JOC Article
pubs.acs.org/joc

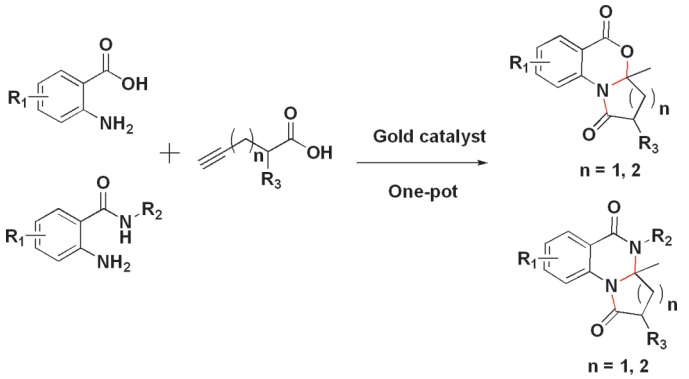
Gold(I)-Catalyzed Tandem Transformation: A Simple Approach for the Synthesis of Pyrrolo/Pyrido[2,1-*a*][1,3]benzoxazinones and Pyrrolo/Pyrido[2,1-*a*]quinazolinones

Enguang Feng, Yu Zhou, Dengyou Zhang, Lei Zhang, Haifeng Sun, Hualiang Jiang, and Hong Liu*

State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, China

hliu@mail.shcnc.ac.cn

Received February 17, 2010



We have developed a simple method for the synthesis of pyrrolo/pyrido[2,1-*a*][1,3]benzoxazinones and pyrrolo/pyrido[2,1-*a*]quinazolinones from 2-amino benzoic acids and 2-amino benzamides via a gold(I)-catalyzed tandem coupling/cyclization process. The tricyclic or polycyclic molecular architectures were constructed in one pot with the formation of three new bonds.

Introduction

Gold catalysts are considered to be attractive reagents in organic synthesis for converting simple starting materials into diverse and valuable synthetic products. In recent years, gold-catalyzed reactions emerged as a powerful tool and were applied in broad reactions, such as the nucleophilic addition,[1] Friedel−Crafts reaction,[2] C−H activation,[3] hydrogenation,[4] oxidation,[5] and so on. Heterocyclic compounds, especially some fused heterocycles, are considered as "privileged structures"[6] and play very important roles in the pharmaceutical and agrochemical industries. Therefore, the development of new and effective strategies for the synthesis of these fused heterocycles is being actively pursued for obtaining novel

(1) For selected examples of gold-catalyzed nucleophilic addition, see: (a) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 11260. (b) Morita, N.; Krause, N. *Org. Lett.* **2004**, *6*, 4121. (c) Zhang, Z. B.; Bender, C. F.; Widenhoefer, R. A. *Org. Lett.* **2007**, *9*, 2887. (d) Nishina, N.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 3314. (e) Nishina, N.; Yamamoto, Y. *Synlett* **2007**, 1767.

(2) For selected examples of gold-catalyzed Friedel−Crafts reaction, see: (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J. H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285. (b) Hashmi, A. S. K.; Blanco, M. C. *Eur. J. Org. Chem.* **2006**, 4340. (c) Nguyen, R. V.; Yao, X. Q.; Li, C. J. *Org. Lett.* **2006**, *8*, 2397. (d) Reich, N. W.; Yang, C. G.; Shi, Z. J.; He, C. *Synlett* **2006**, 1278.

(3) For selected examples of gold-catalyzed C−H activation, see: (a) Hashmi, A. S. K.; Schafer, S.; Wolfle, M.; Gil, C. D.; Fischer, P.; Laguna, A.; Blanco, M. C.; Gimeno, M. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 6184. (b) Wei, C. M.; Li, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 9584. (c) Yao, X. Q.; Li, C. J. *Org. Lett.* **2006**, *8*, 1953. (d) Skouta, R.; Li, C. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 1117.

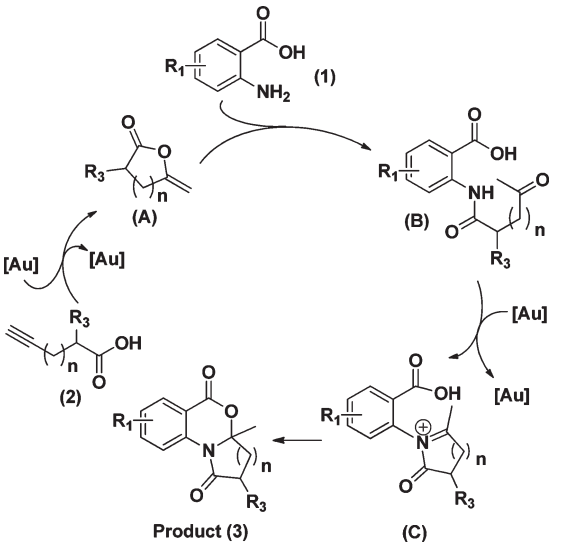
(4) For selected examples of gold-catalyzed hydrogenation, see: (a) Zhang, X.; Shi, H.; Xu, B. Q. *Angew. Chem., Int. Ed.* **2005**, *44*, 7132. (b) Comas-Vives, A.; Gonzalez-Arellano, C.; Corma, A.; Iglesias, M.; Sanchez, F.; Ujaque, G. *J. Am. Chem. Soc.* **2006**, *128*, 4756. (c) Astruc, D.; Lu, F.; Aranzaes, J. R. *Angew. Chem., Int. Ed.* **2005**, *44*, 7852.

(5) For selected examples of gold-catalyzed oxidation, see: (a) Haruta, M. *Nature* **2005**, *437*, 1098. (b) Hughes, M. D.; Xu, Y. J.; Jenkins, P.; McMorn, P.; Landon, P.; Enache, D. I.; Carley, A. F.; Attard, G. A.; Hutchings, G. J.; King, F.; Stitt, E. H.; Johnston, P.; Griffin, K.; Kiely, C. J. *Nature* **2005**, *437*, 1132. (c) Nijhuis, T. A. R.; Visser, T.; Weckhuysen, B. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1115. (d) Christensen, C. H.; Jorgensen, B.; Rass-Hansen, J.; Egeblad, K.; Madsen, R.; Klitgaard, S. K.; Hansen, S. M.; Hansen, M. R.; Andersen, H. C.; Riisager, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4648. (e) Gonzalez-Arellano, C.; Corma, A.; Iglesias, M.; Sanchez, F. *Chem. Commun.* **2005**, 1990.

(6) For selected reviews, see: (a) Clement, N. D.; Cavell, K. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3845. (b) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (c) Patil, N. T.; Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3395. (d) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054.

Published on Web 04/28/2010 DOI: 10.1021/jo100228u

SCHEME 1. Proposed One-Pot Synthesis of Pyrrolo/Pyrido[1,2-*a*][3,1]benzoxazinones

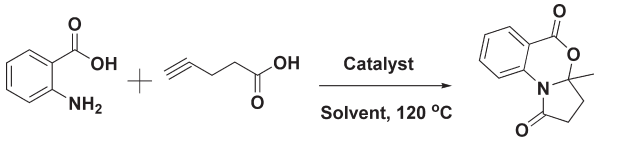


bioactive lead compounds.[7] To this end, transition-metal-catalyzed domino reactions, which allow the formation or cleavage of multiple bonds in one synthetic operation, have been used for the preparation of various compounds. However, the majority of reported gold-catalyzed cascade sequences involve the intramolecular reaction of a single starting compound that contains multiple functional groups strategically positioned along a chain, terminating with alkyne functionality. In addition, the rapid and convenient synthesis of complex and diverse organic molecules in a one-pot operation/reaction remains one of the most important concerns of the chemistry community.[8]

Recently, we successfully achieved the gold-catalyzed tandem transformation of pyrrolo[1,2-*a*]quinolin-1(2*H*)-ones[9] and pyrrolo/pyrido[2,1-*b*]benzo[*d*][1,3]oxazin- 1-ones.[10] Herein, we describe a simple and efficient one-pot gold-catalyzed cascade coupling/cyclization reaction for the synthesis of pyrrolo/pyrido[2,1-*a*][1,3]benzoxazinones and pyrrolo/pyrido[2,1-*a*]-quinazolinones by a gold-catalyzed cascade coupling/cyclization process. To the best of our knowledge, this is the first report of the formation of pyrrolo/pyrido[2,1-*a*][1,3]benzoxazinones and pyrrolo/pyrido[2,1-*a*]quinazolinones via a transition-metal-catalyzed domino reaction.

