EurJOC
European Journal of Organic Chemistry

A Journal of ChemPubSoc Europe

Accepted Article

Title: Synthesis of N-fused Seven-Membered Indoline-3-ones via Palladium-Catalyzed One-Pot Insertion Reaction from 2-Alkynyl Arylazides and Cyclic β-diketones

Authors: Ping Li, Rong Sheng, Zhiqiang Zhou, Guiwen Hu, and Xiaoxiang Zhang

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.202000243

Link to VoR: http://dx.doi.org/10.1002/ejoc.202000243

Supported by ACES Asian Chemical Editorial Society

WILEY-VCH

FULL PAPER WILEY-VCH

Synthesis of *N*-fused Seven-Membered Indoline-3-ones *via* Palladium-Catalyzed One-Pot Insertion Reaction from 2-Alkynyl Arylazides and Cyclic *β*-diketones

Ping Li,[a] Rong Sheng,[a] Zhiqiang Zhou,[a] Guiwen Hu,[a] and Xiaoxiang Zhang*[a]

[a] P. Li, R. Sheng, Z. Zhou, G. Hu, Prof. Dr . X. Zhang
Jiangsu key lab of Biomass-based Green Fuels and Chemicals, College of Chemical Engineering,
Nanjing Forestry University
Nanjing 210037, China
E-mail: zhangxiaoxiang@njfu.edu.cn

Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

Abstract: A novel strategy to synthesize *N*-fused seven-membered multifunctional polycyclic indoline-3-one derivatives *via* insertion reaction of cyclic *C*-acylimines into cyclic *β*-diketones has been described. The reaction was proceeded well under mild reaction conditions *via* one-pot three steps method, which has shown good tolerance of various functional groups.

Introduction

Indolin-3-ones with a *N*-fused ring as an important kind of heterocycles have unique biological and pharmaceutical activities which exist as core scaffold in a number of natural products [1], such as (-)-isatisine A [2], (-)-melokhanine E [3], fluorocarpamine [4] (Figure 1). Thus, the methods for the synthesis of indolin-3-ones containing a *N*-fused ring have been

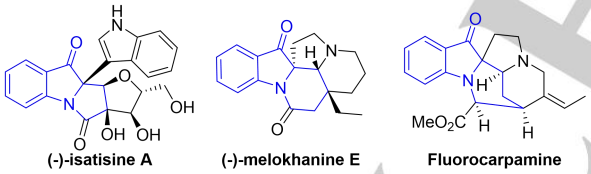
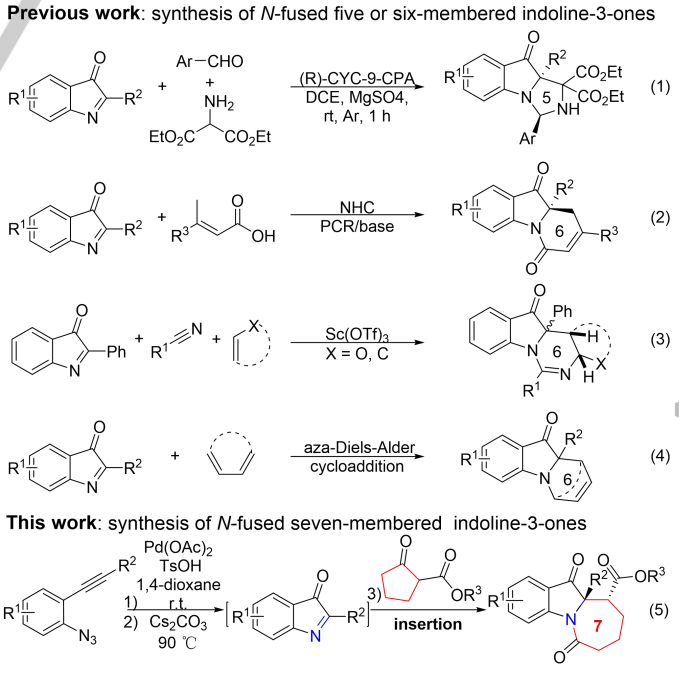


