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Silver- and Gold-Mediated Domino Transformation: A Strategy for Synthesizing Benzo[*e*]indolo[1,2-*a*]pyrrolo/pyrido[2,1-*c*][1,4]-diazepine-3,9-diones

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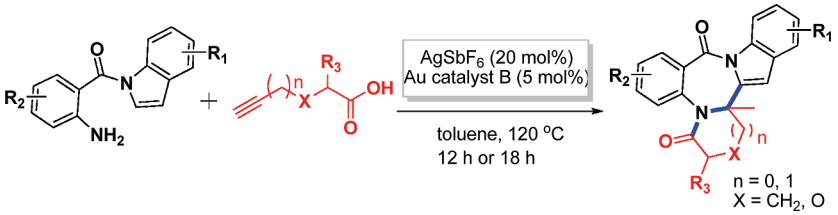

We reported a strategy for the synthesis of fused heterocyclic compounds benzo[*e*]indolo[1,2-*a*]pyrrolo/pyrido[2,1-*c*][1,4]diazepine-3,9-diones via an $AgSbF_6$/gold-complex catalyzed one-pot cascade transformation. The strategy is tolerant of a broad range of substrates and affords a series of intriguing fused diazepinedione heterocycles.

Introduction

The increasing resource consciousness of the chemical community has led to a search for more efficient and atom-economical methods for chemical synthesis. One of the most practical strategies is to develop a cascade reaction in which multiple bond formation and/or bond cleavage events occur in one synthetic sequence.[1] Heterocyclic scaffolds, especially some fused heterocyles, have generally played a very important role in pharmaceutical and agrochemical fields.[2] Therefore, an increasing number of studies are being carried out to develop new approaches for the synthesis of these heterocyclic molecules, which in turn can be used to obtain bioactive lead compounds. Recently, transition-metal-catalyzed cascade transformations have attracted vast attention owing to their intriguing selectivity and high atom economy.[3] Among the numerous catalysts available, silver salts and/or gold complexes are very attractive catalysts. This is because they are powerful tools for the electrophilic activation of alkynes toward a variety of nucleophiles under mild conditions.[4]

(1) (a) Zhang, Z. W.; Li, W. Z. *Org. Lett.* **2010**, *12*, 1649. (b) Ueda, S.; Nagasawa, H. *J. Am. Chem. Soc.* **2009**, *131*, 15080. (c) Barluenga, J.; Mendoza, A.; Rodríguez, F.; Fañanás, F. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 1644. (d) Yang, T.; Campbell, L.; Dixon, D. J. *J. Am. Chem. Soc.* **2007**, *129*, 12070. (e) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134.

(2) For selected examples, see: (a) Chernyak, N.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2010**, *49*, 2743. (b) Lazarski, K. E.; Hu, D. X.; Stern, C. L.; Thomson, R. J. *Org. Lett.* **2010**, *12*, 3010. (c) Tan, C. J.; Di, Y. T.; Wang, Y. H.; Zhang, Y.; Si, Y. K.; Zhang, Q.; Gao, S.; Hu, X. J.; Fang, X.; Li, S. F.; Hao, X. J. *Org. Lett.* **2010**, *12*, 2370. (d) Murata, Y.; Yamashita, D.; Kitahara, K.; Minasako, Y.; Nakazaki, A.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 1400. (e) Yang, D.; Micalizio, G. C. *J. Am. Chem. Soc.* **2009**, *131*, 17548.

(3) (a) Liu, X.; Che, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 3805. (b) de Meijere, A.; von Zezschwitz, P.; Bräse, S. *Acc. Chem. Res.* **2005**, *38*, 413. (c) Wasilke, J. C.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005**, *105*, 1001. (d) Ajamian, A.; Gleason, J. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 3754.

(4) For selected reviews on gold catalysis, see: (a) Bongers, N.; Krause, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 2178. (b) Patil, N. T.; Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3395. (c) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351. (d) Jimenez-Nunez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (e) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239. (f) Kirsch, S. F. *Synthesis* **2008**, *2008*, 3183. (g) Gorin, D. J.; Toste, D. *Nature* **2007**, *446*, 395. (h) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (i) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180.

(5) For selected examples see: (a) Toullec, P. Y.; Blarre, T.; Michelet, V. *Org. Lett.* **2009**, *11*, 2888. (b) Baskar, B.; Bae, H. J.; An, S. E.; Cheong, J. Y.; Rhee, Y. H.; Duschek, A.; Kirsch, S. F. *Org. Lett.* **2008**, *10*, 2605. (c) Witham, C. A.; Mauleón, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 5838. (d) Shapiro, N. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 4160.

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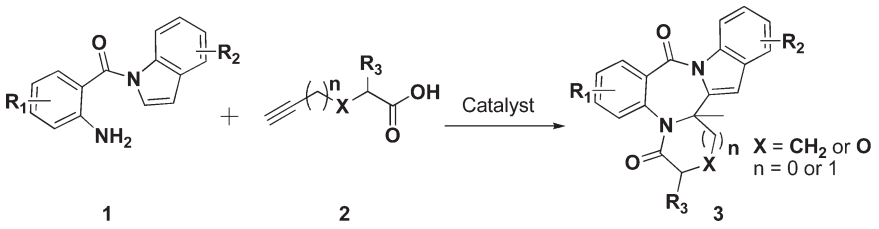
SCHEME 1. Synthesis of Benzo[*e*]indolo[1,2-*a*]pyrrolo/pyrido[2,1-*c*][1,4]diazepine-3,9-diones



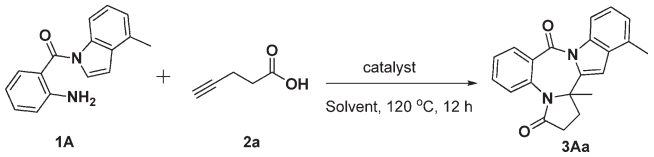
Although significant improvements have been made to domino sequences, most of the reported reactions employ intramolecular ring-closing reaction of a single starting material.[5] It is still a synthetic challenge for the one-pot synthesis of fused heterocycles through an intermolecular reaction of multiple simple starting materials.

Recently, we carried out gold and/or silver catalysts-catalyzed cascade transformations for the efficient synthesis of pyrrolo[1,2-*a*]quinolin-1(2*H*)-ones,[6a] pyrrolo/pyrido[2,1-*b*]benzo[*d*][1,3]oxazin-1-ones,[6b] pyrrolo/pyrido [2,1-*a*][1,3]-benzoxazinones, and pyrrolo/pyrido[2,1-*a*]quinazolinones.[6c] As part of our ongoing efforts to develop new convenient and efficient protocols for the synthesis of potential bioactive fused heterocyles using transition-metal catalysts,[7] we report our recent findings for the synthesis of benzo[*e*]indolo[1,2-*a*]-pyrrolo[2,1-*c*][1,4]diazepine-3,9-diones via a silver-/gold-mediated one-pot domino process (Scheme 1); analogues of these diazepinediones are distributed in various biologically interesting natural products and synthetic molecules.[8] However, to the best of our knowledge, there is no published report on the synthesis of these intriguing molecular scaffolds referred to here. The advantage of this chemical transformation is the formation of one new C−C bond and two new C−N bonds to construct polycyclic heterocycles in one-pot cascade reaction using two simple starting materials.

Results and Discussion

To identify the optimal reaction conditions for one-pot synthesis of benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazepine-3,9-diones, we carried out the experiments using (2-aminophenyl)(4-methyl-1*H*-indol-1-yl)methanone (**1A**) and 4-pentynoic acid (**2a**) as model substrates (as shown in Table 1). In our previous studies, we found that some gold-complexes and/or silver salts are highly efficient catalysts for cascade reactions between less reactive aromatic amines and alkynoic acids.[6] Therefore, in the present study, different gold catalysts and silver salts, such as $AuCl(PPh_3)$, [Au{1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene}]Cl (Au catalyst A), $[Au\{P(t\text{-}Bu)_2(o\text{-biphenyl})\}\{CH_3CN\}]SbF_6$ (Au catalyst B), $AgSbF_6$, AgOTf, and $AgBF_4$ were first investigated at 120 °C for 12 h in a sealed tube using dry toluene as the solvent. However, an excellent yield was not obtained, and only a moderate yield product was formed under the presence of $AgSbF_6$ or AgOTf catalyst (Table 1, entries 1−6). Protonic acid (TFA) was also explored, but no product was detected (Table 1, entry 7). In addition, the desired product was not formed in the absence of catalyst and only the starting materials were recovered (Table 1, entry 8). In our past studies, we

TABLE 1. Optimization of the Reaction Conditions[a]



entry	catalyst system (mol %)[b]	solvent	yield (%)
1	$AuCl(PPh_3)$ (5)	toluene	< 5
2	Au catalyst A (5)	toluene	20
3	Au catalyst B (5)	toluene	23
4	$AgSbF_6$ (5)	toluene	50
5	AgOTf (5)	toluene	49
6	$AgBF_4$ (5)	toluene	45
7	TFA (5)	toluene	0
8	–	toluene	0
9	$AgSbF_6$ (5)/Au catalyst B (5)	toluene	66
10	**$AgSbF_6$** (20)/**Au catalyst B** (5)	**toluene**	**92**
11	$AgSbF_6$ (30)/Au catalyst B (5)	toluene	90
12	$AgSbF_6$ (20)	toluene	84
13	$AgSbF_6$ (20)/TfOH (5)	toluene	85
14	AgOTf (20)/Au catalyst B (5)	toluene	87
15	$AgSbF_6$ (20)/Au catalyst B (5)	CH_2Cl_2	83
16	$AgSbF_6$ (20)/Au catalyst B (5)	Cl CH_2CH_2Cl	80
17	$AgSbF_6$ (20)/Au catalyst B (5)	dioxane	10
18	$AgSbF_6$ (20)/Au catalyst B (5)	CH_3OH	
19	$AgSbF_6$ (20)/Au catalyst B (5)	H_2O	0
20	$AgSbF_6$ (20)/Au catalyst B (5)	THF	0
21	$AgSbF_6$ (20)/Au catalyst B (5)	toluene	88[c]
22	$AgSbF_6$ (20)/Au catalyst B (5)	toluene	78[d]
23	$AgSbF_6$ (20)/Au catalyst B (5)	toluene	87[e]
24	$AgSbF_6$ (20)/Au catalyst B (5)	toluene	91[f]

[a] **1A** (0.1 mmol), **2a** (0.15 mmol), Au catalyst, 120 °C for 12 h. [b] Au catalyst A = [Au{1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene}]Cl; Au catalyst B = $[Au\{P(t\text{-}Bu)_2(o\text{-biphenyl})\}\{CH_3CN\}]SbF_6$. [c] The reaction time was prolonged to 24 h. [d] The reaction temperature was below 100 °C. [e] The reaction temperature was 140 °C. [f] Reaction performed under Ar protection.