Our proposed approach is summarized in Scheme 1. Alkynoic acids are first activated by a gold(I) catalyst to afford cyclic activated enol-lactone intermediate **A**.[11] Subsequently, the amino group of 2-amino benzoic acids **1** attacks this intermediate to form ammonolysis products. In the presence of an appropriate gold catalyst, the resulting ketoamide **B** might be converted into the transition-state complex **C** via *N*-acyliminium ion formation/cyclization.[12] Finally, nucleophilic attack by the hydroxyl group could yield the final product **3**.

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



1A 2a 3Aa

entry	catalyst system	temp (°C)	solvent	yield (%)
1	$AuCl_3$	120	DCE	56
2		120	DCE	0
3	$AuBr_3$	120	DCE	50
4	AuI	120	DCE	30
5	$AuCl(PPh_3)$	120	DCE	56
6	Au^1 catalyst	120	DCE	60
7	**Au^2 catalyst**	**120**	**DCE**	**95/95[b]**
8	Au^2 catalyst	120	toluene	86[b]
9	Au^2 catalyst	120	DME	71[b]
10	Au^2 catalyst	120	DCM	85[b]
11	Au^2 catalyst	120	DMF	30[b]
12	Au^2 catalyst	120	H_2O	0[b]
13	Au^2 catalyst	120	dioxane	64[b]
14	Au^2 catalyst	120	THF	75[b]
15	Au^2 catalyst	120	DCE	85[c]
16	$AgSbF_6$	120	DCE	41[d]/85[e]
17	Au^2 catalyst/$AgSbF_6$	120	DCE	93[b]
18	Au^2 catalyst/TFA	120	DCE	92[b]
19	Au^2 catalyst	120	DCE	80[f]
20	Au^2 catalyst	100	DCE	75[b]

[a]Reaction conditions: **1A** (0.1 mmol), **2a** (0.15 mmol), and Au catalyst (1.5 mol %) in solvent (2.0 mL), oil bath for 12 h under argon protection. Au^1 catalyst = [Au{P(*t*-Bu)$_2$(*o*-biphenyl)}]Cl; Au^2 catalyst = [Au{P(*t*-Bu)$_2$-(*o*-biphenyl)} {CH_3CN}]SbF_6. [b]Reaction performed without argon protection. [c]Reaction performed in the presence of 0.5 mol % Au^2 catalyst and without argon protection. [d]Reaction performed in the presence of 1.5 mol % $AgSbF_6$. [e]Reaction performed in the presence of 10 mol % $AgSbF_6$. [f]Reaction performed for 6 h without argon protection.

Results and Discussion

In the preliminary experiments, we selected 2-amino benzoic acid **1A** and 4-pentynoic acid **2a** as the model substrates. The initial reactions were carried out in dichloroethane (DCE) using $AuCl_3$ (1.5 mol %) as the catalyst at 120 °C in a sealed tube under argon atmosphere. The starting materials were completely consumed, and the expected product **3Aa** was obtained in a moderate yield after 12 h (Table 1, entry 1), whereas the reaction did not proceed in the absence of gold catalysts (Table 1, entry 2). [Au{P(*t*-Bu)$_2$(*o*-biphenyl)}{CH_3-CN}]SbF_6 (Au^2 catalyst) turned out to be better than the other gold catalysts, such as AuI, $AuBr_3$, $AuCl(PPh_3)$, and [Au-{P(t-Bu)$_2$(*o*-biphenyl)}]Cl (Au^1 catalyst) (Table 1, entries 3−7). Furthermore, unlike the air- and water-sensitive AuI and $AuBr_3$, the reaction carried out with Au^2 catalyst afforded

(7) For selected examples, see: (a) Murata, Y.; Yamashita, D.; Kitahara, K.; Minasako, Y.; Nakazaki, A.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 1400. (b) Barluenga, J.; Mendoza, A.; Rodriguez, F.; Fananas, F. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 1644. (c) Zhao, Y. B.; Mariampillai, B.; Candito, D. A.; Laleu, B.; Li, M. Z.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 1849. (d) Bender, C. F.; Yoshimoto, F. K.; Paradise, C. L.; De Brabander, J. K. *J. Am. Chem. Soc.* **2009**, *131*, 11350. (e) Wu, X. X.; Zhou, J. Y.; Snider, B. B. *Angew. Chem., Int. Ed.* **2009**, *48*, 1283.

(8) For selected reviews, see: (a) Enders, D.; Grondal, C.; Huttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (b) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115.

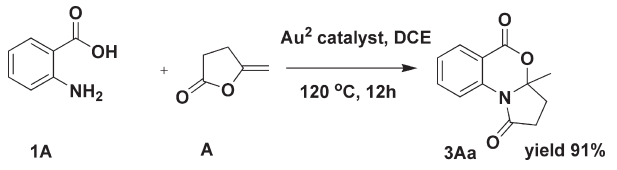
(9) Zhou, Y.; Feng, E. G.; Liu, G. N.; Ye, D. J.; Li, J.; Jiang, H. L.; Liu, H. *J. Org. Chem.* **2009**, *74*, 7344.

(10) Zhou, Y.; Zhai, Y.; Ji, X.; Liu, G. N.; Feng, E. G.; Ye, D. J.; Zhao, L. X.; Jiang, H. L.; Liu, H. *Adv. Synth. Catal.* **2010**, *352*, 373.

(11) (a) Genin, E.; Toullec, P. Y.; Antoniotti, S.; Brancour, C.; Genet, J. P.; Michelet, V. *J. Am. Chem. Soc.* **2006**, *128*, 3112. (b) Harkat, H.; Weibel, J.-M.; Pale, P. *Tetrahedron Lett.* **2006**, *47*, 6273. (c) Muratore, M. E.; Holloway, C. A.; Pilling, A. W.; Storer, R. I.; Trevitt, G.; Dixon, D. J. *J. Am. Chem. Soc.* **2009**, *131*, 10796.

(12) Liu, X. Y.; Che, C. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3805.

SCHEME 2. Reaction of the Enol-lactone Intermediate A with 2-Amino Benzoic acid 1A



3Aa in high yield even without argon protection. This confirmed that the reaction system was not sensitive to air and moisture at low catalyst loadings (Table 1, entry 7). Subsequently, probing solvent effect revealed that DCE was superior to the others (Table 1, entries 8−14). However, the product yield obtained with 0.5 mol % Au^2 catalyst was slightly lower than that obtained with 1.5 mol % Au^2 catalyst (Table 1, entry 15). A lower yield was obtained when $AgSbF_6$ (1.5 mol %) was tested for this reaction, and the yield increased to 85% when 10 mol % $AgSbF_6$ was used (Table 1, entry 16). Furthermore, it was determined whether acids such as $AgSbF_6$ and trifluoroacetic acid (TFA), respectively, could be used as cocatalysts to increase the speed of the reaction; however, reactions carried out using these acids as the cocatalyst did not give better results than that using Au^2 catalyst only (Table 1, entries 17 and 18). Finally, reducing the reaction time (6 h) or decreasing the reaction temperature led to worse results (Table 1, entries 19 and 20). Briefly, the optimum results were obtained when 2-amino benzoic acid (0.1 mmol, **1A**) and 4-pentynoic acid (0.15 mmol, **2a**) in DCE were treated with 1.5 mol % of Au^2 catalyst in a sealed tube at 120 °C for 12 h.