Figure 1. Representative natural products containing *N*-fused indoline-3-ones.

reported extensively [5]. Among those reported reactions, the substituted 2-aryl-3*H*-indol-3-ones **G** [6] were used as the key substrates, which could be attacked easily by various nucleophilic reagents. Recently, Fu's group [7] demonstrated a synthetic strategy of imidazo[1,5-a]indol-3-ones by chiral phosphoric acid catalyzed sequential additions of **G**, aldehydes and diethyl 2-aminomalonate [Scheme 1, (1)]. Later, an NHC-catalyzed [4 + 2] annulation reaction of **G** with *α,β*-unsaturated carboxylic acids to produce *N*-fused six-membered indoline-3-ones has been developed by Du's group [8] [Scheme 1, (2)]. In 2012, Lavilla and co-workers [9] reported a method for the synthesis of dihydropyrimido[1,6-a]indoline-3-ones through multicomponent reaction between dihydropyran, nitrile and **G** with $Sc(OTf)_3$ catalysis [Scheme 1, (3)]. Besides, three different aza-Diels-Alder cycloaddition methods to generate a series of *N*-fused six-membered indoline-3-ones have been described by Raja's group [10a], Luque's group [10b] and Chen's group [10c], respectively [Scheme 1, (4)]. However, the methods for the synthesis of *N*-fused five- or six-membered indoline-3-ones have been reported, the preparation of *N*-fused seven-membered indoline-3-ones has not been studied. Thus, studies on synthesis of *N*-fused seven-membered indoline-3-ones have great necessary.

Recently, the insertion of unsaturated bonds into carbon-carbon σ-bonds provided an efficient strategy to synthesize polyfunctional molecules [11]. Especially, the cyclic *β*-diketones were employed as the key substrates to construct the medium-size ring in various insertion reactions [12]. On the basis of previous studies [11-12] as well as our ongoing efforts on synthesis of various indolin-3-ones [13], we envisaged that the *N*-fused seven-membered indoline-3-ones could be obtained through Palladium-catalyzed one-pot insertion reaction of 3*H*-indol-3-ones into cyclic *β*-diketones from 2-alkynyl arylazides [Scheme 1, (5)].



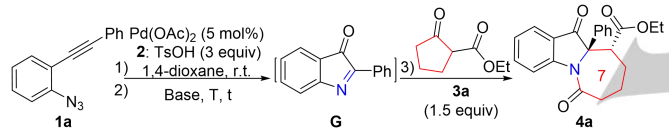
Scheme 1. Synthesis of *N*-fused indoline-3-ones.

Results and Discussion

Based on our previous work [13], the reaction conditions were optimized in Table 1. Initially, the 1-azido-2-(phenylethynyl)benzene **1a** (0.1 mmol) was chosen as a model substrate under the conditions of $Pd(OAc)_2$ (5 mol%), TsOH (3 equiv) in 1,4-dioxane (1 mL) at room temperature for 10 min to form the intermediate 2-phenyl-1*H*-indol-3-yl 4-methylbenzenesulfonate **E**. Then Cs_2CO_3 (3.5 equiv) and ethyl 2-oxocyclopentane-1-carboxylate **3a** (1.5 equiv) were added into the reaction, which was stirred at 90 ℃ for 5 h. The desired product *trans*-ethyl 6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*]indole-10-carboxylate **4a** was obtained in 81% yield (entry 1). The structure of product **4a** was confirmed by the analysis of ^{1}H NMR and determination of X-ray crystal structure (Figure 2).