(6) (a) Zhou, Y.; Feng, E. G.; Liu, G. N.; Ye, D. J.; Li, J.; Jiang, H. L.; Liu, H. *J. Org. Chem.* **2009**, *74*, 7344. (b) 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. (c) Feng, E.; Zhou, Y.; Zhang, D.; Zhang, L.; Sun, H.; Jiang, H.; Liu, H. *J. Org. Chem.* **2010**, *75*, 3274.

(7) (a) Liu, F.; Ding, X.; Zhang, L.; Zhou, Y.; Zhao, L.; Jiang, H.; Liu, H. *J. Org. Chem.* **2010**, *75*, 5810. (b) Zhang, L.; Ye, D.; Zhou, Y.; Liu, G.; Feng, E.; Jiang, H.; Liu, H. *J. Org. Chem.* **2010**, *75*, 3671. (c) Ye, D.; Zhang, X.; Zhou, Y.; Zhang, D.; Zhang, L.; Wang, H.; Jiang, H.; Liu, H. *Adv. Synth. Catal.* **2009**, *351*, 2770. (d) Liu, G.; Zhou, Y.; Ye, D.; Zhang, D.; Ding, X.; Jiang, H.; Liu, H. *Adv. Synth. Catal.* **2009**, *351*, 2605. (e) Ye, D.; Wang, J.; Zhang, X.; Zhou, Y.; Ding, X.; Feng, E.; Sun, H.; Liu, G.; Jiang, H.; Liu, H. *Green Chem.* **2009**, *11*, 1201. (f) Huang, H.; Jiang, H.; Chen, K.; Liu, H. *J. Org. Chem.* **2009**, *74*, 5476. (g) Feng, E.; Huang, H.; Zhou, Y.; Ye, D.; Jiang, H.; Liu, H. *J. Org. Chem.* **2009**, *74*, 2846. (h) Li, Z.; Sun, H.; Jiang, H.; Liu, H. *Org. Lett.* **2008**, *10*, 3263.

(8) (a) Barata, T.; Jenkins, T. C.; Parkinson, G. N.; Howard, P. W.; Thurston, D. E.; Zloh, M. *Biochemistry* **2008**, *47*, 11818. (b) Wang, J.-J.; Shen, Y.-K.; Hu, W.-P.; Hsieh, M.-C.; Lin, F.-L.; Hsu, M.-K.; Hsu, M.-H. *J. Med. Chem.* **2006**, *49*, 1442. (c) Correa, A.; Tellitu, I.; Dominguez, E.; Moreno, I.; SanMartin, R. *J. Org. Chem.* **2005**, *70*, 2256. (d) Langlois, N.; Rojas-Rousseau, A.; Gaspard, C.; Werner, G. H.; Darro, F.; Kiss, R. *J. Med. Chem.* **2001**, *44*, 3754. (e) Mountzouris, J. A.; Wang, J.-J.; Thurston, D.; Hurley, L. H. *J. Med. Chem.* **1994**, *37*, 3132.

found that some silver salts and gold catalysts can be used as cocatalysts for certain organic transformations.[6a,7a,b] Therefore, $AgSbF_6$ and Au catalyst B was first selected as a cocatalyst for this tandem transformation. Treatment of the model substrates with $AgSbF_6$ (5 mol %) in the presence of 5 mol % of Au catalyst B resulted in a slight improvement of the product yield (Table 1, entry 9). Further investigations revealed that the yield could be improved to 92% by increasing the amount of $AgSbF_6$ to 20 mol % (Table 1, entry 10). However, the product yield did not further increase when the amount of $AgSbF_6$ was increased beyond 20 mol % (Table 1, entry 11). 84% yield was obtained by using only 20 mol % $AgSbF_6$ as a catalyst (Table 1, entry 12). In addition, TfOH was added as a cocatalyst, 85% yield was detected (Table 1, entry 13). AgOTf (20 mol %) was also investigated under the presence of 5 mol % of Au catalyst B, but an improved result was not obtained (Table 1, entry 14). Subsequently, we screened different solvents with the use of an $AgSbF_6$ (20 mol %)/ Au catalyst B (5 mol %) as a catalyst system. Among the solvents tested, nonpolar solvents such as CH_2Cl_2 and $ClCH_2CH_2Cl$ gave relatively better results (Table 1, entries 15−16). However, when toluene was replaced with dioxane, CH_3OH, H_2O or THF, the product yield became poor (Table 1, entries 17−20). Therefore, toluene appeared to be the most effective solvent for this transformation (Table 1, entry 10). We also attempted to increase the product yields by prolonging the reaction time to 24 h, but the yield did not improve (Table 1, entry 21). In addition, we found that the reaction temperature played an important role in this domino transformation, the product yield decreased drastically when the reaction temperature was decreased to 100 °C (Table 1, entry 22). When the reaction temperature was elevated to 140 °C, the yield also showed a slight decrease (Table 1, entry 23). Although this tandem transformation was also performed under argon gas protection, no further improvement of the yield of **3Aa** was afforded (Table 1, entry 24). Therefore, the optimal yield was obtained when (2-aminophenyl)(4-methyl-1*H*-indol-1-yl)methanone (**1A**, 0.1 mmol) reacted with 4-pentynoic acid (**2a**, 0.15 mmol) in dry toluene in the presence 20 mol % of $AgSbF_6$ and 5 mol % of Au catalyst B in a sealed tube at 120 °C for 12 h.

To explore the application scopes of this cascade reaction, we tried to survey the diversity of the substrates by probing the changes in both the substituted (2-aminophenyl)(1*H*-indol-1-yl)methanones and the alkynoic acids. As demonstrated in Table 2, different substituted 2-aminophenyl(1*H*-indol-1-yl)methanones could furnished the corresponding benzodiazepinones products **3Aa-3Gb** in good to excellent yields (70%-92%). However, we found that the type of substituent and its site on the 2-aminophenyl(1*H*-indol-1-yl)-methanones (**1B**) were important such that the yield of products was influenced (Table 2, entries 1−17). When the 4-position of the indole-ring of **1B** was substituted by a methyl group, we obtained high yields (Table 2, entry 1). No substituent or introduction of the methyl function at the 5- or 6-position of the indole ring of 2-aminophenyl(1*H*-indol-1-yl)methanones resulted in a decrease in the yield of the target products (Table 2, entries 2−4). Replacement of the 5-methyl group in the indole-ring of **1C** with a methoxyl group also led to a slight decrease in the yield (Table 2, entry 5). Introduction of a strong electron-withdrawing group (−CN) at the 5-position of the indole-ring in **1B** resulted in a drastic reduction in the yield of the product, presumably because of the influence of the electronic effects (Table 2, entry 6). A good yield of the product was obtained when the 5′-fluoro-substituted substrate **1F** was treated with 4-pentynoic acid (**2a**) under the optimized reaction conditions (Table 2, entry 7). Subsequently, we obtained substrates **1I**−**R** by introducing methyl, chloro, and fluoro groups in the benzene ring of **1B**. Results of further investigations demonstrated that all the tested substrates were tolerated in this cascade transformation (Table 2, entries 8−17). Furthermore, substitution of an alkyl group (*n*-hexyl group) into the alkynoic acid chain was also tolerated, and excellent yields were obtained (Table 2, entries 18−19). The target product **3Ba** was crystallized from dichloromethane and characterized by X-ray crystallography.[9]

Subsequently, we have investigated whether this protocol can be used to prepare benzo[*e*]indolo[1,2-*a*] pyrido[2,1-*c*]-[1,4]diazepine-3,9-diones (**3Ac-3Rc**) by the treatment of substituted (2-aminophenyl)(1*H*-indol-1-yl)methanones (**1A-1R**) and 5-hexynoic acid (**2c**) under the optimized reaction conditions. Although we have observed good yields in the abovementioned experimental examples under the optimal conditions, a relatively longer time (18 h) was needed to complete the substrate conversion fully when 5-hexynoic acid (**2c**) was used as one of substrates. As shown in Table 3, substituted 2-aminophenyl(1*H*-indol-1-yl)methanones having substituents with steric and electronic properties were tolerated in these cascade reactions (Table 3, entries 1−17). However, introduction of a strong electron-withdrawing group (−CN) at the 5-position of the indole ring in **1B** led to a dramatic decrease in the yield of the target product. Even if the reaction time was prolonged to 24 h, we have still detected a small amount of keto-amide intermediate[10] that did not fully convert into the end product, probably owing to the strong electronic effects (Table 3, entry 6). In addition, we also used 2-(prop-2-ynyloxy)acetic acid (**2d**) as a substrate to investigate the scope of this domino transformation. Treatment of **1B**, **1G**, and **1I** with 2-(prop-2-ynyloxy)acetic acid (**2d**) in toluene at 120 °C for 18 h afforded the expected products, **3Bd**, **3Gd**, and **3Id**, respectively, in good yields (Table 3, entries 18−20). In view of these findings, we feel that this synthetic strategy will be an effective approach for the synthesis of intriguing polycyclic molecular architectures.