To further explore the proposed mechanism, we have treated one of the commercially available intermediates **A** (α-angelica lactone) from Scheme 1 with 2-amino benzoic acid **1A** under the above optimal reaction conditions, and the desired product **3Aa** was obtained in 91% yield (Scheme 2).

With the optimal conditions established, we then investigated the scope of this method. First, we examined the reactions of various substituted 2-amino benzoic acids **1** with **2a** (Table 2, entries 1−14). 2-Amino benzoic acids bearing both electron-withdrawing (4-F, 6-F, 4-Cl, 5-Cl, and 5-NO_2) and electron-donating groups (3-CH_3 and 5-CH_3, 4,5-dimethoxy, 3,4-dimethyl) appeared to be reactive and afforded the products in good to excellent yields (Table 2, entries 2−11). It is worthwhile to note that the unprotected phenolic hydroxyl group was also tolerated in the reaction (Table 2, entry 9). Substitution at the 5-position of 2-amino benzoic acids helped achieve high yields of the product. However, treatment of 3-amino-2-naphthoic acid (**1M**) resulted in a decrease of yield (65%), and more reaction time (24 h) was required (Table 2, entry 13). In addition, owing to the poor solubility of 2-amino nicotinic acid (**1N**) in DCE, the product was obtained in a low yield even when the reaction time was extended to 24 h (Table 2, entry 14). Furthermore, the replacement of 4-pentynoic acid with 5-hexynoic acid (**2b**) also achieved good yields (Table 2, entries15−17). Substitution of an alkyl group (*n*-hexyl group) with an alkynoic acid chain afforded the product in excellent yields (Table 2, entries 18−20). The product **3Ha** was recrystallized from a component solvent of petroleum ether and ethyl acetate and characterized with crystallography (see Supporting Information for details).

Subsequently, we investigated whether the protocol can be extended to the reaction of 2-amino benzamides **4** with alkynoic acids **2**. As shown in Table 3, the desired products, pyrrolo/pyrido[2,1-*a*]quinazolinones **5**, were obtained in good yields. Alkyl- and aryl-substituted 2-amino benzamides, which were prepared from the corresponding 2-amino benzoic acids,[13] were efficiently converted into their corresponding products in high yields (Table 3, entries1−4). As shown in Table 2, substituents with both electron-donating groups (5-OCH_3, 5-CH_3) and electron-withdrawing groups (5-Cl) were successfully converted to the products (Table 3, entries 5−8). Similarly, good yields were obtained when 4-pentynoic acid was replaced with 5-hexynoic acid (**2b**) (Table 3, entries 9, 10, 12, and 13). However, steric effect was significant when 2-amino-*N*-(*sec*-butyl) benzamide (**4C**) was treated with 5-hexynoic acid (**2b**) (Table 3, entry 11). The substitution of an alkyl group (*n*-hexyl group) at the alkynoic acid chain was also tolerated, and excellent yields were obtained (Table 3, entries 14−17).

Conclusion

In summary, a facile and practical protocol for the synthesis of pyrrolo/pyrido[2,1-*a*][1,3]benzoxazinones and pyrrolo/pyrido[2,1-*a*]quinazolinones was developed via a gold(I)-catalyzed tandem coupling/cyclization. Three new bonds were formed from two simple starting materials in this transformation. A plausible reaction mechanism based on the results was also described. Using this method, a variety of products could be conveniently synthesized in good to excellent yields. We expect these novel molecules to find several applications in medicinal chemistry and/or agrochemistry.

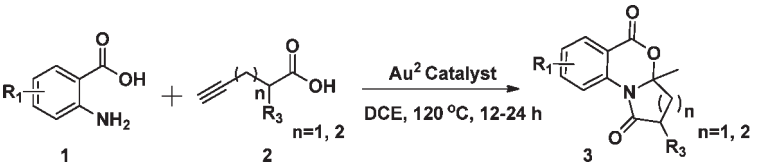
Experimental Section

General Procedure for Synthesis of Pyrrolo/Pyrido[2,1-*a*][1,3]-benzoxazinones and Pyrrolo/Pyrido[2,1-*a*]quinazolinones. To a solution of 2-amino benzoic acids or 2-amino benzamides (0.1 mmol) and alkynoic acids (0.15 mmol) in DCE (2.0 mL) was added Au^2 catalyst ([Au{P(*t*-Bu)$_2$(*o*-biphenyl)}{CH_3CN}]SbF_6, 1.5 mol %). The vial was sealed, and this mixture was then heated in an oil bath and stirred at 120 °C for 12−24 h. After the starting materials were consumed monitored with TLC, the cold mixture was concentrated in a vacuum, and the resulting residue was purified by flash column chromatography (petroleum ether (PE)/ethyl acetate (EA) = 4:1 to 1:1) to afford the expected tricyclic heterocyclic products. For a selected example, compound **3Aa**, the characterization data obtained are as follows: white solid, mp 115−117 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.66 (s, 3H), 2.40−2.73 (m, 4H), 7.29 (td, J = 7.8 Hz, 0.9 Hz, 1H), 7.86 (td, J = 7.8 Hz, 0.9 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 8.06 (dd, J = 7.8 Hz, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.6, 29.3, 32.2, 95.2, 116.1, 120.9, 125.6, 130.2, 135.2, 136.0, 161.5, 171.5; ESI-MS m/z $[M + H]^+$ 217.9; HRMS (ESI) calcd for $C_{12}H_{11}NO_3Na$ $[M + Na]^+$ 240.0637, found 240.0648.

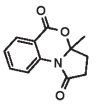
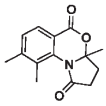
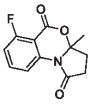
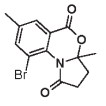
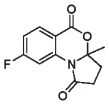
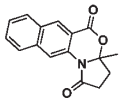
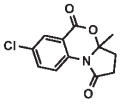
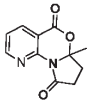
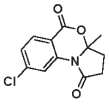
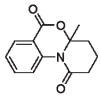
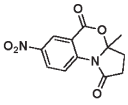
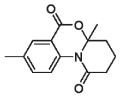
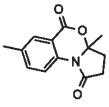
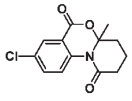
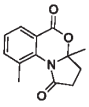
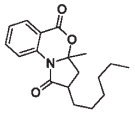
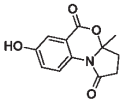
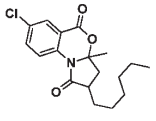
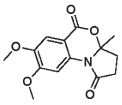
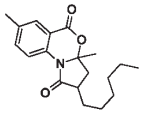
6-Fluoro-3a-methyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Ba). Compound **3Ba** was obtained as a white solid after the purification by flash chromatography (PE/EA = 4:1), mp 139−140 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.73 (s, 3H), 2.42−2.78 (m, 4H), 7.07 (t, J = 9 Hz, 1H), 7.66 (td, J = 8.4 Hz, 5.1 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.6, 27.5, 32.1, 95.2, 114.0 (d, 20.9 Hz,), 117.1 (d, 3.8 Hz), 136.5 (d, 112 Hz), 137.3, 161.4, 164.1, 171.7;

(13) Mizutani, T.; Nagase, T.; Ito, S.; Miyamoto, Y.; Tanaka, T.; Takenaga, N.; Tokita, S.; Sato, N. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 6041.