Subsequently, the reaction was found to accomplish in 0.7 h by adding **3a** after the formation of intermediate 2-phenyl-3*H*-indol-3-one **G**, which also provided the desired product **4a** in 81% yield (entry 2). Therefore, all the reactions were carried out in three steps. When the reaction was conducted at 60 ℃, it took longer time and generated lower yield of 63% (entry 3). Afterwards, various bases were investigated (entries 4-7). However, switching Cs_2CO_3 to K_2CO_3 was found to result in long reaction time and low product yield (entry 4). When K_3PO_4 was used as a base, the desired product **4a** was obtained in 22% yield due to the low intermediate conversion of **E** to **G** (entry 5). When strong base *t*-BuOK and organic base DBU were employed, the desired product was obtained in yields of 19-33%. In these reactions, many byproducts were detected by TLC analysis (entries 6-7). The desired product **4a** could not be detected without any base (entry 8). When the amount of Cs_2CO_3 was decreased to 2.5 equiv, the desired product **4a** was also obtained in 73% yield after long reaction time (entry 9).

Table 1. Optimization of the reaction conditions. [a]



Entry	Base	T (℃)	Time (h)	Yield/%[b]
1	Cs_2CO_3	90	5.0	81[c]
2	Cs_2CO_3	90	0.7	81
3	Cs_2CO_3	60	4.5	63
4	K_2CO_3	90	2.5	69
5	K_3PO_4	90	28	22
6	*t*-BuOK	90	1.5	33
7	DBU	90	4.0	19
8	----	90	28	n.r.[d][e]
9	Cs_2CO_3	90	4.5	73[f]

[a] Reaction conditions: **1a** (0.1 mmol), $Pd(OAc)_2$ (5 mol%), **2a** (3 equiv), 1,4-dioxane (1 mL), base (3.5 equiv), and **3a** (1.5 equiv) was added after the formation of 2-phenyl-3*H*-indol-3-one **G**. [b] Isolated yield. [c] Cs_2CO_3 and **3a** were added in the same time after the first step. [d] Without base. [e] No desired product was detected. [f] 2.5 equiv of Cs_2CO_3 was used.

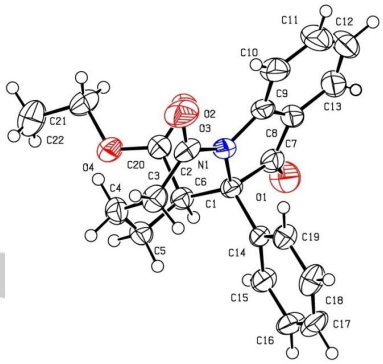


Figure 2. ORTEP drawing of **4a** with thermal ellipsoids at 50% probability.

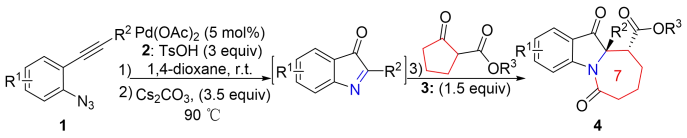
With the optimal reaction conditions in hand, we began to evaluate the generality of this method with a variety of 2-alkynyl arylazides **1** and cyclic *β*-diketones **3**. As shown in Table 2, 2-alkynyl arylazides **1** containing an electron-withdrawing or electron-donating group on the aromatic ring could be reacted with ethyl 2-oxocyclopentane-1-carboxylate **3a** to produce corresponding compounds in moderate to good yields of 52-81% (**4a**, **4c-4j**). When the substituted group CF_3 was on the aromatic ring, the desired product **4k** was afforded in slightly low yield of 52%. Substrates with different substituted aryl or hetero aryl groups on the terminal alkyne carbon were also suitable for the insertion reaction, which gave the desired products **4l**, **4n-4p**, **4r-4s** and **4u** in the yields of 62-77%. However, the yield of **4t** was decreased to 45%. Substrates bearing aliphatic pendant groups were also examined and provided the desired product **4v** and **4w** in yields of 55% and 45%, respectively. In contrast, substrate with R^2 = *t*-butyl group **1x** was failed to the reaction and only the first-step intermediate 2-(*tert*-butyl)-1*H*-indol-3-yl 4-methylbenzenesulfonate [13b] could be isolated, which was probably due to the steric hindrance. Likewise, methyl 2-oxocyclopentane-1-carboxylate **3b** was also proved to be a good substrate for the insertion reaction to construct *N*-fused seven-membered indoline-3-ones (**4b**, **4m** and **4q**). Furthermore, the desired products **4h-4i**, **4k** and **4v-4w** were obtained using two-step method, which was probably due to the unstability of 3*H*-indol-3-ones with strong electron-withdrawing group on the aromatic ring or aliphatic group on the terminal alkyne carbon.

