-1-one (3a). Brown solid; mp = 106−108 °C; R_f = 0.39 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (dd, J = 7.6, 1.5 Hz, 1H), 6.90 (dt, J = 7.6, 1.5 Hz, 1H), 6.77 (t, J = 6.8 Hz, 1H), 6.60 (d, J = 6.8 Hz, 1H), 4.11 (brs, 1H), 2.76−2.67 (m, 1H), 2.54−2.32 (m, 3H), 1.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 142.7, 126.5, 125.2, 120.1, 115.3, 110.5, 85.5, 37.6, 33.6, 26.1; IR (KBr) ν_{max} 3320, 2969, 1692, 1603, 1491, 1202, 1163, 1050, 746 cm^{-1}; HRMS calcd for $C_{11}H_{13}N_2O$ (M^+ + H) 189.1027, found 189.1029.

2,2,3a-Trimethyl-2,3,3a,4-tetrahydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]-imidazol-1-one (3b). Brown solid; mp = 148−150 °C; R_f = 0.46 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (d, J = 7.6 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 6.78 (t, J = 7.6 Hz, 1H), 6.59 (d, J = 8.3 Hz, 1H), 4.12 (brs, 1H), 2.27 (ABq, J = 12.8 Hz, 2H), 1.56 (s, 3H), 1.39 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.9, 142.9, 128.8, 125.3, 119.6, 116.1, 110.2, 82.3, 50.9, 44.2, 28.0, 26.6, 26.5; IR (KBr) ν_{max} 3299, 2965, 2862, 1690, 1493, 1255, 1193, 828, 741 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O$ (M^+ + H) 217.1341, found 217.1332.

3a-Methyl-3a,4-dihydrospiro[benzo[*d*]pyrrolo[1,2-*a*]imidazole-2,1′-cyclopentan]-1(3*H*)-one (3c). White solid; mp = 180−182 °C; R_f = 0.71 (hexane/EtOAc = 80/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J = 7.2 Hz, 1H), 6.90 (t, J = 7.6 Hz, 1H), 6.78 (t, J = 7.5 Hz, 1H), 6.59 (d, J = 7.6 Hz, 1H), 3.89 (brs, 1H), 2.32 (ABq, J = 12.5 Hz, 2H), 2.31−2.22 (m, 1H), 2.14−2.03 (m, 1H), 1.96−1.59 (m, 5H), 1.55 (s, 3H), 1.51−1.42 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.6, 142.9, 128.9, 125.1, 119.9, 115.8, 110.3, 82.6, 54.2, 51.4, 39.0, 37.8, 28.0, 26.0, 25.2; IR (KBr) ν_{max} 3303, 3062, 2953, 2862, 1687, 1601, 1491, 1469, 1425, 1261, 1054, 736 cm^{-1}; HRMS calcd for $C_{15}H_{19}N_2O$ (M^+ + H) 243.1497, found 243.1503.

3a-Methyl-3a,4-dihydrospiro[benzo[*d*]pyrrolo[1,2-*a*]imidazole-2,1′-cyclohexan]-1(3*H*)-one (3d). Yellow solid; mp = 186−188 °C; R_f = 0.56 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J = 7.6 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 6.79 (t, J = 7.6 Hz, 1H), 6.62 (d, J = 7.6 Hz, 1H), 4.03 (brs, 1H), 2.32 (ABq, J = 12.8 Hz, 2H), 1.89−1.58 (m, 6H), 1.55 (s, 3H), 1.51−1.34 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.9, 142.9, 129.1, 125.3, 119.8, 116.3, 110.3, 82.8, 48.8, 46.6, 35.3, 33.8, 28.7, 25.2, 22.5, 21.9; IR (KBr) ν_{max} 3282, 3056, 2932, 2854, 1683, 1490, 1256, 1053, 740 cm^{-1}; HRMS calcd for $C_{16}H_{21}N_2O$ (M^+ + H) 257.1653, found 257.1663.

4a-Methyl-1,2,3,4,4a,5-hexahydrobenzo[4,5]imidazo[1,2-*a*]pyridin-1-one (3e). White solid; mp = 146−148 °C; R_f = 0.62 (DCM/MeOH = 95/05); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (dd, J = 7.6, 1.5 Hz, 1H), 6.88 (dt, J = 7.6, 1.5 Hz, 1H), 6.80 (dt, J = 7.6, 1.5 Hz, 1H), 6.64 (dd, J = 7.6, 1.5 Hz, 1H), 3.91 (brs, 1H), 2.63−2.41 (m, 2H), 2.16−1.87 (m, 4H), 1.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 139.2, 131.3, 124.6, 120.4, 117.2, 110.7, 80.1, 34.7, 30.6, 26.2, 17.5; IR (KBr) ν_{max} 3253, 2966, 2917, 1638, 1592, 1266, 1207, 1081, 740 cm^{-1}; HRMS calcd for $C_{12}H_{15}N_2O$ (M^+ + H) 203.1184, found 203.1181.