TABLE 2. One-Pot Tandem Synthesis of 3 from 2-Amino Benzoic Acids 1 and Alkynoic Acids 2[a]

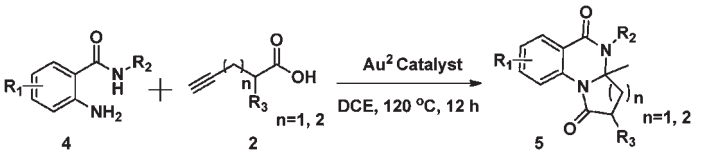


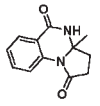
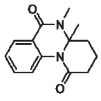
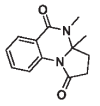
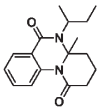
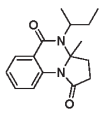
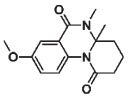
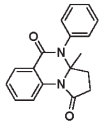
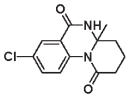
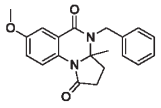
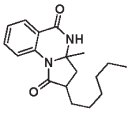
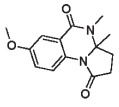
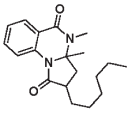
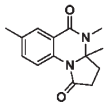
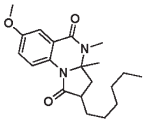
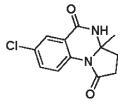
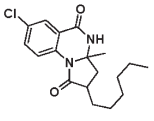
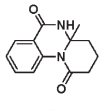
1 2 3

Entry	Product		Yield(%)	Entry	Product		Yield(%)
1		3Aa	95	11		3Ka	80
2		3Ba	96	12		3La	85
3		3Ca	83	13		3Ma	65/90[b]
4		3Da	95	14		3Na	60[b]
5		3Ea	91	15		3Ab	88
6		3Fa	91	16		3Gb	89
7		3Ga	95	17		3Db	86
8		3Ha	93	18		3Ac	92 (1.4:1 dr)
9		3Ia	89	19		3Dc	95 (1.5:1 dr)
10		3Ja	90	20		3Gc	91 (1.2:1 dr)

[a]Reaction conditions: **1** (0.1 mmol), **2** (0.15 mmol) and Au^2 catalyst (1.5 mol %) in DCE (2.0 mL) at 120 °C for 12 h. [b]The reaction time was prolonged to 24 h.

TABLE 3. One-Pot Tandem Synthesis of 5 from 2-Amino Benzamides 4 and Alkynoic Acids 2[a]



Entry	Product		Yield (%)	Entry	Product		Yield (%)
1		4Aa	94	10		4Bb	86
2		4Ba	90	11		4Cb	trace
3		4Ca	85	12		4Fb	85
4		4Da	91	13		4Hb	82
5		4Ea	89	14		4Ac	92 (1.3:1 dr)
6		4Fa	94	15		4Bc	89 (1.3:1 dr)
7		4Ga	94	16		4Fc	82 (4:1 dr)
8		4Ha	93	17		4Hc	90 (1.2:1 dr)
9		4Ab	92				

[a]Reaction conditions: **1** (0.1 mmol), **2** (0.15 mmol) and Au^2 catalyst (1.5 mol %) in DCE (2.0 mL) at 120 °C for 12 h.

ESI-MS *m*/*z* $[M + H]^+$ 235.9; HRMS (ESI) calcd for $C_{12}H_{10}FNO_3Na$ $[M + Na]^+$ 258.0542, found 258.0549.

8-Fluoro-3a-methyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Ca). Compound **3Ca** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 51−53 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.69 (s, 3H), 2.44−2.75 (m, 4H), 7.00 (td, J = 8.1 Hz, 2.4 Hz, 1H), 7.84 (dd, J = 9.6 Hz, 2.4 Hz, 1H), 8.11 (dd, J = 8.7 Hz, 6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.6, 29.4, 32.3, 95.3, 108.2 (d, 26.8 Hz), 112.1, 113.4 (d, 22.3 Hz), 133.1 (d, 10.4 Hz),

138.0 (d, 12.6 Hz), 160.8, 166.8(d, 255.9 Hz), 171.3; MS (EI) *m*/*e* 235; HRMS (EI) *m*/*e* (M^+) calcd for $C_{12}H_{10}FNO_3$ 235.0645, found 235.0636.

7-Chloro-3a-methyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Da). Compound **3Da** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 117−118 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.70 (s, 3H), 2.44−2.77 (m, 4H), 7.64 (dd, J = 8.7 Hz, 3 Hz, 1H), 8.06 (d, J = 8.7 Hz, 1H), 8.09 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.7, 29.4, 32.3, 95.5, 117.5, 122.5, 130.0, 131.4, 134.6, 135.5, 160.5, 171.5; ESI-MS *m*/*z* $[M + H]^+$ 251.9; HRMS (ESI) calcd for $C_{12}H_{10}ClNO_3Na$ $[M + Na]^+$ 274.0247, found 274.0242.

8-Chloro-3a-methyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Ea). Compound **3Ea** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 158−160 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.70 (s, 3H), 2.44−2.78 (m, 4H), 7.31 (dd, J = 8.1 Hz, 2.4 Hz, 1H), 8.04 (d, J = 8.1 Hz, 1H), 8.13 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.7, 29.4, 32.3, 95.4, 114.3, 121.0, 126.2, 131.6, 136.9, 142.0, 160.9, 171.4; MS (EI) *m*/*e* 251 HRMS (EI) *m*/*e* (M^+) calcd for $C_{12}H_{10}ClNO_3$ 251.0349, found 251.0343.

3a-Methyl-7-nitro-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Fa). Compound **3Fa** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 177−179 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.73 (s, 3H), 2.52−2.82 (m, 4H), 8.38 (d, J = 9 Hz, 1H), 8.52 (dd, J = 9 Hz, 2.4 Hz, 1H), 8.98 (d, J = 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.8, 29.5, 32.4, 92.3, 116.2, 121.3, 126.3, 130.2, 140.7, 144.5, 159.6, 171.3; MS (EI) *m*/*e* 262 HRMS (EI) *m*/*e* (M^+) calcd for $C_{12}H_{10}N_2O_5$ 262.0590, found 262.0587.

3a,7-Dimethyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Ga). Compound **3Ga** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 135−136 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.68 (s, 3H), 2.38−2.47 (m, 4H), 2.66−2.76 (m, 3H), 7.49 (dd, J = 8.4 Hz, 1.8 Hz, 1H), 7.90 (d, J = 1.8 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 20.9, 24.7, 29.4, 32.3, 95.4, 116.1, 121.0, 130.4, 133.7, 135.8, 136.3, 161.9, 171.6; ESI-MS *m*/*z* $[M + H]^+$ 231.9; HRMS (ESI) calcd for $C_{13}H_{13}NO_3Na$ $[M + Na]^+$ 254.0793, found 254.0795.

3a,9-Dimethyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Ha). Compound **3Ha** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 140−142 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.63 (s, 3H), 2.33−2.43 (m, 1H), 2.35 (s, 3H), 2.62−2.76 (m, 3H), 7.33 (t, J = 7.8 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.92 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 18.2, 25.0, 28.8, 31.7, 96.8, 120.4, 127.2, 127.6, 134.8, 135.4, 137.0, 162.5, 174.7; ESI-MS *m*/*z* $[M + H]^+$ 232.0; HRMS (ESI) calcd for $C_{13}H_{13}NO_3Na$ $[M + Na]^+$ 254.0793, found 254.0802.

7-Hydroxy-3a-methyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*]-[1,3]oxazine-1,5(2*H*)-dione (3Ia). Compound **3Ia** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 173−174 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.67 (s, 3H), 2.40−2.75 (m, 4H), 7.19 (dd, J = 9 Hz, 2.4 Hz, 1H), 7.56 (d, J = 2.4 Hz, 1H), 7.83 (d, J = 9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.7, 29.3, 32.1, 96.1, 115.8, 117.5, 123.0, 126.4, 128.7, 154.5, 162.2, 172.2; ESI-MS *m*/*z* $[M + H]^+$ 233.9; HRMS (ESI) calcd for $C_{12}H_{11}NO_4Na$ $[M + Na]^+$ 256.0586, found 256.0598.