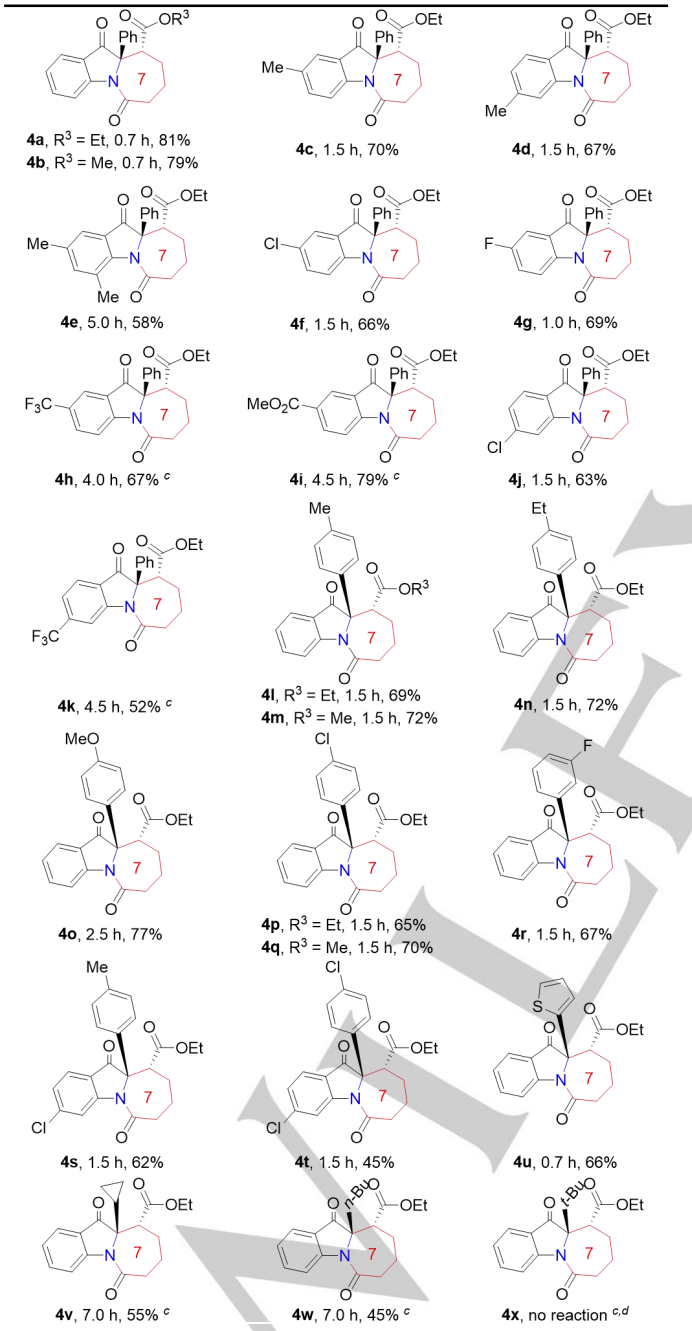
Under the standard reaction conditions, 1*H*-indene-1,3(2*H*)-dione **3c** was next explored for the insertion reaction (Table 3). However, no desired insertion product was obtained. The intermolecular addition intermediate **5a** was isolated in 44% yield. When the substituted group R^2 was changed from Ph to *n*-butyl, the reacion was still afforded the intermediate **5b** in 40% yield after 8 h.