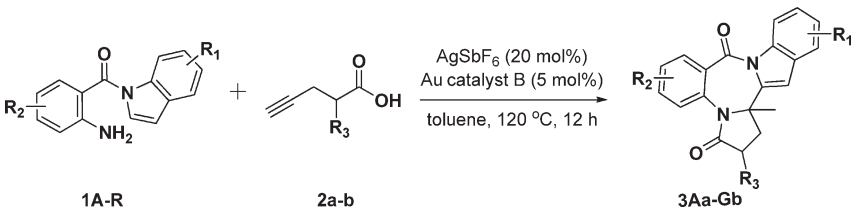
Scheme 2 depicts a plausible mechanism for the present domino transformation. We presumed that the catalyst would induce the cyclization of the alkynoic acid **2** to generate the activated enol-lactone intermediate **A**,[11] and then the amino group of aromatic primary amine **1** attacked this intermediate to afford the ketoamide **B**,[10] which was further converted to *N*-acyl iminium ion **C** via nucleophilic addition and

(9) CCDC 779689 contains the supplementary crystallographic data for **3Ba**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

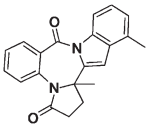
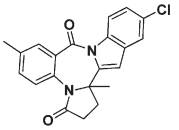
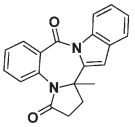
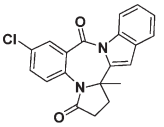
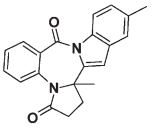
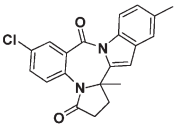
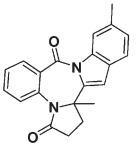
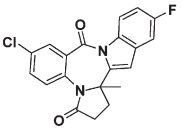
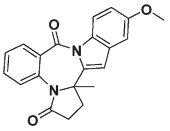
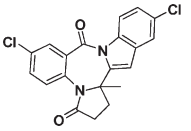
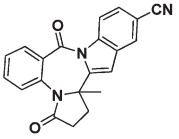
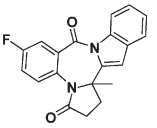
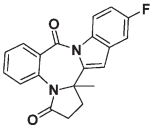
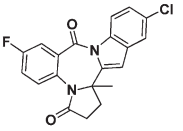
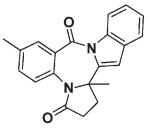
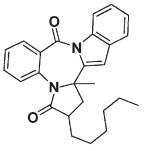
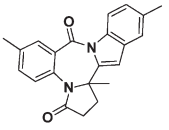
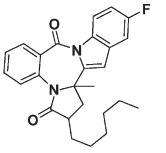
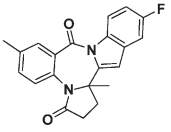
(10) In fact, when we treated 1-(2-aminobenzoyl)-1*H*-indole-5-carbonitrile (**1F**) with 5-hexynoic acid (**2c**) under the optimal reaction conditions, the keto-amide intermediate *N*-(2-(5-cyano-1*H*-indole-1-carbonyl)phenyl)-5-oxohexanamide (**3Fc-M**) was isolated. Characteristic data for **3Fc-M**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.2 (br, 1H), 8.40 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 8.7 Hz, 1H), 7.96 (s, 1H), 7.62−7.67 (m, 2H), 7.49 (d, J = 7.2 Hz, 1H), 7.43 (d, J = 3.9 Hz, 1H), 7.22 (t, 1H), 6.71 (d, J = 3.3 Hz, 1H), 2.54 (t, 2H), 2.41 (t, 2H), 2.11 (s, 3H), 1.92−1.98 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 208.2, 171.2, 168.5, 138.7, 137.8, 133.7, 130.9, 130.4, 129.9, 128.1, 125.9, 123.3, 123.1, 121.6, 119.4, 117.1, 108.3, 107.5, 42.2, 36.5, 29.9, 19.1. LRMS (ESI) m/z 396 $[M + Na]^+$; HRMS (ESI) m/z calcd $C_{22}H_{19}N_3O_3Na$ $[M + Na]^+$ 396.1324, found 396.1327.

(11) Genin, E.; Toullec, P. Y.; Antoniotti, S.; Brancour, C.; Genêt, J.-P.; Michelet, V. *J. Am. Chem. Soc.* **2006**, *128*, 3112.

TABLE 2. Silver- and Gold-Mediated One-Pot Domino Synthesis of 3[a]

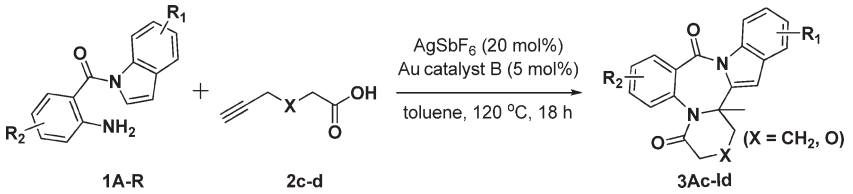


1A-R 2a-b 3Aa-Gb

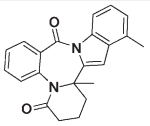
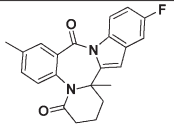
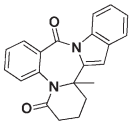
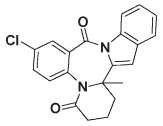
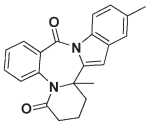
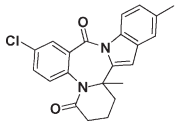
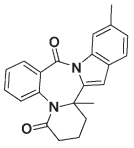
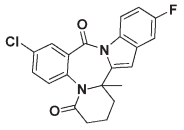
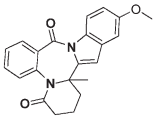
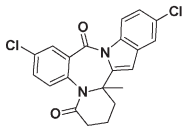
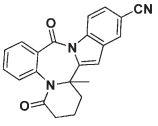
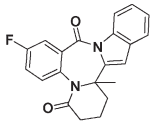
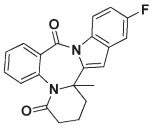
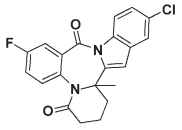
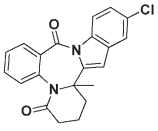
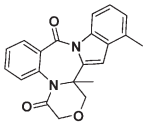
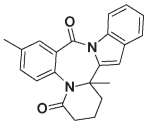
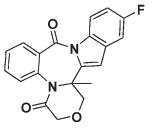
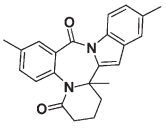
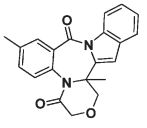
entry	product		Yield (%)	entry	product		Yield (%)
1		**3Aa**	92	11		**3La**	78
2		**3Ba**	90	12		**3Ma**	83
3		**3Ca**	86	13		**3Na**	81
4		**3Da**	79	14		**3Oa**	87
5		**3Ea**	84	15		**3Pa**	76
6		**3Fa**	70	16		**3Qa**	85
7		**3Ga**	91	17		**3Ra**	83
8		**3Ia**	80	18		**3Ab**	88 (1:1.1 *dr*)
9		**3Ja**	81	19		**3Gb**	90 (1:1.3 *dr*)
10		**3Ka**	85				

[a] **1** (0.1 mmol), **2** (0.15 mmol), Au catalyst **B** (5 mol %), $AgSbF_6$ (20 mol %), toluene (2−3 mL), 120 °C for 12 h. [b] The reaction time was prolonged to 24 h.

TABLE 3. Scopes of Silver-/Gold-Catalyzed Domino Transformation[a]

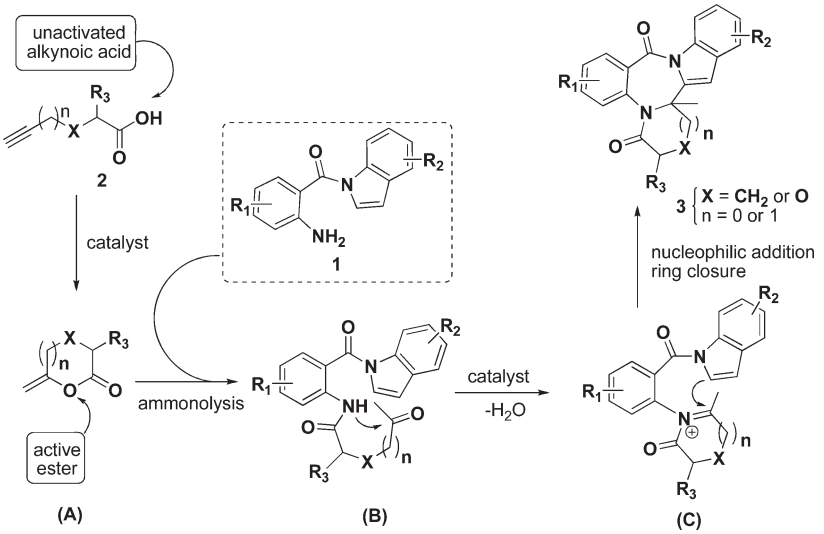


1A-R 2c-d 3Ac-Id

entry	product		Yield (%)	entry	product		Yield (%)
1		**3Ac**	86	11		**3Kc**	84
2		**3Bc**	85	12		**3Mc**	75
3		**3Cc**	81	13		**3Nc**	78
4		**3Dc**	70	14		**3Oc**	78
5		**3Ec**	80	15		**3Pc**	68
6		**3Fc**	40[b]	16		**3Qc**	79
7		**3Gc**	85	17		**3Rc**	75
8		**3Hc**	79	18		**3Bd**	86
9		**3Ic**	78	19		**3Gd**	78
10		**3Jc**	77	20		**3Id**	80

[a] **1** (0.1 mmol), **2** (0.15 mmol), Au catalyst **B** (5 mol %), $AgSbF_6$ (20 mol %), toluene (2−3 mL), 120 °C for 18 h. [b] The reaction time was prolonged to 24 h.

SCHEME 2. A Plausible Mechanism



subsequent dehydration (cascade process). Finally, nucleophilic addition of **C** to the alkene moiety in the indole ring of the substrate yielded the ring-closure product **3**. In order to further support the proposed mechanism, we treated one intermediate (**A**, α-angelica lactone) with a starting material **1B** under the optimized conditions, and the desired product **3Ba** was obtained in 90% yield.[12]

Conclusion

In summary, a strategy for the one-pot synthesis of intriguing polycyclic heterocycles benzo[*e*]indolo[1,2-*a*]pyrrolo/pyrido[2,1-*c*][1,4]diazepine-3,9-diones was reported via a silver- and gold-mediated domino transformation from simple starting materials. Multiple carbon−carbon and carbon−nitrogen bonds were formed from two simple starting materials through a one-pot reaction operation. In view of a large assortment of biological activities of benzodiazepinones, we believe that this new strategy will open the door to prepare new members of benzodiazepinone derivatives family, and have potential applications in drug discovery.

Experimental Section

Typical Procedure for Synthesis of the Substrates (1A as an Example). To a solution of 2-nitrobenzoic acid (0.5 g) in dry CH_2Cl_2 (15 mL) was added 2 mL of thionylchloride. The resulting mixture was heated to reflux for 3 h, and then the solvent was evaporated under reduced pressure. The residue was quickly dissolved in CH_2Cl_2 (15 mL), then was dropped slowly into a solution of 4-methylindole (0.47 g), DMAP (37 mg), and Et_3N (1.3 mL) in CH_2Cl_2 (15 mL) under an argon atmosphere protection. The resulting mixture was stirred at room temperature for overnight until the starting materials were fully consumed. Then, the mixture was concentrated and purified by flash column chromatography (petroleum ether (PE)/ethyl acetate (EA) = 4/1, v/v, as an eluent) to afford 0.68 g of the intermediate.