7,8-Dimethoxy-3a-methyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*]-[1,3]oxazine-1,5(2*H*)-dione (3Ja). Compound **3Ja** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 146−147 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.66 (s, 3H), 2.38−2.72 (m, 4H), 3.90 (s, 3H), 3.96 (s, 3H), 7.45 (s, 1H), 7.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.3, 29.5, 32.2, 56.1, 56.4, 95.3, 103.3, 107.8, 110.7, 131.5, 146.8, 154.9, 161.6, 171.4; ESI-MS *m*/*z* $[M + H]^+$ 277.9; HRMS (ESI) calcd for $C_{14}H_{15}NO_5Na$ $[M + Na]^+$ 300.0848, found 300.0835.

3a,8,9-Trimethyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Ka). Compound **3Ka** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 158−159 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.64 (s, 3H), 2.22 (s, 3H), 2.35−2.42 (m, 1H), 2.40 (s, 3H), 2.63−2.77 (m, 3H), 7.23 (d, J = 7.8 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 15.1, 20.9, 25.1, 28.9, 31.7, 96.9, 118.1, 127.4, 128.9, 133.4, 135.2, 145.9, 162.7, 174.9; ESI-MS *m*/*z* $[M + H]^+$ 245.9; HRMS (ESI) calcd for $C_{14}H_{15}NO_2Na$ $[M + Na]^+$ 268.0950, found 268.0942.

9-Bromo-3a,7-dimethyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]oxazine-1,5(2*H*)-dione (3La). Compound **3La** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 208−209 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.64 (s, 3H), 2.35−2.46 (m, 1H), 2.40 (s, 3H), 2.61−2.74 (m, 3H), 7.71 (d, J = 0.9 Hz, 1H), 7.85 (d, J = 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 20.7, 24.8, 28.6, 31.5, 97.3, 119.3, 122.0, 129.5, 133.8, 139.2, 139.6, 161.4, 173.9; ESI-MS *m*/*z* $[M + H]^+$ 309.8; HRMS (ESI) calcd for $C_{13}H_{12}BrNO_3Na$ $[M + Na]^+$ 331.9898, found 331.9896.

3a-Methyl-3,3a-dihydro-1*H*-naphtho[2,3-*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Ma). Compound **3Ma** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 244−245 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.72 (s, 3H), 2.44−2.51 (m, 1H), 2.62−2.81 (m, 3H), 7.51−7.67 (m, 2H), 7.89−7.97 (m, 2H), 8.44 (s, 1H), 8.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 25.5, 29.4, 32.1, 95.5, 115.5, 119.3, 126.7, 127.8, 129.6, 129.7, 130.3, 130.9, 133.0, 136.5, 162.1, 171.5; MS (EI) *m*/*e* 267 HRMS (EI) *m*/*e* (M^+) calcd for $C_{16}H_{13}NO_3$ 267.0895, found 267.0891.

6a-Methyl-7,8-dihydro-5*H*-pyrido[2,3-*d*]pyrrolo[2,1-*b*][1,3]-oxazine-5,9(6a*H*)-dione (3Na). Compound **3Na** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 196−197 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.72 (s, 3H), 2.42−2.51 (m, 1H), 2.59−2.69 (m, 1H), 2.73−2.82 (m, 2H), 7.36 (dd, J = 7.8 Hz, 2.4 Hz, 1H), 8.42 (d, J = 7.5 Hz, 1H), 8.82 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 25.2, 29.6, 32.1, 95.9, 112.8, 121.8, 139.3, 148.9, 155.0, 161.2, 171.4; ESI-MS *m*/*z* $[M + H]^+$ 218.9; HRMS (ESI) calcd for $C_{11}H_{10}N_2O_3Na$ $[M + Na]^+$ 241.0589, found 241.0594.

4a-Methyl-2,3,4,4a-tetrahydrobenzo[*d*]pyrido[2,1-*b*][1,3]oxazine-1,6-dione (3Ab). Compound **3Ab** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 66−68 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.61 (s, 3H), 1.84−1.90 (m, 1H), 2.10−2.17 (m, 2H), 2.39−2.43 (m, 1H), 2.60−2.65 (m, 2H), 7.35 (t, J = 7.5 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 8.06 (d, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 16.6, 26.7, 33.4, 36.0, 92.4, 120.3, 126.2, 126.3, 129.3, 134.1, 138.5, 162.5, 169.4; ESI-MS *m*/*z* $[M + Na]^+$ 231.9; HRMS (ESI) calcd for $C_{13}H_{13}NO_3Na$ $[M + Na]^+$ 254.0793, found 254.0785.

8-Chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[*d*]pyrido[2,1-*b*]-[1,3]oxazine-1,6-dione (3Db). Compound **3Db** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 102−103 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.64 (s, 3H), 1.85−1.91 (m, 1H), 2.07−2.22 (m, 2H), 2.40−2.47 (m, 1H), 2.61−2.67 (m, 2H), 7.60 (dd, J = 8.7 Hz, 1.8 Hz, 1H), 7.77 (d, J = 8.7 Hz, 1H), 8.04 (d, J = 2.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 16.5, 26.7, 33.4, 35.9, 92.7, 127.6, 129.0, 132.0, 134.1, 137.0, 161.5, 169.4, 171.4; MS (EI) *m*/*e* 265; HRMS (EI) *m*/*e* (M^+) calcd for $C_{13}H_{12}ClNO_3$ 265.0506, found 265.0502.

4a,8-Dimethyl-2,3,4,4a-tetrahydrobenzo[*d*]pyrido[2,1-*b*][1,3]-oxazine-1,6-dione (3Gb). Compound **3Gb** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1), mp 119−121 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.60 (s, 3H),

1.82−1.88 (m, 1H), 2.04−2.20 (m, 2H), 2.32−2.44 (m, 1H), 2.40 (s, 3H), 2.58−2.64 (m, 2H), 7.44 (dd, J = 8.4 Hz, 2.1 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 2.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 16.6, 20.9, 26.7, 33.4, 36.0, 92.4, 120.0, 125.9, 129.4, 135.0, 136.1, 136.3, 162.8, 169.4; ESI-MS m/z $[M + H]^+$ 245.9; HRMS (ESI) calcd for $C_{14}H_{15}NO_3Na$ $[M+Na]^+$ 268.0950, found 268.0966.

2-Hexyl-3a-methyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*][1,3]-oxazine-1,5(2*H*)-dione (3Ac). Compound **3Ac** was obtained after purification by flash chromatography (PE/EA = 4:1), and the two diastereomers were separable by chromatography (dr = 1.4:1). **Diastereomer 1**: white wax solid, mp < 50 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.87−0.92 (m, 3H), 1.31−1.51 (m, 8H), 1.52−1.55 (m, 1H), 1.69 (s, 3H), 1.97−2.04 (m, 1H), 2.21−2.28 (m, 1H), 2.58−2.71 (m, 2H), 7.32 (td, J = 8,7 Hz, 0.9 Hz, 1H), 7.69 (td, J = 8.1 Hz, 1.5 Hz, 1H), 8.11 (dd, J = 8.1 Hz, 1.8 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.6, 24.4, 26.9, 29.0, 30.4, 31.6, 39.2, 40.7, 93.5, 115.6, 120.4, 125.4, 130.4, 135.5, 136.2, 161.6, 173.2; ESI-MS m/z $[M + H]^+$ 302.0; HRMS (ESI) calcd for $C_{18}H_{23}NO_3Na$ $[M + Na]^+$ 324.1576, found 324.1584. **Diastereomer 2**: white wax solid, mp < 50 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.88−0.92 (m, 3H), 1.32−1.57 (m, 9H), 1.72 (s, 3H), 1.97−2.16 (m, 2H), 2.80−2.85 (m, 2H), 7.37 (td, J = 7.8 Hz, 0.9 Hz, 1H), 7.71 (td, J = 7.8 Hz, 1.5 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 8.02 (dd, J = 7.8 Hz, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 26.3, 27.2, 29.0, 31.6, 31.8, 38.2, 40.6, 94.6, 117.7, 122.5, 126.1, 130.2, 135.3, 136.3, 162.1, 175.4; ESI-MS m/z $[M + H]^+$ 302.0; HRMS (ESI) calcd for $C_{18}H_{23}NO_3Na$ $[M + Na]^+$ 324.1576, found 324.1581.