According to our previous research [13] and above experiment results, we proposed a plausible mechanism for the synthesis of *N*-fused seven-membered indolin-3-ones in scheme 2. At the outset, the triple bond of **1a** was activated by Palladium catalyst and delivered the complex **A**. Intramolecular cyclization of azide group to the activated alkyne led to the formation of complex **B**. Then the α-imino palladium carbene **C** [14] generated *in situ* by releasing the N_2 could be trapped by TsOH to afford the complex **D**, which followed by protodemetalation to form 1*H*-indole-3-sulfonate **E** [13b]. Basic conditions produce the 2-phenyl-3*H*-indol-3-one **G** [15] *via* 1,3-Ts shift [16] of **E** and further reductive desulfonation [17] of α-amino sulfone **F**. Nucleophilic addition [6-10] of **3a** to **G** afforded the complex **H**, which resulted in a four-membered ring complex **I** after intramolecular addition [11]. Finally,

the desired product **4aa** was obtained by protonation of complex **J**, which was generated from the ring expansion of **I** [12].

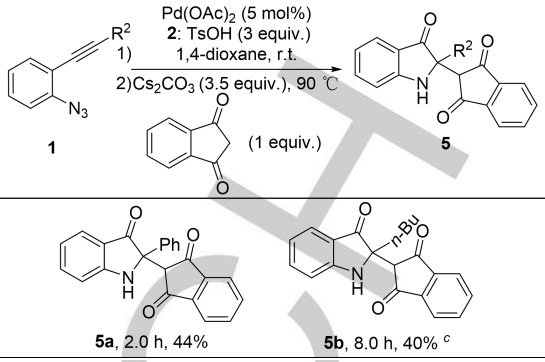
Table 2. Exploration of Substrate Scope. [a] [b]



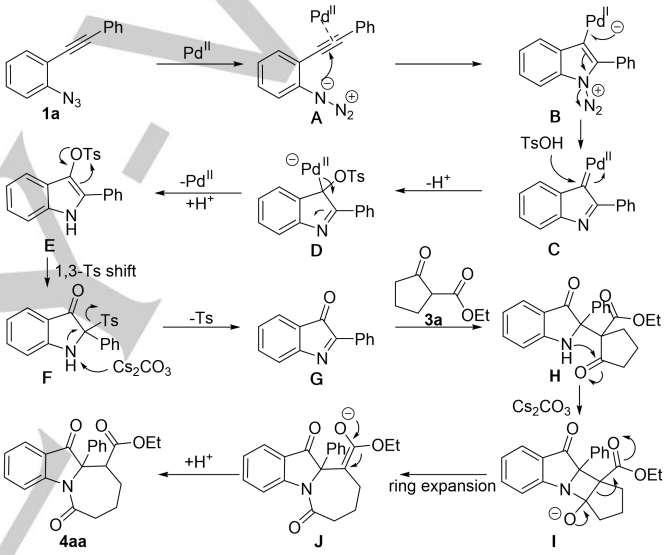


[a] Reaction conditions: **1a** (0.1 mmol), $Pd(OAc)_2$ (5 mol%), TsOH (3 equiv), 1,4-dioxane (1 mL), Cs_2CO_3 (3.5 equiv), and **3** (1.5 equiv) was added after the formation of 3*H*-indol-3-ones. [b] Isolated yield. [c] Cs_2CO_3 and **3a** were added in the same time after the first step. [d] The first-step product 2-(*tert*-butyl)-1*H*-indol-3-yl 4-methylbenzenesulfonate was isolated.

Table 3. Reactions of 1*H*-indene-1,3(2*H*)-dione **3c**.[a] [b]



[a] Reaction conditions: **1a** (0.1 mmol), $Pd(OAc)_2$ (5 mol%), TsOH (3 equiv), 1,4-dioxane (1 mL), Cs_2CO_3 (3.5 equiv), and **3c** (1.5 equiv) was added after the formation of 3*H*-indol-3-ones. [b] Isolated yield. [c] Cs_2CO_3 and **3c** were added in the same time after the first step.



Scheme 2. A plausible reaction mechanism.

Conclusion

In conclusion, we have disclosed a novel insertion reaction from 2-alkynyl arylazides and cyclic *β*-diketones in one-pot three steps. The corresponding *N*-fused seven-membered indoline-3-ones were obtained in moderate to good yields under mild reaction conditions. The results indicate that the reaction can tolerate various functional groups. Further applications of this strategy are currently underway and will be reported in future.