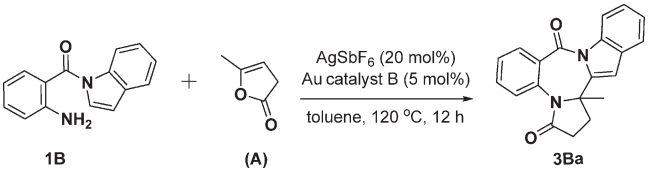
To a mixture of 0.5 g of the above intermediate and 0.4 g of Sn in 25 mL of C_2H_5OH was added 1.5 mL of concentrated hydrochloric acid, and further stirred at 70 °C for 2 h. The reaction was monitored by TLC. After cooling, the mixture was added H_2O (40 mL) and neutralized with saturated $NaHCO_3$. Then, the solution was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with water and dried by anhydrous Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography (PE/EA = 5/1, v/v, as an eluent) to give the desirable substrate **1A**. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.13 (d, J = 8.7 Hz, 1H), 7.24−7.38 (m, 4H), 7.11 (d, J = 7.5 Hz, 1H), 6.71−6.81 (m, 2H), 6.65 (d, J = 3.9 Hz, 1H), 4.78 (br, 2H), 2,58 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 148.9, 135.7, 133.2, 131.4, 130.4, 130.3, 127.4, 124.6, 124.0, 117.0, 116.6, 116.1, 113.6, 106.3, 18.5; LRMS (EI) m/z 250 (M^+); HRMS (EI) m/z calcd $C_{16}H_{14}N_2O$ (M^+) 250.1106, found 250.1107.

(2-Aminophenyl)(1*H*-indol-1-yl)methanone (1B): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.31 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.35 (7.28−7.40, 5H), 6.72−6.81 (m, 2H), 6.61 (d, J = 3.9 Hz, 1H), 5.03 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 149.0, 136.0, 133.2, 131.4, 130.8, 128.0, 124.6, 123.6, 120.9, 117.0, 116.6, 116.1, 116.0, 107.9; LRMS (EI) m/z 236 (M^+); HRMS (EI) m/z calcd $C_{15}H_{14}N_2O$ (M^+) 236.0950, found 236.0951.

(2-Aminophenyl)(5-methyl-1*H*-indol-1-yl)methanone (1C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.18 (d, J = 8.4 Hz, 1H), 7.28−7.39 (m, 4H), 7.19 (d, J = 8.7 Hz, 1H), 6.71−6.80 (m, 2H), 6.54 (d, J = 3.6 Hz, 1H), 4.67 (br, 2H), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 148.8, 134.2, 133.2, 133.1, 131.3, 131.0, 128.0, 125.9, 120.8, 117.0, 116.6, 116.2, 115.7, 107.8, 21.4; LRMS (EI) m/z 250 (M^+); HRMS (EI) m/z calcd $C_{16}H_{14}N_2O$ (M^+) 250.1106, found 250.1103.

(2-Aminophenyl)(6-methyl-1*H*-indol-1-yl)methanone (1D): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.18 (s, 1H), 7.48 (d, J = 8.1 Hz,

(12) To further explore the proposed mechanism, we treated **1B** with the tautomer of intermediate **A** (α-*angelica lactone*, as shown below) under the optimized reaction conditions. *Operational procedure*: To a solution of α-angelica lactone (1.5 mmol) in dry toluene (3 mL) were added Au catalyst B (5 mol %) and AgSbF6 (20 mol%). After stirring at room temperature for 10 min, **1B** (1 mmol) were added. Subsequently, the reaction vial was sealed, the mixture was heated to 120 °C for 12 h, and then, the cold mixture was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford **3Ba** in 90% yield.



1H), 7.24−7.38 (m, 3H), 7.14 (d, J = 8.1 Hz, 1H), 6.67−6.80 (m, 2H), 6.55 (d, J = 3.6 Hz, 1H), 5.04 (br, 2H), 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 148.9, 136.4, 134.7, 133.1, 131.3, 128.5, 127.5, 125.1, 120.4, 117.0, 116.6, 116.3, 107.8, 21.9; LRMS (EI) m/z 250 (M^+); HRMS (EI) m/z calcd $C_{16}H_{14}N_2O$ (M^+) 250.1106, found 250.1115.

(2-Aminophenyl)(5-methoxy-1*H*-indol-1-yl)methanone (1E): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.23 (d, J = 9.0 Hz, 1H), 7.28−7.38 (m, 3H), 7.07 (d, J = 2.7 Hz, 1H), 6.98 (dd, J = 9.0 Hz, 2.7 Hz, 1H), 6.76 (q, 2H), 6.53 (d, J = 3.6 Hz, 1H), 5.03 (br, 2H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.8, 156.5, 148.8, 133.0, 131.8, 131.2, 130.7, 128.6, 117.0, 116.9, 116.6, 116.1, 113.1, 107.9, 103.5, 55.6; LRMS (EI) m/z 266 (M^+); HRMS (EI) m/z calcd $C_{16}H_{14}N_2O_2$ (M^+) 266.1055, found 266.1054.

1-(2-Aminobenzoyl)-1*H*-indole-5-carbonitrile (1F): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.31 (d, J = 8.4 Hz, 1H), 7.95 (s, 1H), 7.59 (dd, J = 8.4 Hz, 1.5 Hz, 1H) 7.51 (d, J = 3.9 Hz, 1H), 7.34−7.39 (m, 2H), 6.82 (d, J = 9.0 Hz, 1H), 6.75 (t, 1H), 6.67 (d, J = 3.6 Hz, 1H), 5.30 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 149.7, 137.9, 134.2, 131.5, 130.6, 130.2, 127.5, 125.8, 119.7, 117.4, 116.8, 116.7, 114.4, 107.2, 106.8; LRMS (EI) m/z 261 (M^+); HRMS (EI) m/z calcd $C_{16}H_{11}N_3O$ (M^+) 261.0902, found 261.0894.

(2-Aminophenyl)(5-fluoro-1*H*-indol-1-yl)methanone (1G): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.28 (q, 1H), 7.23−7.41 (m, 4H), 7.09 (td, 1H), 6.72−6.81 (m, 2H), 6.57 (d, J = 3.9 Hz, 1H), 5.00 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 159.6 (d, J = 238.7 Hz), 149.0, 133.4, 132.3, 131.7 (d, J = 10.0 Hz), 131.2, 129.5, 117.1, 117.0 (d, J = 8.6 Hz), 116.6, 115.6, 112.3 (d, J = 24.6 Hz), 107.5, 106.3 (d, J = 23.6 Hz); LRMS (EI) m/z 254 (M^+); HRMS (EI) m/z calcd $C_{15}H_{11}FN_2O$ (M^+) 254.0855, found 254.0860.

(2-Aminophenyl)(5-chloro-1*H*-indol-1-yl)methanone (1H): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.22 (d, J = 8.7 Hz, 1H), 7.57 (s, 1H), 7.26−7.40 (m, 4H), 6.72−6.81 (m, 2H), 6.54 (d, J = 3.3 Hz, 1H), 5.10 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 149.2, 134.3, 133.5, 131.9, 131.3, 129.3, 129.1, 124.7, 120.4, 117.1, 117.0, 116.6, 115.3, 107.1; LRMS (EI) m/z 270 (M^+); HRMS (EI) m/z calcd $C_{15}H_{11}ClN_2O$ (M^+) 270.0560, found 270.0565.

(2-Amino-5-methylphenyl)(1*H*-indol-1-yl)methanone (1I): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.31 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 6.9 Hz, 1H), 7.30−7.37 (m, 3H), 7.13−7.17 (m, 2H), 6.72 (d, J = 8.4 Hz, 1H), 6.61 (d, J = 3.9 Hz, 1H), 4.86 (br, 2H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 146.5, 136.0, 134.1, 131.1, 130.8, 128.1, 126.0, 124.5, 123.6, 120.8, 117.2, 116.3, 116.1, 107.8, 20.3; LRMS (EI) m/z 250 (M^+); HRMS (EI) m/z calcd $C_{16}H_{14}N_2O$ (M^+) 250.1106, found 250.1108.

(2-Amino-5-methylphenyl)(5-methyl-1*H*-indol-1-yl)methanone (1J): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.18 (d, J = 8.4 Hz, 1H), 7.40 (s, 1H), 7.32 (d, J = 3.9 Hz, 1H), 7.12−7.20 (m, 3H), 6.71 (d, J = 8.1 Hz, 1H), 6.54 (d, J = 3.9 Hz, 1H), 4.80 (br, 2H), 2.48 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 146.3, 134.1, 133.9, 133.2, 131.0, 128.1, 126.0, 125.9, 120.7, 117.2, 116.6, 115.7, 107.7, 21.4, 20.3; LRMS (EI) m/z 264 (M^+); HRMS (EI) m/z calcd $C_{17}H_{16}N_2O$ (M^+) 264.1263, found 264.1259.

(2-Amino-5-methylphenyl)(5-fluoro-1*H*-indol-1-yl)methanone (1K): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27 (q, 1H), 7.40 (d, J = 3.6 Hz, 1H), 7.223−7.30 (m, 1H), 7.7.05−7.16 (m, 3H), 6.72 (d, J = 6.6 Hz, 1H), 6.56 (d, J = 3.9 Hz, 1H), 4.84 (br, 2H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 159.6 (d, J = 238.3 Hz), 146.6, 134.3, 132.4, 131.7 (d, J = 10.1 Hz), 131.0, 129.6, 126.0, 117.3, 117.1 (d, J = 9.1 Hz), 115.9, 112.3 (d, J = 24.6 Hz), 107.5, 106.3 (d, J = 23.7 Hz), 20.3; LRMS (EI) m/z 268 (M^+); HRMS (EI) m/z calcd $C_{16}H_{13}FN_2O$ (M^+) 268.1012, found 268.1007.

(2-Amino-5-chlorophenyl)(1*H*-indol-1-yl)methanone (1M): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.31 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 7.2 Hz, 1H), 7.25−7.38 (m, 5H), 6.73 (d, J = 9.0 Hz, 1H), 6.65 (d, J = 4.2 Hz, 1H), 5.02 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8, 147.3, 135.9, 133.1, 130.8, 130.3, 127.5, 124.8, 123.9, 121.3, 121.0, 118.3, 117.1, 116.1, 108.7; LRMS (EI) m/z 270 (M^+); HRMS (EI) m/z calcd $C_{15}H_{11}ClN_2O$ (M^+) 270.0560, found 270.0559.

(2-Amino-5-chlorophenyl)(5-methyl-1*H*-indol-1-yl)methanone (1N): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.18 (d, J = 8.4 Hz, 1H), 7.39 (s, 1H), 7.34 (d, J = 2.4 Hz, 1H), 7.24−7.29 (m, 2H), 7.19 (d, J = 8.4 Hz, 1H), 6.73 (d, J = 8.7 Hz, 1H), 6.57 (d, J = 3.9 Hz, 1H), 4.97 (br, 2H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.6, 147.1, 134.1, 133.6, 132.9, 131.1, 130.3, 127.5, 126.2, 121.3, 120.9, 118.3, 117.3, 115.7, 108.5, 21.4; LRMS (EI) m/z 284 (M^+); HRMS (EI) m/z calcd $C_{16}H_{13}ClN_2O$ (M^+) 284.0716, found 284.0723.