10a-Methyl-3,4,10,10a-tetrahydro-1*H*-benzo[4,5]imidazo[2,1-*c*][1,4]oxazin-4-one (3f). Yellow solid; mp = 182−184 °C; R_f = 0.31 (hexane/EtOAc = 50/50); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 7.6 Hz, 1H), 6.93 (t, J = 7.6 Hz, 1H), 6.82 (t, J = 7.6 Hz, 1H), 6.67 (d, J = 7.6 Hz, 1H), 4.26 (ABq, J = 17.4 Hz, 2H), 3.81 (ABq, J = 10.6 Hz, 2H), 3.75 (brs, 1H), 1.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 139.3, 129.8, 125.5, 120.7, 117.2, 110.6, 77.9, 72.2, 66.9, 24.9; IR (KBr) ν_{max} 3248, 2976, 2880, 1652, 1491, 1236, 1104, 941, 751 cm^{-1}; HRMS calcd for $C_{11}H_{13}N_2O_2$ (M^+ + H) 205.0977, found 205.0968.

4b-Methyl-4b,11-dihydro-5*H*-benzo[4,5]imidazo[2,1-*a*]isoindol-11-one (3g). White solid; mp = 186−188 °C; R_f = 0.56 (hexane/EtOAc = 30/70); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 7.6 Hz, 1H), 7.60−7.45 (m, 4H), 6.96−6.83 (m, 2H), 6.67 (d, J = 7.6 Hz, 1H), 4.20 (brs, 1H), 1.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 149.6, 145.1, 133.4, 132.0, 130.6, 129.6, 125.4, 125.1, 121.9, 120.9, 117.2, 111.4, 86.1, 26.8; IR (KBr) ν_{max} 3355, 3056, 2922, 2853, 1702, 1601, 1482, 1324, 1123, 1015, 738, 697 cm^{-1}; HRMS calcd for $C_{15}H_{13}N_2O$ (M^+ + H) 237.1028, found 237.1021.

3a-Ethyl-2,3,3a,4-tetrahydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazol-1-one (3h). Brown solid; mp = 118−120 °C; R_f = 0.47 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (d, J = 7.6 Hz, 1H), 6.87 (t, J = 7.6 Hz, 1H), 6.73 (t, J = 7.4 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 4.32 (brs, 1H), 2.76−2.64 (m, 1H), 2.50−2.20 (m, 3H), 1.87−1.68 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 142.9, 129.7, 125.1, 119.8, 115.3, 109.8, 87.8, 35.6, 33.4, 32.9, 17.8; IR (KBr) ν_{max} 3326, 2969, 1698, 1601, 1490, 1210, 1153, 1051, 747 cm^{-1}; HRMS calcd for $C_{12}H_{15}N_2O$ (M^+ + H) 203.1184, found 203.1191.

3a,5-Dimethyl-2,3,3a,4-tetrahydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]-imidazol-1-one (3i). Red solid; mp = 164−166 °C; R_f = 0.32 (DCM/MeOH = 95/05); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (dd, J = 6.8, 2.3 Hz, 1H), 6.76−6.69 (m, 2H), 3.78 (brs, 1H), 2.83−2.65 (m, 1H), 2.54−2.31 (m, 3H), 2.12 (s, 3H), 1.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 141.0, 128.0, 126.4, 120.1, 120.0, 112.8, 85.4, 37.7, 33.5, 26.3, 16.4; IR (KBr) ν_{max} 3282, 3055, 2958, 1662, 1592, 1483, 1387, 1329, 1227, 1180, 898, 740 cm^{-1}; HRMS calcd for $C_{12}H_{15}N_2O$ (M^+ + H) 203.1184, found 203.1175.

9,10a-Dimethyl-3,4,10,10a-tetrahydro-1*H*-benzo[4,5]imidazo-[2,1-*c*][1,4]oxazin-4-one (3j). Yellow solid; mp = 186−188 °C; R_f = 0.36 (DCM/MeOH = 95/05); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (dd, J = 6.0, 3.0 Hz, 1H), 6.79−6.73 (m, 2H), 4.25 (ABq, J = 16.6 Hz, 2H), 3.84 (ABq, J = 10.6 Hz, 2H), 3.50 (brs, 1H), 2.15 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 137.6, 129.6, 126.8, 121.0, 120.0, 115.0, 77.8, 72.3, 67.0, 25.5, 16.5; IR (KBr) ν_{max} 3273, 2963, 2923, 2860, 1651, 1587, 1479, 1393, 1224, 1159, 948, 757 cm^{-1}; HRMS calcd for $C_{12}H_{14}N_2O_2Na$ (M^+ + H) 241.0943, found 241.0952.

6-Ethoxy-3a-methyl-2,3,3a,4-tetrahydro-1*H*-benzo[*d*]pyrrolo-[1,2-*a*]imidazol-1-one (3k). Dark brown solid; mp = 122−124 °C; R_f = 0.37 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, J = 8.3 Hz, 1H), 6.26 (dd, J = 8.3, 2.3 Hz, 1H), 6.19 (d, J = 2.3 Hz, 1H), 4.03 (brs, 1H), 3.93 (q, J = 6.9 Hz, 2H), 2.87−2.67 (m, 1H), 2.53−2.27 (m, 3H), 1.51 (s, 3H), 1.38 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 157.4, 144.1, 122.3, 115.6, 104.3, 98.9, 86.1, 63.8, 37.4, 33.5, 26.1, 14.9; IR (KBr) ν_{max} 3268, 2971, 2923, 1680, 1610, 1499, 1343, 1161, 1045, 836, 782, 738 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O_2$ (M^+ + H) 233.1290, found 233.1292.