Experimental Section

General experimental procedure for the synthesis of 4/5a in three steps: To a 10 mL of flask was added 2-alkynyl arylazides **1** (0.1 mmol, 1 equiv), TsOH **2** (0.3 mmol, 3 equiv), $Pd(OAc)_2$ (5 mol%), and 1,4-dioxane (1 mL). The reaction mixture was stirred at room temperature. After the 2-alkynyl arylazides **1** disappeared monitored by TLC, Cs_2CO_3 (0.35 mmol, 3.5 equiv) was added to the reaction solution, which was then stirred at 90 ℃. When 3*H*-indol-3-one was completely formed, **3**

(0.15 mmol, 1.5 equiv) was added into the above mixture at 90 ℃. On completion monitored by TLC, the reaction mixture was directly subjected to purification by flash column chromatography on silica gel to give the desired **4**. (eluent: petrol ether: ethyl acetate = 40:1 to 8:1).

General experimental procedure for the synthesis of 4/5b in two steps: To a 10 mL of flask was added 2-alkynyl arylazides **1** (bearing strong electron-withdrawing group on the aromatic ring or aliphatic group on the terminal alkyne carbon) (0.1 mmol, 1 equiv), TsOH **2** (0.3 mmol, 3 equiv), $Pd(OAc)_2$ (5 mol%), and 1,4-dioxane (1 mL). The reaction mixture was stirred at room temperature. After the 2-alkynyl arylazides **1** disappeared, Cs_2CO_3 (0.35 mmol, 3.5 equiv) and **3** (0.15 mmol, 1.5 equiv) were added to the reaction solution together, which was then stirred at 90 ℃ and monitored by TLC analysis. On completion, the reaction mixture was directly subjected to purification by flash column chromatography on silica gel to give the desired **4**. (eluent: petrol ether: ethyl acetate = 40:1 to 8:1).

***trans*-Ethyl 6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*]indole-10- carboxylate (4a):** Isolated yield = 81%; yellow solid; m.p. 133.3-134.2 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.88 (t, *J* = 6.6 Hz, 3 H), 1.71-1.83 (m, 2 H), 1.97-2.03 (m, 1 H), 2.28-2.33 (m, 1 H), 2.44-2.47 (m, 1 H), 2.59-2.63 (m, 1 H), 3.92-3.98 (m, 2 H), 4.30 (t, *J* = 4.2 Hz, 1 H), 7.22-7.31 (m, 4 H), 7.34-7.37 (m, 2 H), 7.68-7.71 (m, 2 H), 8.80 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.6, 19.9, 25.4, 38.5, 47.6, 60.5, 73.6, 117.8, 121.7, 123.7, 123.8, 127.5, 128.8, 134.0, 135.9, 152.7, 169.4, 172.7, 195.7; HRMS (ESI) calcd for $C_{22}H_{22}NO_4$ $[M+H]^+$ 364.1549, found 364.1555.

***trans*-Methyl 6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*]indole-10- carboxylate (4b):** Isolated yield = 79%; yellow solid; m.p. 185.6-186.3 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.71-1.82 (m, 2 H), 1.99-2.05 (m, 1 H), 2.28-2.33 (m, 1 H), 2.43-2.46 (dd, J_1 = 14.4 Hz, J_2 = 3.6 Hz, 1 H), 2.60-2.64 (dd, J_1 = 14.4 Hz, J_2 = 6.6 Hz, 1 H), 3.51 (s, 3 H), 4.33 (t, *J* = 4.2 Hz, 1 H), 7.22-7.24 (m, 1 H), 7.27-7.31 (m, 3 H), 7.35-7.37 (m, 2 H), 7.69-7.72 (m, 2 H), 8.81 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 20.1, 25.4, 38.5, 47.8, 51.4, 73.6, 117.8, 121.6, 123.7, 123.9, 127.6, 1288, 133.9, 136.0, 152.6, 170.1, 172.7, 195.8; HRMS (ESI) calcd for $C_{21}H_{20}NO_4$ $[M+H]^+$ 350.1392, found 350.1397.