7-Chloro-2-hexyl-3a-methyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo-[2,1-*b*][1,3]oxazine-1,5(2*H*)-dione (3Dc). Compound **3Dc** was obtained after purification by flash chromatography (PE/EA = 4:1), and the two diastereomers were separable by chromatography (dr = 1.5:1). **Diastereomer 1**: white wax solid, mp < 50 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.85−0.90 (m, 3H), 1.25−1.55 (m, 9H), 1.67 (s, 3H), 1.95−2.02 (m, 1H), 2.19−2.26 (m, 1H), 2.57−2.72 (m, 2H), 7.61 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 8.05 (d, J = 2.4 Hz, 1H), 8.13 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 24.3, 26.8, 29.0, 30.3, 31.5, 39.2, 40.7, 93.6, 116.8, 121.7, 129.9, 130.8, 134.6, 135.4, 160.4, 173.0; ESI-MS m/z $[M + H]^+$ 335.9; HRMS (ESI) calcd for $C_{18}H_{22}ClNO_3Na$ $[M + Na]^+$ 358.1186, found 358.1191. **Diastereomer 2**: white wax solid, mp < 50 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.87−0.90 (m, 3H), 1.26−1.56 (m, 9H), 1.71 (s, 3H), 1.93−2.15 (m, 2H), 2.76−2.83 (m, 2H), 7.64 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 26.2, 27.1, 28.9, 31.5, 31.7, 38.1, 40.5, 94.7, 118.9, 123.9, 129.9, 131.8, 134.8, 135.2, 160.9, 175.3; ESI-MS m/z $[M + H]^+$ 335.9; HRMS (ESI) calcd for $C_{18}H_{22}ClNO_3Na$ $[M + Na]^+$ 358.1186, found 358.1190.

2-Hexyl-3a,7-dimethyl-3,3a-dihydro-1*H*-benzo[*d*]pyrrolo[2,1-*b*]-[1,3]oxazine-1,5(2*H*)-dione (3Gc). Compound **3Gc** was obtained after purification by flash chromatography (PE/EA = 4:1), and the two diastereomers were separable by chromatography (dr = 1.2:1). **Diastereomer 1**: white wax solid, mp < 50 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.86−0.91 (m, 3H), 1.29−1.56 (m, 9H), 1.66 (s, 3H), 1.95−2.02 (m, 1H), 2.19−2.26 (m, 1H), 2.40 (s, 3H), 2.55−2.69 (m, 2H), 7.49 (dd, J = 8.4 Hz, 2.1 Hz, 1H), 7.90 (d, J = 0.9 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 20.9, 22.5, 24.3, 26.8, 29.0, 30.4, 31.6, 39.2, 40.7, 93.5, 115.4, 120.2, 130.3, 133.7, 135.3, 136.3, 161.8, 173.1; ESI-MS m/z $[M + H]^+$ 316.0; HRMS (ESI) calcd for $C_{19}H_{25}NO_3Na$ $[M + Na]^+$ 338.1732, found 338.1732. **Diastereomer 2**: white solid, mp 117−118 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.87−0.91 (m, 3H), 1.25−1.55 (m, 9H), 1.69 (s, 3H), 1.94−2.12 (m, 2H), 2.40 (s, 3H), 2.75−2.81 (m, 2H), 7.49 (dd, J = 8.4 Hz, 2.1 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.90 (d, J = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 20.9, 22.5, 26.1, 27.1, 29.0, 31.6, 31.8, 38.2, 40.6, 94.6, 117.5, 122.3, 130.2, 133.9, 136.0, 136.1, 162.3, 175.4; ESI-MS m/z $[M + H]^+$ 316.0; HRMS (ESI) calcd for $C_{19}H_{25}NO_3Na$ $[M+Na]^+$ 338.1732, found 338.1730.

3a-Methyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (4Aa). Compound **4Aa** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 165−167 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.67(s, 3H), 2.37−2.42 (m, 2H), 2.68−2.74 (m, 2H), 7.28 (td, J = 7.8 Hz, 0.9 Hz, 1H), 7.60 (td, J = 7.8 Hz, 1.8 Hz, 1H), 8.06 (dd, J = 7.8 Hz, 1.8 Hz, 1H), 8.16 (d, J = 7.8 Hz, 1H), 8.28 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 26.9, 30.0, 32.9, 74.5, 119.5, 120.7, 125.0, 128.3, 133.8, 135.8, 163.5, 171.7; ESI-MS m/z $[M + H]^+$ 217.0; HRMS (ESI) calcd for $C_{12}H_{12}N_2O_2Na$ $[M + Na]^+$ 239.0796, found 239.0796.

3a,4-Dimethyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (4Ba). Compound **4Ba** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 96−97 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.45 (s, 3H), 2.25−2.32 (m, 1H), 2.38−2.49 (m, 1H), 2.63−2.9 (m, 2H), 3.06 (s, 3H), 7.24 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 8.07 (d, J = 7.8 Hz, 1H), 8.25 (d, J = 7.8 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 21.6, 27.6, 30.1, 32.2, 78.4, 119.2, 119.5, 124.8, 128.4, 133.2, 135.0, 161.9, 171.1; ESI-MS m/z $[M + H]^+$ 230.9; HRMS (ESI) calcd for $C_{13}H_{14}N_2O_2Na$ $[M + Na]^+$ 253.0953, found 253.0958.

4-(*sec*-Butyl)-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (4Ca). Compound **4Ca** was obtained as a white wax solid after purification by flash chromatography (PE/EA = 1:1), mp < 50 °C, and the two diastereomers were inseparable by chromatography. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.93 (q, J = 7.5 Hz, 3H), 1.48−155 (m, 6H), 1.81−1.90 (m, 1H), 1.99−2.07 (m, 1H), 2.30−2.50 (m, 2H), 2.61−2.66 (m, 2H), 3.14−3.23 (m, 1H), 7.22 (t, J = 8.4 Hz, 1H), 7.50 (t, J = 8.4 Hz, 1H), 8.00 (t, J = 7.2 Hz, 1H), 8.20 (dd, J = 8.1 Hz, 15 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 12.0, 12.5, 18.0, 18.5, 24.3, 24.4, 27.5, 27.8, 30.0, 30.2, 32.2, 32.7, 54.5, 79.4, 119.2, 119.4, 121.0, 124.7, 124.8, 128.0, 128.1, 132.7, 132.8, 134.5, 134.7, 161.2, 171.0, 171.1; ESI-MS m/z $[M + H]^+$ 273.0; HRMS (ESI) calcd for $C_{16}H_{20}N_2O_2Na$ $[M + Na]^+$ 295.1422, found 295.1406.

3a-Methyl-4-phenyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (4Da). Compound **4Da** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 223−224 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.77 (s, 3H), 1.80−1.86 (m, 1H), 2.28−2.39 (m, 1H), 2.59−2.65 (m, 2H), 7.25−7.33 (m, 3H), 7.39−7.51 (m, 3H), 7.61 (td, J = 8.1 Hz, 1.5 Hz, 1H), 8.13 (dd, J = 7.3 Hz, 1.2 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 25.4, 30.2, 31.7, 79.3, 120.0, 125.0, 128.5, 129.0, 129.4, 129.6, 133.6, 135.4, 137.0, 162.2, 171.5; ESI-MS m/z $[M + Na]^+$ 314.9; HRMS (ESI) calcd for $C_{18}H_{16}N_2O_2Na$ $[M + Na]^+$ 315.1109, found 315.1112.