(3l). A mixture of regioisomers (70:30); thick liquid; R_f = 0.34 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.19 (m, 1H), 6.71−6.20 (m, 2H), 4.06 (brs, 1H), 2.82−2.66 (m, 1H), 2.54−2.24 (m, 3H), 1.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 143.0, 140.4, 135.2, 126.3, 125.4, 120.3, 116.1, 115.0, 111.5, 110.6, 85.8, 37.6, 36.0, 33.8, 33.6, 29.7, 26.0, 21.5, 21.0; IR (film) ν_{max} 3311, 2970, 2921, 1690, 1500, 1463, 1393, 1202, 1085, 982, 858, 802, 753, 659 cm^{-1}; HRMS calcd for $C_{12}H_{12}F_3N_2O$ (M^+ + H) 257.0902, found 257.0913.

(3m). A mixture of regioisomers (90:10); brown solid; mp = 110−112 °C; R_f = 0.37 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (dd, J = 8.3, 5.3 Hz, 1H), 6.43 (dt, J = 9.1, 2.3 Hz, 1H), 6.32 (dd, J = 9.1, 2.3 Hz, 1H), 4.42 (brs, 1H), 2.79−2.65 (m, 1H), 2.53−2.29 (m, 3H), 1.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 162.5, 159.3, 144.0, 124.5, 115.5, 115.4, 110.5, 110.4, 105.3, 104.9, 98.7, 98.3, 86.4, 37.6, 37.4, 33.4, 33.2, 26.0; IR (KBr) ν_{max} 3302, 2976, 2919, 1692, 1614, 1500, 1349, 1138, 1087, 971, 833, 792, 715, 625 cm^{-1}; HRMS calcd for $C_{11}H_{12}FN_2O$ (M^+ + H) 207.0934, found 207.0923.

(3n). A mixture of regioisomers (80:20); pale Yellow solid; mp = 92−94 °C; R_f = 0.33 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J = 1.5 Hz, 0.3H), 7.28 (d, J = 8.3 Hz, 0.8H), 6.87 (dd, J = 8.3, 2.3 Hz, 0.2H), 6.75 (dd, J = 8.3, 2.3 Hz, 0.8H), 6.58 (d, J = 1.5 Hz, 0.8H), 6.52 (d, J = 7.6 Hz, 0.2H), 4.18 (brs, 1H), 2.84−2.68 (m, 1H), 2.56−2.30 (m, 3H), 1.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 144.0, 130.3, 127.2, 124.9, 119.4, 115.8, 110.9 110.6, 86.2, 37.7, 37.6, 33.4, 26.2, 26.1; IR (KBr) ν_{max} 3265, 2969, 2921, 1700, 1606, 1498, 1334, 1262, 1049, 932, 778, 658 cm^{-1}; HRMS calcd for $C_{11}H_{12}ClN_2O$ (M^+ + H) 223.0638, found 223.0629.

(3o). A mixture of regioisomers (70:30); dark red solid; mp = 136−138 °C; R_f = 0.57 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 1.5 Hz, 0.3H), 7.23 (d, J = 8.3 Hz, 0.7H), 7.01 (dd, J = 8.3, 2.3 Hz, 0.3H), 6.89 (dd, J = 8.3, 2.3 Hz, 0.7H), 6.74 (d, J = 1.5 Hz, 0.7H), 6.47 (d, J = 8.3 Hz, 0.3H), 4.30 (brs, 1H), 2.77−2.67 (m, 1H), 2.61−2.34 (m, 3H), 1.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 144.2, 127.9, 127.6, 122.5, 118.4, 117.9, 116.3, 113.4, 111.5, 86.2, 37.9, 37.6, 33.4, 27.7, 26.2; IR (KBr) ν_{max} 3302, 2972, 2921, 1680, 1595, 1474, 1328, 1078, 980, 744, 655 cm^{-1}; HRMS calcd for $C_{11}H_{12}N_2OBr$ (M^+ + H) 267.0133, found 267.0132.

(2*S*,3a*R*)-3a-Methyl-2-phenyl-2,3,3a,4-tetrahydro-1*H*-benzo-[*d*]pyrrolo[1,2-*a*]imidazol-1-one (3q). Yellow solid; mp = 178−180 °C; R_f = 0.42 (hexane/EtOAc = 70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49−7.25 (m, 6H), 6.94 (t, J = 6.9 Hz, 1H), 6.82 (t, J = 6.9 Hz, 1H), 6.65 (d, J = 7.7 Hz, 1H), 4.15 (brs, 1H), 4.02 (dd, J = 13.0, 7.6 Hz, 1H), 2.77 (dd, J = 12.3, 7.6 Hz, 1H), 2.59 (dd, J = 12.5, 7.5 Hz, 1H), 1.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 142.7, 137.1, 128.7, 128.5, 127.3, 125.2, 120.0, 115.5, 110.5, 82.5, 50.6, 47.2, 25.6; IR (KBr) ν_{max} 3298, 3052, 2963, 2861, 1690, 1490, 1253, 1191, 738 cm^{-1}; HRMS calcd for $C_{17}H_{17}N_2O$ (M^+ + H) 265.1341, found 265.1337.