***trans*-Ethyl 2-methyl-6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4c):** Isolated yield = 70%; yellow solid; m.p. 138.7-139.8 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.93 (t, *J* = 6.6 Hz, 3 H), 1.70-1.82 (m, 2 H), 1.96-2.02 (m, 1 H), 2.26-2.31 (m, 1 H), 2.37 (s, 3 H), 2.44-2.47 (m, 1 H), 2.58-2.62 (m, 1 H), 3.94-3.99 (m, 2 H), 4.29 (t, *J* = 3.6 Hz, 1 H), 7.26-7.30 (m, 3 H), 7.34-7.36 (m, 2 H), 7.47 (s, 1 H), 7.51-7.52 (dd, J_1 = 9 Hz, J_2 = 1.8 Hz, 1 H), 8.68 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.7, 19.9, 20.0, 25.4, 38.4, 47.7, 60.5, 73.8, 117.6, 121.8, 123.4, 127.5, 128.7, 133.8, 134.2, 137.1, 150.8, 169.5, 172.5, 195.7; HRMS (ESI) calcd for $C_{23}H_{24}NO_4$ $[M+H]^+$ 378.1705, found 378.1710.

***trans*-Ethyl 3-methyl-6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4d):** Isolated yield = 67%; yellow solid; m.p. 139.8-140.7 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.92 (t, *J* = 7.2 Hz, 3 H), 1.71-1.83 (m, 2 H), 1.97-2.03 (m, 1 H), 2.27-2.32 (m, 1 H), 2.43-2.46 (m, 1 H), 2.51 (s, 3 H), 2.58-2.62 (m, 1 H), 3.94-3.98 (m, 2 H), 4.28 (t, *J* = 3.6 Hz, 1 H), 7.05 (d, *J* = 7.8 Hz, 1 H), 7.26-7.30 (m, 3 H), 7.34-7.36 (m, 2 H), 7.57 (d, *J* = 7.8 Hz, 1 H), 8.65 (s, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.7, 20.0, 22.0, 25.4, 38.5, 47.4, 60.5, 73.8, 118.1, 119.5, 123.5, 125.2, 127.4, 128.7, 134.3, 147.8, 153.0, 169.5, 172.8, 195.1; HRMS (ESI) calcd for $C_{23}H_{24}NO_4$ $[M+H]^+$ 378.1705, found 378.1708.

***trans*-Ethyl 2,4-dimethyl-6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4e):** Isolated yield = 58%; yellow solid; m.p. 158.8-160.2 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.98 (t, *J* = 7.2 Hz, 3 H), 1.67-1.71 (m, 2 H), 1.79-1.85 (m, 1 H), 2.32 (s, 3 H), 2.37 (s, 3 H), 2.39-2.44 (m, 2 H), 2.63-2.66 (m, 1 H), 3.97-4.04 (m, 2 H), 4.33 (t, *J* = 4.2 Hz, 1 H), 7.26-7.28 (m, 1 H), 7.32-7.35 (m, 4 H), 7.43 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.8, 19.8, 20.1, 20.9, 25.2, 37.4, 48.7, 60.6, 74.3, 120.9, 124.1, 125.1, 127.4, 128.0, 128.5, 134.1, 134.7, 139.3, 150.0, 169.7, 171.1, 197.0; HRMS (ESI) calcd for $C_{24}H_{26}NO_4$ $[M+H]^+$ 392.1862, found 392.1868.

***trans*-Ethyl 2-chloro-6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4f):** Isolated yield = 66%; yellow solid; m.p. 152.9-153.8 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.99 (t, *J* = 7.2 Hz, 3 H), 1.73-1.77 (m, 2 H), 1.95-2.01 (m, 1 H), 2.26-2.31 (m, 1 H), 2.46-2.49 (m, 1 H), 2.60-2.64 (m, 1 H), 3.97-4.03 (m, 2 H), 4.30 (t, *J* = 4.2 Hz, 1 H), 7.25-7.28 (m, 2 H), 7.30-7.33 (m, 1 H), 7.36-7.38 (m, 2 H), 7.63-7.64 (m, 2 H), 8.77 (d, *J* = 9.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.8, 19.9, 25.4, 38.4, 47.9, 60.7, 74.1, 119.0, 123.2, 123.3, 127.5, 127.8, 128.9, 129.3, 135.6, 151.0, 169.5, 172.6, 194.6; HRMS (ESI) calcd for $C_{22}H_{21}ClNO_4$ $[M+H]^+$ 398.1159, found 398.1164.