4-Benzyl-7-methoxy-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]-quinazoline-1,5-dione (4Ea). Compound **4Ea** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 126−128 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.47 (s, 3H), 2.04−2.21 (m, 1H), 2.38−2.61 (m, 3H), 3.86 (s, 3H), 4.30 (d, J = 15.9 Hz, 1H), 5.24 (d, J = 15.9 Hz, 1H), 7.14 (dd, J = 9 Hz, 3 Hz, 1 H), 7.25−7.35 (m, 5H), 7.65 (d, J = 3 Hz, 1H), 8.17 (d, J = 9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 23.3, 30.0, 31.1, 45.5, 55.6, 79.1, 111.4, 120.5, 120.8, 121.3, 126.8, 127.3, 128.7, 128.8, 137.8, 156.6, 162.4, 170.9; ESI-MS m/z $[M + H]^+$ 337.0; HRMS (ESI) calcd for $C_{20}H_{20}N_2O_3Na$ $[M + Na]^+$ 359.1372, found 359.1394.

7-Methoxy-3a,4-dimethyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]-quinazoline-1,5-dione (4Fa). Compound **4Fa** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 116−118 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.41(s, 3H), 2.23−2.46 (m, 2H), 2.59−2.65 (m, 2H), 3.04 (s, 3H),

3.82 (s, 3H), 7.07 (dd, J = 8.7 Hz, 3 Hz, 1H), 7.54 (d, J = 3 Hz, 1H), 8.13 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 21.4, 27.7, 30.0, 32.1, 55.5, 78.4, 111.2, 120.3, 120.4, 121.1, 128.5, 156.5, 161.7, 170.7; ESI-MS m/z $[M + H]^+$ 260.9; HRMS (ESI) calcd for $C_{14}H_{16}N_2O_3Na$ $[M + Na]^+$ 283.1059, found 283.1048.

3a,4,7-Trimethyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (4Ga). Compound **4Ga** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 130−132 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.42 (s, 3H), 2.23−2.30 (m, 1H), 2.36 (s, 3H), 2.40−2.43 (m, 1H), 2.61−2.67 (m, 2H), 3.05 (s, 3H), 7.33 (dd, J = 8.4 Hz, 2.1 Hz, 1H), 7.86 (d, J = 2.1 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 20.9, 21.5, 27.6, 30.1, 32.2, 78.3, 119.0, 119.4, 128.5, 132.6, 133.9, 134.6, 162.1, 170.9; ESI-MS m/z $[M + H]^+$ 245.0; HRMS (ESI) calcd for $C_{14}H_{16}N_2O_2Na$ $[M+Na]^+$ 267.1109, found 267.1114.

7-Chloro-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (4Ha). Compound **4Ha** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 217−218 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.55 (s, 3H), 2.38−2.43 (m, 2H), 2.67−2.73 (m, 2H), 7.53 (dd, J = 8.7 Hz, 2.7 Hz, 1H), 8.01 (d, J = 2.4 Hz, 1H), 8.13 (d, J = 8.7 Hz, 1H), 8.96 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 26.8, 29.9, 32.7, 74.4, 120.8, 122.1, 128.0, 130.5, 122.7, 134.2, 162.5, 171.7; ESI-MS m/z $[M + H]^+$ 250.9; HRMS (ESI) calcd for $C_{12}H_{11}ClN_2O_2$ $[M - H]^-$ 249.0431, found 249.0431.

4a-Methyl-3,4,4a,5-tetrahydro-1*H*-pyrido[1,2-*a*]quinazoline-1,6(2*H*)-dione (4Ab). Compound **4Ab** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 201−203 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.51 (s, 3H), 1.89−1.95 (m, 1H), 2.02−2.06 (m, 1H), 2.17−2.20 (m, 2H), 2.60−2.66 (m, 2H), 7.31 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.78 (br, 1H), 8.01 (d, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 17.0, 28.6, 33.5, 36.2, 71.4, 123.1, 125.7, 126.3, 127.3, 132.5, 138.1, 164.1, 169.0; ESI-MS m/z $[M+H]^+$ 231.0; HRMS (ESI) calcd for $C_{13}H_{14}N_2O_2Na$ $[M + Na]^+$ 253.0953, found 253.0966.

4a,5-Dimethyl-3,4,4a,5-tetrahydro-1*H*-pyrido[1,2-*a*]quinazoline-1,6(2*H*)-dione (4Bb). Compound **4Bb** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 139−141 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.39 (s, 3H), 1.86−1.96 (m, 2H), 2.09−2.18 (m, 1H), 2.35−2.73 (m, 3H), 3.12 (s, 3H), 7.30 (td, J = 8.1 Hz, 1.5 Hz, 1H), 7.51 (td, J = 8.1 Hz, 1.5 Hz, 1H), 7.63 (dd, J = 7.5 Hz, 1.2 Hz, 1H), 8.02 (dd, J = 7.8 Hz, 1.5 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 16.7, 24.3, 27.3, 33.5, 34.2, 75.3, 123.7, 125.8, 126.0, 127.6, 131.8, 137.1, 163.4, 169.2; ESI-MS m/z $[M + H]^+$ 245.0; HRMS (ESI) calcd for $C_{14}H_{16}N_2O_2Na$ $[M+Na]^+$ 267.1109, found 267.1121.

8-Methoxy-4a,5-dimethyl-3,4,4a,5-tetrahydro-1*H*-pyrido[1,2-*a*]-quinazoline-1,6(2*H*)-dione (4Fb). Compound **4Fb** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 140−142 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.37 (s, 3H), 1.83−1.93 (m, 2H), 2.06−2.15 (m, 1H), 2.33−2.41 (m, 1H), 2.51−2.69 (m, 2H), 3.10 (s, 3H), 3.83 (s, 3H), 7.05 (m, 1H), 7.49 (d, J = 3 Hz, 1H), 7.52 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 16.7, 24.2, 27.4, 33.4, 34.1, 55.6, 75.3, 110.1, 119.2, 124.6, 127.3, 130.3, 157.2, 163.2, 169.2; ESI-MS m/z $[M + H]^+$ 275.0; HRMS (ESI) calcd for $C_{15}H_{18}N_2O_3Na$ $[M+Na]^+$ 297.1215, found 297.1214.

8-Chloro-4a-methyl-3,4,4a,5-tetrahydro-1*H*-pyrido[1,2-*a*]quinazoline-1,6(2*H*)-dione (4Hb). Compound **4Hb** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1), mp 187−189 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.52 (s, 3H), 1.89−2.07 (m, 2H), 2.15−2.25 (m, 2H), 2.60−2.66 (m, 2H), 7.51 (dd, J = 8.7 Hz, 2.7 Hz, 1H), 7.75 (d, J = 8.7 Hz, 1H), 7.99 (d, J = 2.7 Hz, 1H), 8.48 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 16.9, 28.6, 33.5, 35.9, 71.5, 124.5, 127.0, 127.8, 131.3, 132.5, 136.6, 163.3, 169.0; ESI-MS m/z $[M + H]^+$ 264.9; HRMS (ESI) calcd for $C_{13}H_{13}ClN_2O_2Na$ $[M + Na]^+$ 287.0563, found 287.0562.