(2*R*,3a*R*)-3a-Methyl-2-phenyl-2,3,3a,4-tetrahydro-1*H*-benzo-[*d*]pyrrolo[1,2-*a*]imidazol-1-one (3q′). Yellow solid; mp = 174−176 °C; R_f = 0.41 (hexane/EtOAc = 70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, J = 7.5 Hz, 1H), 7.40−7.20 (m, 5H), 6.93 (t, J = 8.5 Hz, 1H), 6.79 (t, J = 8.1 Hz, 1H), 6.30 (d, J = 7.5 Hz, 1H), 4.07 (brs, 1H), 4.06 (dd, J = 10.7, 2.2 Hz, 1H), 2.92 (dd, J = 12.8, 10.7 Hz, 1H), 2.45 (dd, J = 12.8, 2.2 Hz, 1H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 142.9, 139.4, 128.8, 127.4, 127.1, 125.7, 120.3, 116.5, 110.5, 85.2, 50.8, 44.4, 28.5; IR (KBr) ν_{max} 3324, 2965, 2928, 2871, 1691, 1603, 1490, 1416, 1256, 743 cm^{-1}; HRMS calcd for $C_{17}H_{17}N_2O$ (M^+ + H) 265.1341, found 265.1343.

(2*R*,3a*R*)-2-Ethyl-3a-methyl-2,3,3a,4-tetrahydro-1*H*-benzo[*d*]-pyrrolo[1,2-*a*]imidazol-1-one (3r). Brown solid; mp = 142−144 °C; R_f = 0.62 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J = 7.6 Hz, 1H), 6.89 (dt, J = 7.6, 1.1 Hz, 1H), 6.77 (dt, J = 7.6, 1.1 Hz, 1H), 6.60 (d, J = 7.6 Hz, 1H), 4.10 (brs, 1H), 2.75−2.65 (m, 1H), 2.52−2.46 (m, 1H), 2.07−1.89 (m, 1H), 1.50 (s, 3H), 1.46−1.34 (m, 1H), 0.97 (t, J = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2, 142.6, 128.6, 124.9, 120.1, 115.4, 110.5, 82.9, 45.8, 44.1, 26.1, 23.1, 11.6; IR (KBr) ν_{max} 3276, 2964, 2928, 1683, 1604, 1492, 1258, 1056, 743, 681 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O$ (M^+ + H) 217.1341, found 217.1339.

(2*S*,3a*R*)-2-Ethyl-3a-methyl-2,3,3a,4-tetrahydro-1*H*-benzo[*d*]-pyrrolo[1,2-*a*]imidazol-1-one (3r′). Brown solid; mp = 94−96 °C; R_f = 0.61 (hexane/EtOAc = 70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, J = 8.4 Hz, 1H), 6.89 (t, J = 7.3 Hz, 1H), 6.75 (t, J = 7.3 Hz, 1H), 6.60 (d, J = 7.3 Hz, 1H), 4.40 (brs, 1H), 2.60−2.55 (m, 1H), 2.53 (ABq, J = 10.5 Hz, 2H), 1.95−1.86 (m, 1H), 1.63−1.54 (m, 1H), 1.49 (s, 3H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.8, 142.8, 129.3, 125.5, 120.1, 116.5, 110.5, 84.9, 47.0, 40.5, 29.2, 26.1, 12.3; IR (KBr) ν_{max} 3286, 3056, 2942, 1680, 1596, 1484, 1232, 1034, 745, 693 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O$ (M^+ + H) 217.1341, found 217.1339.

(2*R*,3a*R*)-2-(4-Isobutylphenyl)-2,3a-dimethyl-2,3,3a,4-tetra-hydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazol-1-one (3s). White solid; mp = 158−160 °C; R_f = 0.81(hexane/EtOAc = 70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 7.3 Hz, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 6.97 (t, J = 8.4 Hz, 1H), 6.85 (t, J = 7.3 Hz, 1H), 6.67 (d, J = 7.3 Hz, 1H), 4.05 (brs, 1H), 2.92 (d, J = 12.5 Hz, 1H), 2.61 (d, J = 12.5 Hz, 1H), 2.46 (d, J = 7.3 Hz, 2H), 1.89−1.81 (m, 1H), 1.53 (s, 3H), 1.13 (s, 3H), 0.89 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5, 143.0, 141.6, 140.0, 129.4, 128.9, 125.7, 125.4, 119.8, 116.1, 110.3, 89.2, 82.6, 52.9, 44.9, 30.2, 28.3, 26.6, 22.5; IR (KBr) ν_{max} 3290, 3062, 2927, 1667,1497, 1380, 1261, 1156, 1028, 756, 691 cm^{-1}; HRMS calcd for $C_{22}H_{27}N_2O$ (M^+ + H) 335.2123, found 335.2126.