(2-Amino-5-chlorophenyl)(5-fluoro-1*H*-indol-1-yl)methanone (1O): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27 (q, 1H), 7.33−7.37 (m, 2H), 7.24−7.29 (m, 2H), 7.10 (td, 1H), 6.74 (d, J = 9.0 Hz, 1H), 6.61 (d, J = 3.6 Hz, 1H), 4.96 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.6, 159.8 (d, J = 239.2 Hz), 147.4, 133.2, 132.3, 131.8 (d, J = 10.1 Hz), 130.3, 129.1, 121.4, 118.4, 117.1 (d, J = 9.1 Hz), 116.7, 112.6 (d, J = 25.1 Hz), 108.4, 106.5 (d, J = 23.7 Hz); LRMS (EI) m/z 288 (M^+); HRMS (EI) m/z calcd $C_{15}H_{10}ClFN_2O$ (M^+) 288.0466, found 288.0471.

(2-Amino-5-chlorophenyl)(5-chloro-1*H*-indol-1-yl)methanone (1P): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.22 (d, J = 9.0 Hz, 1H), 7.59 (d, J = 4.5 Hz, 1H), 7.25−7.40 (m, 4H), 6.74 (d, J = 8.7 Hz, 1H), 6.59 (d, J = 3.3 Hz, 1H), 4.98 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.7, 147.6, 134.3, 133.4, 132.0, 130.3, 129.4, 128.8, 125.0, 121.4, 120.6, 118.5, 117.1, 116.4, 107.9; LRMS (EI) m/z 304 (M^+); HRMS (EI) m/z calcd $C_{15}H_{10}Cl_2N_2O$ (M^+) 304.0170, found 304.0178.

(2-Amino-5-fluorophenyl)(1*H*-indol-1-yl)methanone (1Q): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.31 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 7.5 Hz, 1H), 7.29−7.41 (m, 3H), 7.05−7.11 (m, 2H), 6.73−6.78 (m, 1H), 6.64 (d, J = 3.9 Hz, 1H), 4.84 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.0, 154.1 (d, J = 236.0 Hz), 145.1, 135.9, 130.8, 127.5, 124.8, 123.9, 121.0, 120.6 (d, J = 22.8 Hz), 118.3 (d, J = 7.3 Hz), 116.7 (d, J = 23.7 Hz), 116.1, 108.6; LRMS (EI) m/z 254 (M^+); HRMS (EI) m/z calcd $C_{15}H_{11}FN_2O$ (M^+) 254.0855, found 254.0861.

(2-Amino-5-fluorophenyl)(5-chloro-1*H*-indol-1-yl)methanone (1R): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.23 (d, J = 8.7 Hz, 1H), 7.58 (d, J = 1.8 Hz, 1H), 7.30−7.38 (m, 2H), 7.06−7.13 (m, 2H), 6.73−6.79 (m, 1H), 6.58 (d, J = 3.9 Hz, 1H), 4.81 (br, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8, 154.1 (d, J = 236.4 Hz), 145.3, 134.3, 132.0, 129.4, 128.8, 125.0, 121.1 (d, J = 22.8 Hz), 120.6, 118.4 (d, J = 7.3 Hz), 117.1, 116.6 (d, J = 23.7 Hz), 107.8; LRMS (EI) m/z 288 (M^+); HRMS (EI) m/z calcd $C_{15}H_{10}ClFN_2O$ (M^+) 288.0466, found 288.0465.

General Procedure for Synthesis of Benzo[*e*]indolo[1,2-*a*]pyrrolo/pyrido[2,1-*c*][1,4]diazepine-3,9-diones (3Aa as an Example). To a solution of 4-pentynoic acids (**2a**, 1.5 mmol) in dry toluene (3 mL) were added Au catalyst B (5 mol %) and $AgSbF_6$ (20 mol %). After stirring for 10 min at room temperature, (2-aminophenyl)-(4-methyl-1*H*-indol-1-yl)methanone (**1A**, 1 mmol) was added. Subsequently, the reaction vial was sealed, and the mixture was heated to 120 °C for 12 h, and then, the cold mixture was concentrated under reduced pressure. The resulting reside was purified by flash column chromatography (PE/EA = 4/1, v/v, as an eluent) to afford the desired product **3Aa** in 92% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.61 (d, J = 8.7 Hz, 1H), 8.41 (d, J = 8.4 Hz, 1H), 7.62−7.68 (m, 2H), 7.42−7.48 (m, 1H), 7.24−7.29 (m, 1H), 7.11 (d, J = 7.5 Hz 1H), 6.62 (s, 1H), 2.96−3.0 (m, 1H), 2.65−2.73 (m, 2H), 2.54 (s, 3H), 2.29−2.36 (m, 1H), 1.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 164.0, 139.9, 138.7, 134.5, 134.1, 133.7, 129.9, 128.3, 127.3, 126.7, 125.5, 124.9, 115.6, 103.2, 62.4, 34.4, 30.5, 27.7, 18.4; LRMS (EI) m/z 330

(M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{18}N_2O_2$ (M^+) 330.1368, found 330.1376.

15*b*-Methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ba): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.59 (t, 2H), 7.61−7.69 (m, 2H), 7.54 (d, J = 7.6 Hz, 1H), 7.46 (t, 1H), 7.37 (t, 1H), 7.31 (t, 1H), 6.60 (s, 1H), 2.93−2.96 (m, 1H), 2.65−2.71 (m, 2H), 2.28−2.35 (m, 1H), 1.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.4, 163.9, 140.4, 138.8, 134.5, 134.1, 133.7, 128.8, 127.3, 126.7, 126.6, 125.4, 124.4, 120.5, 118.1, 104.9, 62.3, 34.4, 30.4, 27.6; LRMS (EI) *m*/*z* 316 (M^+); HRMS (EI) *m*/*z* calcd $C_{20}H_{16}N_2O_2$ (M^+) 316.1212, found 316.1212.

13,15*b*-Dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ca): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.58 (d, J = 8.1 Hz, 1H), 8.45 (d, J = 8.4 Hz, 1H), 7.60−7.67 (m, 2H), 7.46 (t, 1H), 7.31 (s, 1H), 7.18 (d, J = 8.4 Hz, 1H), 6.52 (s, 1H), 2.9−2.96 (m, 1H), 2.63−2.70 (m, 2H), 2.44 (s, 3H), 2.27−2.35 (m, 1H), 1.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.4, 163.8, 140.4, 137.0, 134.5, 134.1, 134.0, 133.7, 129.0, 127.3, 126.8, 126.7, 120.5, 117.8, 104.8, 62.3, 34.4, 30.4, 27.7, 21.3; LRMS (EI) *m*/*z* 330 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{18}N_2O_2$ (M^+) 330.1368, found 330.1367.

12,15*b*-Dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3 Da): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (d, J = 7.8 Hz, 1H), 8.42 (s, 1H), 7.64 (m, 2H), 7.46 (d, J = 7.2 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.14 (d, J = 7.8 Hz, 1H), 6.54 (s, 1H), 2.90−2.95 (m, 1H), 2.52−2.72 (m, 2H), 2.50 (s, 3H), 2.25−2.34 (m, 1H), 1.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.4, 164.0, 139.8, 139.2, 135.5, 134.5, 134.0, 133.6, 127.2, 126.7, 126.5, 125.7, 120.0, 118.3, 104.8, 62.3, 34.3, 30.4, 27.6, 22.0; LRMS (EI) *m*/*z* 330 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{18}N_2O_2$ (M^+) 330.1368, found 330.1359.

13-Methoxyl-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ea): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.58 (d, J = 8.1 Hz, 1H), 8.50 (d, J = 9.3 Hz, 1H), 7.59−7.68 (m, 2H), 7.45 (t, 1H), 6.94−7.00 (m, 2H), 6.53 (s, 1H), 3.87 (s, 3H), 2.90−2.96 (m, 1H), 2.63−2.70 (m, 2H), 2.28−2.35 (m, 1H), 1.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 163.5, 156.8, 141.1, 134.4, 134.0, 133.6, 133.4, 129.8, 127.3, 126.8, 119.1, 113.3, 104.9, 103.4, 62.3, 55.6, 34.5, 30.4, 27.7; LRMS (EI) *m*/*z* 346 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{18}N_2O_3$ (M^+) 346.1317, found 346.1318.

13-Cyano-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Fa): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.56−8.64 (m, 2H), 7.87 (s, 1H), 7.59−7.72 (m, 3H), 7.48 (t, 1H), 6.64 (s, 1H), 2.93−2.99 (m, 1H), 2.65−2.71 (m, 2H), 2.33−2.41 (m, 1H), 1.54 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 164.1, 143.0, 140.7, 134.8, 133.8, 129.0, 128.3, 127.4, 126.9, 125.7, 125.2, 119.3, 118.8, 107.6, 103.8, 62.1, 34.2, 30.3, 27.4; LRMS (EI) *m*/*z* 341 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{15}N_3O_2$ (M^+) 341.1164, found 341.1166.

13-Fluoro-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ga): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.50−8.59 (m, 2H), 7.61−7.69 (m, 2H), 7.47 (t, 1H), 7.16−7.20 (m, 1H), 7.07−7.12 (m, 1H), 6.56 (s, 1H), 2.90−2.92 (m, 1H), 2.64−2.71 (m, 2H), 2.30−2.34 (m, 1H), 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.4, 163.7, 159.9 (d, J = 239.6 Hz), 142.0, 135.1, 134.5, 134.3, 133.7, 129.9, 127.3, 126.9, 126.5, 119.3 (d, J = 8.7 Hz), 112.9 (d, J = 24.1 Hz), 105.1 (d, J = 23.7 Hz), 104.5, 62.3, 34.4, 30.3, 27.6; LRMS (EI) *m*/*z* 334 (M^+); HRMS (EI) *m*/*z* calcd $C_{20}H_{15}FN_2O_2$ (M^+) 334.1118, found 334.1114.

7,15*b*-Dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ia): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.57 (d, J = 8.4 Hz, 1H), 8.39 (s, 1H), 7.49.7.55 (m, 3H), 7.27−7.39 (m, 2H), 6.59 (s, 1H), 2.91−2.96 (m, 1H), 2.62−2.70 (m, 2H), 2.47 (s, 3H), 2.26−2.35 (m, 1H), 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 164.2, 140.6, 138.8, 136.7, 135.1, 133.7, 132.0, 128.9, 127.2, 126.3, 125.3, 124.3, 120.5, 118.1, 104.8, 62.2, 34.4, 30.4, 27.6, 21.0; LRMS (EI) *m*/*z* 330 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{18}N_2O_2$ (M^+) 330.1368, found 330.1359.