2-Hexyl-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (4Ac). Compound **4Ac** was obtained after purification by flash chromatography (PE/EA = 1:1), and the two diastereomers were separable by chromatography (dr = 1.3:1). **Diastereomer 1**: white solid, mp 98−101 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.85−0.89 (m, 3H), 1.25−1.49 (m, 9H), 1.54 (s, 3H), 1.98−2.10 (m, 2H), 2.54−2.72 (m, 2H), 7.26 (t, J = 7.8 Hz, 1H), 7.58 (td, J = 8.1 Hz, 1.8 Hz, 1H), 8.07 (dd, J = 7.8 Hz, 0.9 Hz, 1H), 8.24 (d, J = 8.1 Hz, 1H), 8.78 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 26.4, 26.9, 29.0, 30.3, 31.5, 39.9, 40.9, 72.5, 119.1, 120.1, 124.6, 128.2, 133.7, 135.8, 163.4, 173.5; ESI-MS m/z $[M + H]^+$ 301.0; HRMS (ESI) calcd for $C_{18}H_{24}N_2O_2Na$ $[M + Na]^+$ 323.1735, found 323.1721. **Diastereomer 2**: white solid, mp 122−123 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.88−0.92 (m, 3H), 1.31−1.57 (m, 9H), 1.60 (s, 3H), 1.97−2.08 (m, 2H), 2.60−2.67 (m, 1H), 2.73−2.79 (m, 1H), 7.32 (t, J = 7.8 Hz, 1H), 7.61 (td, J = 9 Hz, 1.5 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H), 8.76 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 27.3, 29.0, 29.4, 31.6, 32.0, 38.1, 41.2, 73.2, 120.9, 122.6, 125.4, 128.0, 133.5, 136.1, 164.3, 175.4; ESI-MS m/z $[M+H]^+$ 301.0; HRMS (ESI) calcd for $C_{18}H_{24}N_2O_2Na$ $[M + Na]^+$ 323.1735, found 323.1728.

2-Hexyl-3a,4-dimethyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (4Bc). Compound **4Bc** was obtained after purification by flash chromatography (PE/EA = 1:1), and the two diastereomers were separable by chromatography (dr = 1.3:1). **Diastereomer 1**: white wax solid, mp < 50 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.85−0.89 (m, 3H), 1.23−1.43 (m, 9H), 1.45 (s, 3H), 2.00−2.08 (m, 2H), 2.42−2.48 (m, 1H), 2.62−2.68 (m, 1H), 3.06 (s, 3H), 7.22 (t, 7.8 Hz, 1H), 7.51 (t, J = 7.8 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 21.5, 22.5, 26.9, 27.6, 29.1, 30.0, 31.6, 39.3, 40.9, 76.5, 119.1, 119.4, 124.6, 128.4, 133.2, 135.1, 161.9, 173.0; ESI-MS m/z $[M+H]^+$ 315.0; HRMS (ESI) calcd for $C_{19}H_{26}N_2O_2Na$ $[M + Na]^+$ 337.1892, found 337.1907. **Diastereomer 2**: white wax solid, mp < 50 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.86−0.90 (m, 3H), 1.24−1.53 (m, 9H), 1.49 (s, 3H), 1.96−2.00 (m, 2H), 2.66-.277 (m, 2H), 3.07 (s, 3H), 7.26 (t, J = 7.8 Hz, 1H), 7.54 (t, J = 7.8 Hz, 1H), 8.02 (d, J = 7.8 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 25.3, 27.7, 28.1, 28.9, 31.5, 32.2, 36.3, 41.2, 77.5, 120.4, 121.1, 125.2, 128.3, 133.0, 135.1, 162.3, 174.5; ESI-MS m/z $[M + H]^+$ 315.0; HRMS (ESI) calcd for $C_{19}H_{26}N_2O_2Na$ $[M + Na]^+$ 337.1892, found 337.1902.

2-Hexyl-7-methoxy-3a,4-dimethyl-2,3,3a,4-tetrahydropyrrolo-[1,2-*a*]quinazoline-1,5-dione (4Fc). Compound **4Fc** was obtained after purification by flash chromatography (PE/EA = 1:1), and the two diastereomers were separable by chromatography (dr = 4:1). **Diastereomer 1**: white solid, mp 83−85 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.84−0.90 (m, 3H), 1.29−1.48 (m, 12H), 1.99−2.07 (m, 2H), 2.41−2.48 (m, 1H), 2.58−2.67 (m, 1H), 3.07 (s, 3H), 3.85 (s, 3H), 7.09 (dd, J = 8.7 Hz, 3 Hz, 1H), 7.56 (d, J = 3 Hz, 1H), 8.18 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 21.4, 22.5, 27.0, 27.7, 29.1, 30.1, 31.6, 39.3, 40.8, 55.6, 76.5, 111.2, 120.3, 120.4, 121.0, 128.7, 156.4, 172.6; ESI-MS m/z $[M + H]^+$ 345.0; HRMS (ESI) calcd for $C_{20}H_{28}N_2O_3Na$ $[M + Na]^+$ 367.1998, found 367.1986. **Diastereomer 2**: white solid, mp 72−73 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.87−0.92 (m, 3H), 1.25−1.53 (m, 12H), 1.95−2.00 (m, 2H), 2.66−2.77 (m, 2H), 3.07 (s, 3H), 3.85 (s, 3H), 7.11 (dd, J = 9.3 Hz, 3 Hz, 1H), 7.57 (d, J = 3 Hz, 1H), 7.92 (d, J = 9.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.6, 25.2, 27.7, 28.3, 29.0, 31.6, 32.3, 36.4, 41.1, 55.7, 77.6, 111.3, 120.2, 121.7, 122.8, 128.6, 157.0, 162.3, 174.4; ESI-MS m/z $[M + H]^+$ 345.0; HRMS (ESI) calcd for $C_{20}H_{28}N_2O_3Na$ $[M + Na]^+$ 367.1998, found 367.1989.

7-Chloro-2-hexyl-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]-quinazoline-1,5-dione (4Hc). Compound **4Hc** was obtained after purification by flash chromatography (PE/EA = 1:1), and the two diastereomers were separable by chromatography (dr = 1.2:1). **Diastereomer 1**: white solid, mp 148−150 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.85−0.89 (m, 3H), 1.24−1.48 (m, 9H), 1.54 (s, 3H), 1.98−2.09 (m, 2H), 2.55−2.71 (m, 2H), 7.52 (dd, J = 6.6 Hz, 2.1 Hz, 1H), 8.02 (d, J = 1.8 Hz, 1H), 8.21 (d, J = 6.9 Hz, 1H), 8.82 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 26.5, 26.9, 29.1, 30.3, 31.6, 39.9, 41.0, 72.6, 120.5, 121.7, 128.0, 130.2, 133.7, 134.3, 162.4, 173.4; ESI-MS m/z $[M + H]^+$ 334.9; HRMS (ESI) calcd for $C_{18}H_{23}ClN_2O_2Na$ $[M + Na]^+$ 357.1346, found 357.1356. **Diastereomer 2**: white solid, mp 141−142 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.87−0.91 (m, 3H), 1.25−1.57 (m, 9H), 1.59 (s, 3H), 1.96−2.10 (m, 2H), 2.59−2.67 (m, 1H), 2.74−2.79 (m, 1H), 7.56 (dd, J = 8.7 Hz, 2.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 2.4 Hz, 1H), 8.92 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 27.3, 29.0, 29.4, 31.6, 32.0, 38.1, 41.2, 73.3, 122.2, 124.0, 127.9, 131.1, 133.5, 134.5, 163.2, 175.4; ESI-MS m/z $[M + H]^+$ 334.9; HRMS (ESI) calcd for $C_{18}H_{23}ClN_2O_2Na$ $[M + Na]^+$ 357.1346, found 357.1352.

Acknowledgment. We gratefully acknowledge financial support from the National Natural Science Foundation of China (Grants 20721003 and 20872153), International Collaboration Projects (Grants 20720102040), the 863 Hi-Tech Program of China (Grants 2006AA020602 and 2006AA-10A201), and National S&T Major Projects (2009ZX09301-001, 2009ZX09501-001 and 2009ZX09501-010).

Supporting Information Available: Experimental details, general information and ^{1}H and ^{13}C NMR spectra for all products, and crystallographic file in CIF format of **3Ha**. This material is available free of charge via the Internet at http://pubs.acs.org.