3a-Methyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5a). Brown solid; mp = 138−140 °C; R_f = 0.52 (hexane/EtOAc = 30/70); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01−6.97 (m, 2H), 6.73 (t, J = 7.6 Hz, 1H), 6.49 (d, J = 8.1 Hz, 1H), 4.56 (ABq, J = 16.9 Hz, 2H), 3.74 (brs, 1H), 2.59−2.38 (m, 2H), 2.15−2.01 (m, 2H), 1.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 141.7, 127.4, 126.7, 119.0, 117.1, 116.3, 71.8, 38.5, 32.7, 29.6, 25.4; IR (KBr) ν_{max} 3294, 3057, 2908, 1718, 1484, 1383, 1094, 755, 700 cm^{-1}; HRMS calcd for $C_{12}H_{15}N_2O$ (M^+ + H) 203.1184, found 203.1191.

2,2,3a-Trimethyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5b). Brown solid; mp = 148−150 °C; R_f = 0.68 (hexane/EtOAc = 30/70); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99−6.97 (m, 2H), 6.71 (t, J = 8.3 Hz, 1H), 6.47 (d, J = 7.6 Hz, 1H), 4.51 (ABq, J = 16.6 Hz, 2H), 3.78 (brs, 1H), 1.99 (ABq, J = 13.6 Hz, 2H), 1.54 (s, 3H), 1.24 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 141.7, 127.4, 126.8, 118.9, 117.3, 116.2, 69.2, 48.5, 40.5, 38.7, 26.7, 26.5; IR (KBr) ν_{max} 3322, 2966, 2925, 1667, 1494, 1226, 1062, 747 cm^{-1}; HRMS calcd for $C_{14}H_{19}N_2O$ (M^+ + H) 231.1497, found 231.1495.

3a′-Methyl-3′,3a′,4′,9′-tetrahydro-1′*H*-spiro[cyclohexane-1,2′-pyrrolo[2,1-*b*]quinazolin]-1′-one (5c). Pale yellow solid; mp = 200−202 °C; R_f = 0.32 (hexane/EtOAc = 30/70); ^{1}H NMR

(300 MHz, $CDCl_3$) δ 6.99−6.95 (m, 2H), 6.71 (t, J = 7.6 Hz, 1H), 6.47 (d, J = 8.3 Hz, 1H), 4.58 (ABq, J = 16.6 Hz, 2H), 3.70 (brs, 1H), 2.02 (ABq, J = 12.8 Hz, 2H), 1.87−1.60 (m, 6H), 1.54 (s, 3H), 1.42−1.23 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.4, 141.8, 127.4, 126.8, 118.9, 117.3, 116.1, 69.6, 45.4, 44.7, 38.5, 35.0, 33.5, 26.8, 25.2, 22.2, 22.1; IR (KBr) ν_{max} 3323, 2926, 2849, 1664, 1490, 1251, 1207, 1096, 746 cm^{-1}; HRMS calcd for $C_{17}H_{23}N_2O$ (M^+ + H) 271.1810, found 271.1816.

4b-Methyl-4b,5,10,12-tetrahydroisoindolo[1,2-*b*]quinazolin-12-one (5d). Pale yellow solid; mp =222−224 °C; R_f = 0.32 (hexane/EtOAc = 30/70); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.80−7.76 (m, 2H), 7.63 (t, J = 6.7 Hz, 1H), 7.52 (t, J = 6.7 Hz, 1H), 7.10 (d, J = 8.1 Hz, 1H), 7.05 (t, J = 8.1 Hz, 1H), 6.77 (t, J = 8.1 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 5.85 (brs, 1H), 4.83 (ABq, J = 17.5 Hz, 2H), 1.70 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1, 147.6, 140.5, 131.4, 130.3, 128.4, 127.0, 126.1, 123.0, 120.7, 118.1, 116.2, 116.0, 70.5, 37.2, 23.0; IR (KBr) ν_{max} 3291, 2955, 2923, 2864, 1677, 1495, 1393, 1206, 1098, 1016, 841, 744, 694 cm^{-1}; HRMS calcd for $C_{16}H_{15}N_2O$ (M^+ + H) 251.1184, found 251.1170.

3a-Ethyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5e). Brown solid; mp = 148−150 °C; R_f = 0.53 (hexane/EtOAc = 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00−6.95 (m, 2H), 6.72 (t, J = 7.6 Hz, 1H), 6.49 (d, J = 7.6 Hz, 1H), 4.52 (ABq, J = 16.6 Hz, 2H), 4.05 (brs, 1H), 2.59−2.38 (m, 2H), 2.18−2.08 (m, 1H), 1.94−1.78 (m, 3H), 0.94 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6, 141.6, 127.6, 126.9, 119.1, 117.6, 116.3, 74.7, 38.8, 29.8, 29.5, 29.4, 7.7; IR (KBr) ν_{max} 3290, 2964, 2932, 1679, 1608, 1441, 1160, 983, 746 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O$ (M^+ + H) 217.1340, found 217.1341.