7,13,15*b*-Trimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*][1,4]-diazepine-3,9(2*H*,15*bH*)-dione (3Ja): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.45 (d, J = 8.7 Hz, 1H), 8.37 (s, 1H), 7.49 (s, 2H), 7.31 (s, 1H), 7.18 (d, J = 8.7 Hz, 1H), 6.51 (s, 1H), 2.89−2.97 (m, 1H), 2.62−2.69 (m, 2H), 2.47 (s, 3H), 2.45 (s, 3H), 2.22−2.34 (m, 1H), 1.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 164.0, 140.6, 137.0, 136.7, 135.0, 134.0, 133.7, 132.0, 129.1, 127.2, 126.6, 126.5, 120.4, 117.8, 104.8, 62.3, 34.5, 30.4, 27.7, 21.3, 21.0; LRMS (EI) *m*/*z* 344 (M^+); HRMS (EI) *m*/*z* calcd $C_{22}H_{20}N_2O_2$ (M^+) 344.1525, found 344.1528.

7,15*b*-Dimethyl-13-fluoro-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ka): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.51−8.56 (m, 1H), 8.36 (s, 1H), 7.50 (s, 2H), 7.15−7.20 (m, 1H), 7.03−7.11 (m, 1H), 6.55 (s, 1H), 2.89−2.93 (m, 1H), 2.62−2.69 (m, 2H), 2.47 (s, 3H), 2.27−2.36 (m, 1H), 1.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 164.0, 159.8 (d, J = 239.6 Hz), 142.2, 136.8, 135.2, 135.1, 133.7, 132.0, 129.9 (d, J = 10.0 Hz), 127.2, 126.2, 119.4 (d, J = 8.6 Hz), 112.8 (d, J = 24.1 Hz), 106.0 (d, J = 23.7 Hz), 104.4, 62.2, 34.4, 30.3, 27.6, 21.0; LRMS (EI) *m*/*z* 348 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{17}FN_2O_2$ (M^+) 348.1274, found 348.1276.

7,15*b*-Dimethyl-13-chloro-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3La): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.49 (d, J = 9.0 Hz, 1H), 8.36 (s, 1H), 7.48−7.50 (m, 3H), 7.31 (d, J = 9.6, 1H), 6.52 (s, 1H), 2.88−2.91 (m, 1H), 2.62−2.68 (m, 2H), 2.47 (s, 3H), 2.27−2.36 (m, 1H), 1.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 164.0, 142.0, 137.1, 136.9, 135.3, 133.7, 132.0, 130.1, 129.7, 127.2, 126.0, 125.3, 120.0, 119.2, 104.0, 62.2, 34.4, 30.3, 27.5, 21.0; LRMS (EI) *m*/*z* 364 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{17}ClN_2O_2$ (M^+) 364.0979, found 364.0971.

7-Chloro-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ma): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (s, 1H), 8.53 (d, J = 8.1 Hz, 1H), 7.62 (s, 2H), 7.54 (d, J = 7.5, 1H), 7.28−7.40 (m, 2H), 6.60 (s, 1H), 2.93−2.99 (m, 1H), 2.64−2.71 (m, 2H), 2.26−2.35 (m, 1H), 1.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 162.6, 140.0, 138.8, 134.1, 133.2, 133.1, 132.5, 128.8, 128.6, 127.7, 125.6, 124.7, 120.7, 118.0, 105.2, 62.2, 34.2, 30.3, 27.6; LRMS (EI) *m*/*z* 350 (M^+); HRMS (EI) *m*/*z* calcd $C_{20}H_{15}ClN_2O_2$ (M^+) 350.0822, found 350.0828.

7-Chloro-13,15*b*-dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Na): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.58 (s, 1H), 8.41 (d, J = 8.7 Hz, 1H), 7.60 (s, 2H), 7.32 (s, 1H), 7.19 (d, J = 8.7 Hz, 1H), 6.53 (s, 1H), 2.91−2.98 (m, 1H), 2.63−2.70 (m, 2H), 2.45 (s, 3H), 2.25−2.34 (m, 1H), 1.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 162.4, 140.0, 136.9, 134.4, 134.0, 133.2, 133.0, 132.5, 129.0, 128.6, 127.9, 126.9, 120.6, 117.7, 105.2, 62.2, 34.2, 30.3, 27.6, 21.3; LRMS (EI) *m*/*z* 364 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{17}ClN_2O_2$ (M^+) 364.0979, found 364.0982.

7-Chloro-13-fluoro-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]-pyrrolo[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Oa): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.56 (s, 1H), 8.47−8.52 (m, 1H), 7.61 (s, 2H), 7.15−7.19 (m, 1H), 7.05−7.11 (m, 1H), 6.56 (s, 1H), 2.90−2.93 (m, 1H), 2.63−2.69 (m, 2H), 2.28−2.33 (m, 1H), 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 162.4, 141.6, 135.0, 134.2, 133.2, 133.0, 132.6, 129.9, 128.7, 127.6, 119.3 (d, J = 8.6 Hz), 113.1 (d, J = 24.1 Hz), 106.2 (d, J = 23.7 Hz), 104.8, 62.2, 34.2, 30.3, 27.6; LRMS (EI) *m*/*z* 368 (M^+); HRMS (EI) *m*/*z* calcd $C_{20}H_{14}ClFN_2O_2$ (M^+) 368.0728, found 368.0720.

7,13-Dichloro-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo-[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3 Pa): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.56 (s, 1H), 8.45 (d, J = 9.0 Hz, 1H), 7.62 (s, 2H), 7.49 (s, 1H), 7.30−7.34 (m, 1H), 6.54 (s, 1H), 2.90−2.97 (m, 1H), 2.63−2.69 (m, 2H), 2.27−2.36 (m, 1H), 1.51 (s, 3H); ^{13}C NMR ($CDCl_3$,

100 MHz) δ 172.3, 162.5, 141.4, 137.1, 134.3, 133.2, 133.1, 132.6, 130.0, 128.7, 127.4, 125.7, 120.2, 119.1, 104.3, 62.1, 34.1, 30.2, 27.5; LRMS (EI) *m*/*z* 384 (M^+); HRMS (EI) *m*/*z* calcd $C_{20}H_{14}Cl_2N_2O_2$ (M^+) 384.0432, found 384.0427.

7-Fluoro-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Qa): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.55 (d, *J* = 8.1 Hz, 1H), 8.29 (dd, *J* = 10.2 Hz, 3.0 Hz, 1H), 7.60−7.65 (m, 1H), 7.54 (d, *J* = 7.2 Hz, 1H), 7.29−7.42 (m, 3H), 6.61 (s, 1H), 2.93−2.96 (m, 1H), 2.64−2.71 (m, 2H), 2.29−2.34 (m, 1H), 1.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 162.7, 160.6 (d, *J* = 245.5 Hz), 140.2, 138.8, 130.6, 129.2 (d, *J* = 7.8 Hz), 128.8, 128.4, 125.6, 124.6, 121.5 (d, *J* = 22.8 Hz), 120.6, 119.6 (d, *J* = 25.1 Hz), 118.1, 105.3, 62.2, 34.3, 30.3, 27.6; LRMS (EI) *m*/*z* 334 (M^+); HRMS (EI) *m*/*z* calcd $C_{20}H_{15}FN_2O_2$ (M^+) 334.1118, found 334.1123.

7-Fluoro-13-chloro-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo-[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ra): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.47 (d, *J* = 9.0 Hz, 1H), 8.25 (dd, *J* = 10.2 Hz, 3.3 Hz, 1H), 7.59−7.65 (q, 1H), 7.49 (s, 1H), 7.36−7.43 (m, 1H), 7.31 (dd, *J* = 9.0 Hz, 2.4 Hz, 1H), 6.54 (s, 1H), 2.90−2.97 (m, 1H), 2.63−2.69 (m, 2H), 2.29−2.36 (m, 1H), 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 162.5, 160.6 (d, *J* = 245.5 Hz), 141.6, 137.1, 130.6, 130.1, 130.0, 129.3 (d, *J* = 8.2 Hz), 128.1 (d, *J* = 6.9 Hz), 125.6, 121.8 (d, *J* = 22.8 Hz), 120.2, 119.6 (d, *J* = 25.1 Hz), 119.1, 104.4, 62.1, 34.3, 30.2, 27.5; LRMS (EI) *m*/*z* 368 (M^+); HRMS (EI) *m*/*z* calcd $C_{20}H_{14}ClFN_2O_2$ (M^+) 368.0728, found 368.0730.

2-Hexyl-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ab-1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (t, 2H), 7.60−7.67 (m, 2H), 7.54 (d, *J* = 6.6 Hz, 1H), 7.42−7.48 (m, 1H), 7.27−7.39 (m, 1H), 6.58 (s, 1H), 3.10 (q, 1H), 2.67−2.70 (m, 2H), 2.05−2.07 (m, 1H), 1.94 (t, 1H), 1.25−1.55 (m, 12H), 0.92 (t, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.1, 164.0, 140.7, 138.8, 134.8, 134.0, 133.7, 128.9, 127.3, 126.6, 126.5, 125.3, 124.4, 120.5, 118.1, 104.8, 60.1, 41.2, 40.8, 31.7, 30.3, 29.3, 27.7, 27.2, 22.6, 14.1; LRMS (EI) *m*/*z* 400 (M^+); HRMS (EI) *m*/*z* calcd $C_{26}H_{28}N_2O_2$ (M^+) 400.2151, found 400.2143.

2-Hexyl-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*]-[1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Ab-2): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.67 (d, *J* = 8.4 Hz, 1H), 8.41 (d, *J* = 7.8 Hz, 1H), 7.64−7.67 (m, 2H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.42−7.48 (m, 1H), 7.32−7.40 (m, 2H), 6.61 (s, 1H), 2.73−2.78 (m, 2H), 2.53−2.59 (m, 1H), 1.72−1.76 (m, 1H), 1.51 (s, 3H), 1.39−1.45 (m, 3H), 1.24−1.30 (m, 6H), 0.86 (t, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.7, 164.7, 143.7, 138.4, 134.3, 133.7, 133.2, 128.9, 128.3, 127.2, 127.0, 125.3, 124.4, 120.3, 118.4, 106.7, 62.4, 42.0, 40.4, 31.5, 30.6, 28.8, 28.7, 27.6, 22.5, 14.0; LRMS (EI) *m*/*z* 400 (M^+); HRMS (EI) *m*/*z* calcd $C_{26}H_{28}N_2O_2$ (M^+) 400.2151, found 400.2143.