3a-Octyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5f). Brown solid; mp =98−100 °C; R_f = 0.76 (hexane/EtOAc = 70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99−6.95 (m, 2H), 6.71 (t, J = 7.8 Hz, 1H), 6.47 (d, J = 7.8 Hz, 1H), 4.51 (ABq, J = 16.6 Hz, 2H), 2.53−2.39 (m, 2H), 2.15−2.01 (m, 1H), 1.92−1.80 (m, 1H), 1.80−1.69 (m, 2H), 1.35−1.23 (m, 12H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 141.6, 127.5, 126.8, 119.0, 117.4, 116.1, 74.3, 38.7, 37.2, 31.7, 29.9, 29.5, 29.4, 29.1, 23.4, 22.5, 14.0; IR (KBr) ν_{max} 3307, 2926, 2854, 1673, 1449, 1260, 1198, 813, 745 cm^{-1}; HRMS calcd for $C_{19}H_{29}N_2O$ (M^+ + H) 301.2280, found 301.2287.

5a-Methyl-5,6,7,8,9,11-hexahydro-5a*H*-pyrido[2,1-*b*]quinazolin-9-one (5g). Yellow solid; mp = 156−158 °C; R_f = 0.50 (hexane/EtOAc = 30/70); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95−6.92 (m, 2H), 6.69−6.66 (m, 1H), 6.47 (d, J = 7.4 Hz, 1H), 4.22 (ABq, J = 17.5 Hz, 2H), 3.80 (brs, 1H), 2.44−2.26 (m, 2H), 1.98−1.88 (m, 3H), 1.78−1.67 (m, 1H), 1.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 141.0, 128.4, 127.4, 126.8, 119.3, 116.1, 68.3, 39.7, 37.3, 32.9, 26.8, 16.8; IR (KBr) ν_{max} 3293, 2941, 2862, 1619, 1491, 1271, 1113, 749, 541 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O$ (M^+ + H) 217.1341, found 217.1346.

3a,8-Dimethyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5h). Brown solid; mp = 156−158 °C; R_f = 0.53 (hexane/EtOAc = 30/70); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (t, J = 8.3 Hz, 1H), 6.59 (d, J = 7.6 Hz, 1H), 6.36 (d, J = 8.3 Hz, 1H), 4.45 (ABq, J = 16.6 Hz, 2H), 3.75 (brs, 1H), 2.54−2.46 (m, 2H), 2.23 (s, 3H), 2.11−2.02 (m, 2H), 1.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 141.7, 135.7, 127.2, 120.8, 115.9, 114.1, 71.4, 37.4, 32.7, 29.5, 25.2, 18.5; IR (KBr) ν_{max} 3319, 2969, 2923, 1675, 1236, 1200, 1099, 778, 673 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O$ (M^+ + H) 217.1340, found 217.1347.

3a,5,7-Trimethyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5i). Pale yellow solid; mp = 136−138 °C; R_f = 0.37 (hexane/EtOAc = 30/70); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.71 (s, 1H), 6.68 (s, 1H), 4.46 (ABq, J = 16.8 Hz, 2H), 3.39 (brs, 1H), 2.59−2.39 (m, 2H), 2.20 (s, 3H), 2.15−2.09 (m, 2H), 2.05 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 137.3, 129.4, 128.0, 124.8, 123.7, 116.9, 71.9, 38.6, 33.2, 29.5, 25.7, 20.4, 16.9; IR (KBr) ν_{max} 3341, 2964, 2924, 1678, 1489, 1398, 1228, 1101, 1029, 636 cm^{-1}; HRMS calcd for $C_{14}H_{19}N_2O$ (M^+ + H) 231.1497, found 231.1494.

7-Methoxy-3a-methyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]-quinazolin-1-one (5j). Brown solid; mp = 104−106 °C; R_f = 0.48 (hexane/EtOAc = 30/70); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.63−6.49 (m, 3H), 4.53 (ABq, J = 17.4 Hz, 2H), 3.72 (s, 3H), 3.48 (brs, 1H), 2.58−2.39 (m, 2H), 2.15−1.99 (m, 2H), 1.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.0, 153.3, 135.2, 118.9, 118.3, 114.1, 111.4, 72.0, 55.6, 38.7, 32.9, 29.5, 25.0; IR (KBr) ν_{max} 3307, 2964, 1674, 1504, 1229, 1180, 1034, 834, 665 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O_2$ (M^+ + H) 233.1290, found 233.1298.

7-Chloro-3a,5-dimethyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]-quinazolin-1-one (5k). Dark brown solid; mp = 144−146 °C; R_f = 0.33 (hexane/EtOAc = 30/70); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (s, 1H), 6.87 (s, 1H), 4.42 (ABq, J = 17.2 Hz, 2H), 3.63 (brs, 1H), 2.55−2.42 (m, 2H), 2.18−2.20 (m, 2H), 2.07 (s, 3H), 1.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 138.5, 128.4, 125.3, 124.1, 123.2, 118.1, 71.9, 38.3, 32.9, 29.4, 25.7, 16.9; IR (KBr) ν_{max} 3336, 2964, 1678, 1482, 1396, 1227, 1169, 865, 723 cm^{-1}; HRMS calcd for $C_{13}H_{16}ClN_2O$ (M^+ + H) 251.0951, found 251.0968.

8-Chloro-3a-methyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5l). Yellow solid; mp = 128−130 °C; R_f = 0.36 (hexane/EtOAc = 30/70); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (t, J = 7.7 Hz, 1H), 6.76 (d, J = 7.9 Hz, 1H), 6.39 (d, J = 7.9 Hz, 1H), 4.51 (ABq, J = 17.6 Hz, 2H), 4.00 (brs, 1H), 2.51−2.44 (m, 2H), 2.09−2.04 (m, 2H), 1.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 143.6, 128.2, 126.9, 119.5, 116.4, 114.5, 71.9, 37.6, 32.6, 29.5, 25.3; IR (KBr) ν_{max} 3292, 2975, 1682, 1395, 1233, 1200, 821, 780 cm^{-1}; HRMS calcd for $C_{12}H_{14}ClN_2O$ (M^+ + H) 237.0795, found 237.0793.

8-Fluoro-3a-methyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5m). Pale yellow solid; mp = 140−142 °C; R_f = 0.36 (hexane/EtOAc = 30/70); ^{1} H NMR (300 MHz, $CDCl_3$) δ 6.95 (dd, J = 8.2, 6.4 Hz, 1H), 6.44 (t, J = 8.3 Hz, 1H), 6.27 (d, J = 8.1 Hz, 1H), 4.57 (ABq, J = 17.4 Hz, 2H), 4.05 (brs, 1H), 2.58−2.40 (m, 2H), 2.12−2.02 (m, 2H), 1.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 161.8, 158.6, 143.5, 131.9, 128.3, 128.2, 111.3, 105.2, 104.9, 71.6, 33.9, 32.6, 29.4, 25.3; IR (KBr) ν_{max} 3300, 2965, 1681, 1500, 1391, 1233, 1199, 1079, 1025, 763 cm^{-1}; HRMS calcd for $C_{12}H_{14}FN_2O$ (M^+ + H) 221.1090, found 221.1097.

11,11a-Dimethyl-1,3,4,6,11,11a-hexahydro[1,4]oxazino[3,4-*b*]-quinazolin-4-one (5n). Brown solid; mp = 192−194 °C; R_f = 0.32 (DCM/MeOH = 95/05); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 7.4 Hz, 1H), 6.80 (t, J = 7.4 Hz, 1H), 6.71 (d, J = 8.1 Hz, 1H), 4.70 (ABq, J = 16.8 Hz, 2H), 4.12 (ABq, J = 4.1 Hz, 2H), 3.92 (ABq, J = 11.7 Hz, 2H), 2.82 (s, 3H), 1.45 (s, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 144.1, 128.0, 126.3, 121.2, 119.5, 114.5, 72.2, 68.0, 39.3, 33.0, 29.8, 19.8; IR (KBr) ν_{max} 2923, 1670, 1605, 1494, 1458, 1397, 1296, 1110, 1067, 981, 837, 600 cm^{-1}; HRMS calcd for $C_{13}H_{17}N_2O_2$ (M^+ + H) 233.1290, found 233.1296.

(2*R*,3a*R*)-3a-Methyl-2-phenyl-1,2,3,3a,4,9-hexahydropyrrolo-[2,1-*b*]quinazolin-1-one (5p). Pale yellow solid; mp = 170−172 °C; R_f = 0.46 (hexane/EtOAc = 30/70); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.18 (m, 5H), 7.02−6.97 (m, 2H), 6.74 (t, J = 7.6 Hz, 1H), 6.49 (d, J = 8.1 Hz, 1H), 4.40 (ABq, J = 16.8 Hz, 2H), 3.84 (t, J = 9.6 Hz, 1H), 3.82 (brs, 1H), 2.53 (dd, J = 13.0, 9.6 Hz, 1H), 2.12 (dd, J = 13.0, 9.6 Hz, 1H), 1.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9, 141.9, 139.1, 128.8, 128.1, 127.5, 127.1, 126.8, 119.2, 117.5, 116.4, 70.0, 47.1, 42.7, 39.0, 25.8; IR (KBr) ν_{max} 3303, 2974, 1680, 1489, 1228, 1119, 1076, 751, 696 cm^{-1}; HRMS calcd for $C_{18}H_{19}N_2O$ (M^+ + H) 279.1497, found 279.1508.

(2*S*,3a*R*)-3a-Methyl-2-phenyl-1,2,3,3a,4,9-hexahydropyrrolo-[2,1-*b*]quinazolin-1-one (5p′). Yellow solid; mp = 122−124 °C;

R_f = 0.70 (hexane/EtOAc = 30/70); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24−7.19 (m, 4H), 7.18−7.14 (m, 1H), 7.02−6.97 (m, 2H), 6.75 (t, J = 7.2 Hz, 1H), 6.54 (d, J = 7.2 Hz, 1H), 4.37 (ABq, J = 17.6 Hz, 2H), 3.78 (t, J = 9.3 Hz, 1H), 2.63 (dd, J = 13.5, 9.3 Hz, 1H), 2.15 (dd, J = 13.5, 3.1 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 141.2, 128.6, 128.3, 127.6, 127.0, 126.9, 119.3, 116.3, 70.1, 47.6, 43.2, 38.9, 25.2; IR (KBr) ν_{max} 3326, 2994, 2826, 1692, 1497, 1253, 1181, 1074, 753, 695 cm^{-1}; HRMS calcd for $C_{18}H_{19}N_2O$ (M^+ + H) 279.1497, found 279.1509.