2-Hexyl-13-fluoro-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo-[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Gb-1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.51−8.60 (m, 2H), 7.60−7.68 (m, 2H), 7.45 (t, 1H), 7.18 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.04−7.17 (m, 1H), 6.55 (s, 1H), 3.05−3.12 (q, 1H), 2.68−2.70 (m, 1H), 1.89−2.26 (m, 2H), 1.48 (s, 3H), 1.25−1.44 (m, 9H), 0.86−0.93 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.1, 163.8, 159.9 (d, *J* = 240.3 Hz), 148.9, 142.3, 135.0, 134.8, 134.2, 133.7, 130.0, 127.4, 126.7, 126.3, 119.4 (d, *J* = 9.0 Hz), 112.8 (d, *J* = 24.5 Hz), 106.0 (d, *J* = 23.8 Hz), 104.4, 60.1, 41.2, 40.8, 31.7, 30.3, 29.3, 27.7, 27.2, 22.6; LRMS (EI) *m*/*z* 418 (M^+); HRMS (EI) *m*/*z* calcd $C_{26}H_{27}FN_2O_2$ (M^+) 418.2057, found 418.2058.

2-Hexyl-13-fluoro-15*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrrolo-[2,1-*c*][1,4]diazepine-3,9(2*H*,15*bH*)-dione (3Gb-2): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59−8.61 (m, 1H), 8.39 (d, *J* = 7.5 Hz, 1H), 7.63−7.67 (m, 2H), 7.45 (t, 1H), 7.07−7.19 (m, 2H), 6.56 (s, 1H), 2.69−2.75 (m, 2H), 2.52−2.58 (m, 1H), 1.69 (m, 1H), 1.49 (s, 3H), 1.21−1.45 (m, 9H), 0.81−0.88 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.7, 164.5, 160.0, 145.4, 134.7, 134.4, 133.9, 133.3, 130.0, 128.1, 127.3, 127.1, 119.7 (d, *J* = 9.0 Hz), 112.8 (d, *J* = 23.8 Hz), 106.3, 105.9 (d, *J* = 23.8 Hz), 62.4, 42.0, 40.5, 31.5, 30.7, 28.8, 28.7, 27.6, 22.5, 14.0; LRMS (EI) *m*/*z* 418 (M^+); HRMS (EI) *m*/*z* calcd $C_{26}H_{27}FN_2O_2$ (M^+) 418.2057, found 418.2058.

15,16*b*-Dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*][1,4]-diazepine-4,10(2*H*,16*bH*)-dione (3Ac): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.57 (d, *J* = 8.7 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.60 (t, 1H), 7.46 (t, 1H), 7.28−7.32 (m, 2H), 7.12 (d, *J* = 7.2 Hz, 1H), 6.52 (s, 1H), 2.76−2.81 (m, 1H), 2.55−2.64 (m, 2H), 2.52 (s, 3H), 2.10−2.28 (m, 2H), 1.91−1.96 (m, 1H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 165.3, 142.6, 138.1, 137.1, 132.9, 132.4, 131.5, 129.9, 129.6, 128.5, 127.8, 125.5, 125.0, 116.3, 105.1, 60.9, 37.7, 31.8, 31.7, 18.3, 17.1; LRMS (EI) *m*/*z* 344 (M^+); HRMS (EI) *m*/*z* calcd $C_{22}H_{20}N_2O_2$ (M^+) 344.1525, found 344.1527.

16*b*-Methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*][1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Bc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.75 (d, *J* = 8.7 Hz, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 7.62 (t, 1H), 7.45−7.55 (m, 2H), 7.31−7.42 (m, 3H), 6.52 (s, 1H), 2.75−2.80 (m, 1H), 2.57−2.66 (m, 2H), 2.19−2.29 (m, 1H), 2.11−2.14 (m, 1H), 1.92−1.97 (m, 1H), 1.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 165.3, 143.1, 138.3, 137.1, 133.0, 132.5, 131.3, 130.0, 129.1, 127.8, 125.5, 124.5, 120.3, 118.8, 106.8, 60.8, 37.6, 31.9, 31.6, 17.0; LRMS (EI) *m*/*z* 330 (M^+); HRMS (EI) *m*/*z* calcd $C_{21}H_{18}N_2O_2$ (M^+) 330.1368, found 330.1369.

14,16*b*-Dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*][1,4]-diazepine-4,10(2*H*,16*bH*)-dione (3Cc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.60 (d, *J* = 8.4 Hz, 1H), 8.21 (d, *J* = 8.1 Hz, 1H), 7.60 (t, 1H), 7.46 (t, 1H), 7.29−7.31 (m, 2H), 7.18 (d, *J* = 9.0 Hz, 1H), 6.42 (s, 1H), 2.71−2.76 (m, 1H), 2.54−2.63 (m, 2H), 2.45 (s, 3H), 2.16−2.25 (m, 1H), 1.91−2.11 (s, 2H), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 165.0, 143.1, 137.1, 136.5, 134.2, 132.9, 132.5, 131.4, 130.0, 129.3, 127.8, 126.7, 120.2, 118.5, 106.7, 60.8, 37.6, 31.8, 31.5, 21.3, 17.0; LRMS (EI) *m*/*z* 344 (M^+); HRMS (EI) *m*/*z* calcd $C_{22}H_{20}N_2O_2$ (M^+) 344.1525, found 344.1521.

13,16*b*-Dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*][1,4]-diazepine-4,10(2*H*,16*bH*)-dione (3Dc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.60 (s, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.60 (t, 1H), 7.47 (t, 1H), 7.39 (d, *J* = 7.5, 1H), 7.29 (d, *J* = 7.8, 1H), 7.15 (d, *J* = 8.1, 1H), 6.45 (s, 1H), 2.54−2.75 (m, 3H), 2.52(s, 3H), 2.15−2.26 (m, 1H), 2.08−2.11 (m, 1H), 1.89−1.94 (m, 1H), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 165.3, 142.4, 138.7, 137.1, 135.5, 132.9, 132.4, 131.4, 129.9, 127.8, 126.7, 125.8, 119.8, 119.1, 106.8, 60.8, 37.6, 31.8, 31.6, 22.1, 17.0; LRMS (EI) *m*/*z* 344 (M^+); HRMS (EI) *m*/*z* calcd $C_{22}H_{20}N_2O_2$ (M^+) 344.1525, found 344.1529.

14-Methoxyl-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Ec): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.64 (d, *J* = 8.1 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.60 (t, 1H), 7.46 (t, 1H), 7.29 (d, *J* = 7.8 Hz, 1H), 6.95−6.99 (m, 2H), 6.43 (s, 1H), 3.87 (s, 3H), 2.56−2.76 (m, 3H), 1.91−2.26 (m, 3H), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 156.9, 143.7, 137.1, 132.9, 132.5, 131.3, 130.1, 130.0, 127.8, 119.7, 113.2, 106.7, 103.4, 60.7, 55.6, 37.5, 31.8, 31.5, 17.0; LRMS (EI) *m*/*z* 360 (M^+); HRMS (EI) *m*/*z* calcd $C_{22}H_{20}N_2O_3$ (M^+) 360.1474, found 360.1478.

14-Cyano-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Fc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.84 (d, *J* = 9.0 Hz, 1H), 8.19 (d, *J* = 8.1 Hz, 1H), 7.85 (s, 1H), 7.64 (d, *J* = 9.3 Hz, 2H), 7.51 (t, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 6.55 (s, 1H), 2.74−2.76 (m, 1H), 2.57−2.66 (m, 2H), 2.20−2.24 (m, 1H), 1.96−2.00 (m, 2H), 1.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 165.4, 145.7, 140.2, 137.3, 133.6, 132.7, 130.7, 130.2, 129.2, 128.5, 128.1, 124.8, 119.6, 119.4, 107.8, 105.9, 60.7, 37.5, 31.8, 31.4, 17.0; LRMS (EI) *m*/*z* 355 (M^+); HRMS (EI) *m*/*z* calcd $C_{22}H_{17}N_3O_2$ (M^+) 355.1321, found 355.1316.

14-Fluoro-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Gc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.68−8.73 (q, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.62

(t, 1H), 7.47 (t, 1H), 7.30 (d, J = 7.5 Hz, 1H), 7.05−7.18 (m, 2H), 6.46 (s, 1H), 2.56−2.76 (m, 3H), 2.17−2.27 (m, 1H), 2.04−2.09 (m, 1H), 1.92−1.97 (m, 1H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 165.0, 160.0, 144.7, 137.1, 134.6, 133.1, 132.5, 131.0, 130.2, 130.0, 127.9, 120.0 (d, J = 8.2 Hz), 112.8 (d, J = 24.2 Hz), 106.3, 105.8 (d, J = 23.7 Hz), 60.7, 37.5, 31.8, 31.4, 17.0; LRMS (EI) m/z 348 (M^+); HRMS (EI) m/z calcd $C_{21}H_{17}FN_2O_2$ (M^+) 348.12741, found 348.1279.

14-Chloro-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Hc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.67 (d, J = 9.0 Hz, 1H), 8.19 (d, J = 8.1 Hz, 1H), 7.60 (t, 1H), 7.47 (t, 2H), 7.29−7.35 (m, 2H), 6.44 (s, 1H), 2.56−2.76 (m, 3H), 2.17−2.24 (m, 1H), 1.95−2.04 (m, 2H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 165.1, 144.5, 137.1, 136.6, 133.2, 132.5, 131.0, 130.3, 130.0, 129.9, 127.9, 125.4, 119.8, 105.9, 60.7, 37.5, 31.8, 31.4, 17.0; LRMS (EI) m/z 364 (M^+); HRMS (EI) m/z calcd $C_{21}H_{17}ClN_2O_2$ (M^+) 364.0979, found 364.0977.

8,16*b*-Dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*][1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Ic): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.73 (d, J = 8.1 Hz, 1H), 8.00 (s, 1H), 7.52 (d, J = 7.8 Hz 1H), 7.28−7.42 (m, 3H), 7.19 (d, J = 8.1 Hz 1H), 6.49 (s, 1H), 2.72−2.77 (m, 1H), 2.54−2.62 (m, 2H), 2.44 (s, 3H), 2.16−2.25 (m, 1H), 2.05−2.10 (m, 1H), 1.89−1.94 (m, 1H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 165.5, 143.2, 138.3, 137.8, 134.5, 134.0, 132.6, 130.9, 129.7, 129.0, 125.4, 124.4, 120.2, 118.8, 106.8, 60.7, 37.6, 31.9, 31.5, 21.0, 17.0; LRMS (EI) m/z 344 (M^+); HRMS (EI) m/z calcd $C_{22}H_{20}N_2O_2$ (M^+) 344.1525, found 344.1522.