(2*S*,3a*R*)-2-Ethyl-3a-methyl-1,2,3,3a,4,9-hexahydropyrrolo-[2,1-*b*]quinazolin-1-one (5q). Yellow solid; mp = 130−132 °C; R_f = 0.58 (hexane/EtOAc = 30/70); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99−6.95 (m, 2H), 6.72 (t, J = 8.3 Hz, 1H), 6.47 (d, J = 8.3 Hz, 1H), 4.45 (ABq, J = 16.6 Hz, 2H), 3.73 (brs, 1H), 2.58−2.48 (m, 1H), 2.21 (dd, J = 12.8, 9.0 Hz, 1H), 2.05−1.87 (m, 1H), 1.70 (dd, J = 12.8, 9.0 Hz, 1H), 1.55 (s, 3H), 1.51−1.39 (m, 1H), 0.97 (t, J = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5, 141.9, 127.4, 126.8, 119.1, 117.6, 116.3, 70.2, 42.0, 39.0, 38.6, 25.9, 23.9, 11.4; IR (KBr) ν_{max} 3331, 2963, 2925, 2869, 1680, 1487, 1399, 1231, 1032, 747, 695 cm^{-1}; HRMS calcd for $C_{14}H_{19}N_2O$ (M^+ + H) 231.1497, found 231.1506.

(2*R*,3a*R*)-2-Ethyl-3a-methyl-1,2,3,3a,4,9-hexahydropyrrolo-[2,1-*b*]quinazolin-1-one (5q′). Yellow solid; mp = 100−102 °C; R_f = 0.56 (hexane/EtOAc = 70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00−6.96 (m, 2H), 6.73 (t, J = 7.6 Hz, 1H), 6.50 (d, J = 8.7 Hz, 1H), 4.53 (ABq, J = 17.0 Hz, 2H), 3.86 (brs, 1H), 2.53−2.42 (m, 1H), 2.32 (dd, J = 12.5, 7.0 Hz, 1H), 1.97−1.84 (m, 1H), 1.79 (dd, J = 12.5, 7.0 Hz, 1H), 1.57−1.42 (m, 1H), 1.49 (s, 3H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 141.4, 127.6, 127.0, 119.2, 117.1, 116.2, 70.3, 42.7, 39.7, 38.5, 25.4, 24.7, 11.8; IR (KBr) ν_{max} 3309, 2964, 2927, 2867, 1676, 1490, 1408, 1308, 1175, 752, 707 cm^{-1}; HRMS calcd for $C_{14}H_{19}N_2O$ (M^+ + H) 231.1497, found 231.1506.

(2*R*,3a*R*)-2-(4-Isobutylphenyl)-2,3a-dimethyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5r). White solid; mp = 172−174 °C; R_f = 0.74 (hexane/EtOAc = 70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.25 (m, 2H), 7.07−6.97 (m, 4H), 6.74 (t, J = 7.6 Hz, 1H), 6.50 (d, J = 8.3 Hz, 1H), 4.68 (ABq, J = 17.4 Hz, 2H), 3.85 (brs, 1H), 2.39 (ABq, J = 13.6 Hz, 2H), 2.43 (d, J = 6.8 Hz, 2H), 1.90−1.77 (m, 1H), 1.61 (s, 3H), 1.47 (s, 3H), 0.91 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.7, 142.5, 141.5, 139.9, 129.2, 127.5, 126.9, 125.7, 119.1, 117.3, 116.1, 69.4, 50.5, 48.7, 44.9, 38.8, 30.1, 26.4, 26.3, 22.4; IR (KBr) ν_{max} 3296, 3027, 2925, 2854, 1675, 1607, 1487, 1399, 1239, 769, 750 cm^{-1}; HRMS calcd for $C_{23}H_{29}N_2O$ (M^+ + H) 349.2280, found 349.2277.

(2*S*,3a*R*)-2-(4-Isobutylphenyl)-2,3a-dimethyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-1-one (5r′). White solid; mp = 128−130 °C; R_f = 0.72 (hexane/EtOAc = 70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, J = 8.4 Hz, 2H), 6.96−6.95 (m, 4H), 6.69 (t, J = 7.5 Hz, 1H), 6.36 (d, J = 8.4 Hz, 1H), 4.61 (ABq, J = 16.8 Hz, 2H), 2.36 (ABq, J = 13.9 Hz, 2H), 2.33 (d, J = 6.5 Hz, 2H), 1.78−1.70 (m, 1H), 1.57 (s, 3H), 1.50 (s, 3H), 0.82 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5, 142.2, 141.5, 139.8, 129.1, 127.5, 126.9, 125.9, 119.2, 117.3, 116.7, 69.4, 50.8, 48.4, 44.9, 39.0, 30.0, 26.9, 26.7, 22.3; IR (KBr) ν_{max} 3313, 2955, 2866, 1676, 1609, 1489, 1410, 1213, 771, 749 cm^{-1}; HRMS calcd for $C_{23}H_{29}N_2O$ (M^+ + H) 349.2280, found 349.2276.

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Supporting Information Available: All experimental procedures, analytical data, copies of ^{1}H and ^{13}C NMR spectra of all newly synthesized products, and CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.