8,14,16*b*-Trimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Jc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (d, J = 8.4 Hz, 1H), 8.00 (s, 1H), 7.40 (d, J = 8.1 Hz, 1H), 7.29 (s, 1H), 7.16−7.21 (m, 2H), 6.41 (s, 1H), 2.53−2.75 (m, 3H), 2.45 (s, 3H), 2.44 (s, 3H), 2.15−2.24 (m, 1H), 2.03−2.08 (m, 1H), 1.86−1.92 (m, 1H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 165.2, 143.2, 137.8, 136.5, 134.5, 134.1, 133.9, 132.6, 131.0, 129.7, 129.3, 126.6, 120.2, 118.4, 106.6, 60.7, 37.6, 31.9, 31.5, 21.3, 21.0, 17.0; LRMS (EI) m/z 358 (M^+); HRMS (EI) m/z calcd $C_{23}H_{22}N_2O_2$ (M^+) 358.1681, found 358.1685.

8-Chloro-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Mc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.70 (d, J = 7.8 Hz, 1H), 8.21 (d, J = 2.4 Hz, 1H), 7.50−7.58 (m, 2H), 7.30−7.43 (m, 2H), 7.27 (d, J = 8.4 Hz, 1H), 6.51 (s, 1H), 2.55−2.78 (m, 3H), 2.16−2.26 (m, 1H), 1.93−2.13 (m, 2H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 163.8, 142.7, 138.3, 135.7, 133.7, 133.1, 132.5, 132.2, 131.5, 129.0, 125.7, 124.8, 120.4, 118.8, 107.3, 60.7, 37.4, 31.8, 31.6, 17.0; LRMS (EI) m/z 364 (M^+); HRMS (EI) m/z calcd $C_{21}H_{17}ClN_2O_2$ (M^+) 364.0979, found 364.0975.

8-Chloro-14,16*b*-dimethyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Nc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.57 (d, J = 8.7 Hz, 1H), 8.21 (d, J = 1.8 Hz, 1H), 7.54 (dd, J = 8.4 Hz, 2.7 Hz, 1H), 7.28 (d, J = 9.3 Hz, 1H), 7.22 (t, 2H), 6.43 (s, 1H), 2.54−2.77 (m, 3H), 2.45 (s, 3H), 2.15−2.21 (m, 1H), 1.91−2.05 (m, 2H), 1.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 163.6, 142.6, 136.5, 135.7, 134.5, 133.6, 133.0, 132.6, 132.2, 131.5, 129.2, 126.9, 120.4, 118.5, 107.1, 60.7, 37.4, 31.8, 31.5, 21.3, 16.9; LRMS (EI) m/z 378 (M^+); HRMS (EI) m/z calcd $C_{22}H_{19}ClN_2O_2$ (M^+) 378.1135, found 378.1136.

8-Chloro-14-fluoro-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido-[2,1-*c*][1,4]diazepine-4,10(2*H*, 16*bH*)-dione (3Oc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.67 (q, 1H), 8.20 (d, J = 2.7 Hz, 1H), 7.56 (dd, J = 8.7 Hz, 2.4 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 7.06−7.18 (m, 2H), 6.47 (s, 1H), 2.72−2.77 (m, 1H), 2.57−2.64 (m, 2H), 2.17−2.26 (m, 1H), 1.92−2.06 (m, 2H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 163.6, 160.1 (d, J = 241.0 Hz), 144.3, 135.7, 134.6, 133.8, 133.2, 132.3, 132.2, 131.5, 130.1, 120.1 (d, J = 8.7 Hz), 113.1 (d, J = 23.6 Hz), 106.8, 106.1 (d, J = 23.7 Hz), 60.7, 37.3, 31.8, 31.5, 17.0; LRMS (EI) m/z 382 (M^+); HRMS (EI) m/z calcd $C_{21}H_{16}ClFN_2O_2$ (M^+) 382.0884, found 382.0878.

8,14-Dichloro-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Pc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.63 (d, J = 8.7 Hz, 1H), 8.20 (d, J = 2.4 Hz, 1H), 7.56 (dd, J = 8.4 Hz, 1.8 Hz, 1H), 7.48 (d, J = 2.1 Hz, 1H), 7.33 (dd, J = 9.3 Hz, 1.8 Hz, 1H), 7.26 (d, J = 8.1 Hz, 1H), 6.45 (s, 1H), 2.57−2.77 (m, 3H), 2.11−2.22 (m, 1H), 1.94−2.02 (m, 2H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 163.7, 144.1, 136.6, 135.7, 133.8, 133.3, 132.2, 131.6, 130.3, 130.2, 125.7, 120.0, 119.9, 106.3, 60.7, 37.3, 31.8, 31.5, 29.7, 16.9; LRMS (EI) m/z 398 (M^+); HRMS (EI) m/z calcd $C_{21}H_{16}Cl_2N_2O_2$ (M^+) 398.0589, found 398.0589.

8-Fluoro-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido[2,1-*c*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Qc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.71 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.36−7.43 (m, 1H), 7.28−7.36 (m, 3H), 6.51 (s, 1H), 2.73−2.79 (m, 1H), 2.55−2.64 (m, 2H), 2.17−2.27 (m, 1H), 2.07−2.12 (m, 1H), 1.91−1.97 (m, 1H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 163.9, 161.4 (d, J = 246.0 Hz), 142.9, 138.3, 133.2, 133.0, 132.0 (d, J = 8.2 Hz), 129.1, 125.6, 124.8, 120.5 (d, J = 23.7 Hz), 120.4, 118.8, 118.6 (d, J = 24.6 Hz), 107.3, 60.8, 37.5, 31.8, 31.6, 17.0; LRMS (EI) m/z 348 (M^+); HRMS (EI) m/z calcd $C_{21}H_{17}FN_2O_2$ (M^+) 348.1274, found 348.1276.

8-Fluoro-14-chloro-16*b*-methyl-1*H*-benzo[*e*]indolo[1,2-*a*]pyrido-[2,1-*c*][1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Rc): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.63 (d, J = 9.0 Hz, 1H), 7.89 (dd, J = 9.3 Hz, 2.4 Hz, 1H), 7.47 (d, J = 1.8 Hz, 1H), 7.29−7.35 (m, 3H), 6.45 (s, 1H), 2.71−2.77 (m, 1H), 2.55−2.64 (m, 2H), 2.17−2.26 (m, 1H), 2.00−2.05 (m, 1H), 1.92−1.97 (m, 1H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 163.7, 161.3 (d, J = 246.8 Hz), 144.2, 136.6, 133.2, 132.6 (d, J = 7.7 Hz), 132.0 (d, J = 8.2 Hz), 130.3, 130.1, 125.6, 120.7 (d, J = 22.8 Hz), 120.0, 119.9, 118.6 (d, J = 24.6 Hz), 106.3, 60.7, 37.4, 31.8, 31.4, 16.9; LRMS (EI) m/z 382 (M^+); HRMS (EI) m/z calcd $C_{21}H_{16}ClFN_2O_2$ (M^+) 382.0884, found 382.0885.

15,16*b*-Dimethyl-1*H*-benzo[*e*][1,4]oxazino[3,4-*c*]indolo[1,2-*a*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Bd): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.55 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 8.1 Hz, 1H), 7.64 (t, 1H), 7.50 (t, 1H), 7.43 (d, J = 8.1 Hz, 1H), 7.31 (d, J = 7.5 Hz, 1H), 7.13 (d, J = 7.5 Hz, 1H), 6.67 (s, 1H), 4.66 (d, J = 12.0 Hz, 1H), 4.48 (d, J = 16.5 Hz, 1H), 4.35 (d, J = 16.8 Hz, 1H), 4.06 (d, J = 12.3 Hz, 1H), 2.54 (s, 3H), 1.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8, 164.3, 139.4, 138.3, 134.6, 133.2, 133.1, 130.6, 130.0, 129.3, 128.5, 128.1, 125.7, 125.2, 116.1, 105.9, 73.1, 68.0, 59.4, 24.9, 18.4; LRMS (EI) m/z 346 (M^+); HRMS (EI) m/z calcd $C_{21}H_{18}N_2O_3$ (M^+) 346.1317, found 346.1315.

14-Fluoro-16*b*-methyl-1*H*-benzo[*e*][1,4]oxazino[3,4-*c*]indolo-[1,2-*a*][1,4]diazepine-4,10(2*H*, 16*bH*)-dione (3Gd): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.67−8.72 (q, 1H), 8.36 (d, J = 6.9 Hz, 1H), 7.64 (t, 1H), 7.52 (t, 1H), 7.44 (d, J = 8.1 Hz, 1H), 7.19 (dd, J = 8.4 Hz, 2.7 Hz, 1H), 7.10 (td, 1H), 6.60 (s, 1H), 4.63 (d, J = 12.3 Hz, 1H), 4.48 (d, J = 17.1 Hz, 1H), 4.36 (d, J = 16.8 Hz, 1H), 4.06 (d, J = 12.6 Hz, 1H), 1.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.7, 164.0, 160.0, 141.6, 135.0, 134.6, 133.5, 133.2, 130.1, 129.4, 128.2, 119.9 (d, J = 8.6 Hz), 113.1 (d, J = 24.1 Hz), 107.0, 106.3 (d, J = 24.2 Hz), 73.0, 68.0, 59.3, 24.7; LRMS (EI) m/z 350 (M^+); HRMS (EI) m/z calcd $C_{20}H_{15}FN_2O_3$ (M^+) 350.1067, found 350.1067.

8,16*b*-Dimethyl-1*H*-benzo[*e*][1,4]oxazino[3,4-*c*]indolo[1,2-*a*]-[1,4]diazepine-4,10(2*H*,16*bH*)-dione (3Id): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.72 (d, J = 7.8 Hz, 1H), 8.15 (s, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.26−7.44 (m, 4H), 6.63 (s, 1H), 4.62 (d, J = 12.6 Hz, 1H), 4.46 (d, J = 17.4 Hz, 1H), 4.33 (d, J = 17.1 Hz, 1H), 4.04 (d, J = 12.6 Hz, 1H), 2.47 (s, 3H), 1.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8, 164.5, 140.1, 138.5, 138.3, 134.3,

133.2, 132.0, 130.0, 129.1, 129.0, 125.6, 124.6, 120.7, 118.6, 107.4, 73.1, 68.0, 59.3, 24.8, 21.0; LRMS (EI) m/z 346 (M^+); HRMS (EI) m/z calcd $C_{21}H_{18}N_2O_3$ (M^+) 346.1317, found 346.1319.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for all compounds and crystallographic data for compound **3Ba**. This material is available free of charge via the Internet at http://pubs.acs.org.