***trans*-Ethyl 2-fluoro-6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4g):** Isolated yield = 69%; yellow solid; m.p. 136.3-137.3 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.97 (t, *J* = 7.2 Hz, 3 H), 1.73-1.82 (m, 2 H), 1.96-2.02 (m, 1 H), 2.26-2.31 (m, 1 H), 2.45-2.48 (m, 1 H), 2.60-2.64 (m, 1 H), 3.97-4.01 (m, 2 H), 4.29 (t, *J* = 3.6 Hz, 1 H), 7.26-7.29 (m, 2 H), 7.31-7.33 (m, 2 H), 7.36-7.42 (m, 3 H), 8.81-8.83 (dd, J_1 = 9.6 Hz, J_2 = 4.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.8, 19.9, 25.5, 38.4, 48.0, 60.6, 74.2, 109.1 (d, *J* = 22.9 Hz), 119.4 (d, *J* = 6.9 Hz), 122.9, 123.0, 123.3 (d, *J* = 7.7 Hz), 127.7, 128.9, 133.8, 149.1, 158.6 (d, *J* = 245.1 Hz), 169.4, 172.4, 194.9; HRMS (ESI) calcd for $C_{22}H_{21}FNO_4$ $[M+H]^+$ 382.1455, found 382.1459.

***trans*-Ethyl 6,11-dioxo-10a-phenyl-2-(trifluoromethyl)-7,8,9,10,10a,11-hexahydro-6*H*- azepino[1,2-*a*]indole-10-carboxylate (4h):** Isolated yield = 67%; yellow solid; m.p. 160.7-161.4 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.98 (t, *J* = 7.2 Hz, 3 H), 1.74-1.78 (m, 2 H), 1.97-2.03 (m, 1 H), 2.29-2.34 (m, 1 H), 2.48-2.51 (m, 1 H), 2.63-2.67 (m, 1 H), 3.98-4.02 (m, 2 H), 4.34 (t, *J* = 4.2 Hz, 1 H), 7.26-7.29 (m, 2 H), 7.29-7.34 (m, 1 H), 7.37-7.39 (m, 2 H), 7.92-7.95 (m, 2 H), 8.93 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 13.4, 20.6, 25.9, 39.0, 48.7, 61.4, 74.9, 118.7, 121.8 (d, *J* = 3.7 Hz), 122.6, 124.9 (d, *J* = 185.4 Hz), 126.6 (d, *J* = 33.3 Hz), 128.5, 129.6, 133.2 (d, *J* = 3.3 Hz), 133.9, 155.0, 170.1, 173.6, 195.3; HRMS (ESI) calcd for $C_{23}H_{21}F_3NO_4$ $[M+H]^+$ 432.1423, found 432.1428.

***trans*-10-Ethyl 2-methyl 6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-2,10-dicarboxylate (4i):** Isolated yield = 79%; white solid; m.p. 178.3-190.0 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.94 (t, *J* = 7.2 Hz, 3 H), 1.74-1.78 (m, 2 H), 1.98-2.02 (m, 1 H), 2.28-2.33 (m, 1 H), 2.46-2.49 (m, 1 H), 2.61-2.65 (m, 1 H), 3.90 (s, 3 H), 3.94-4.00 (m, 2 H), 4.32 (t, *J* = 3.6 Hz, 1 H), 7.17-7.26 (m, 2 H), 7.29-7.32 (m, 1 H), 7.35-7.38 (m, 2 H), 8.35-8.38 (m, 2 H), 8.85 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.8, 19.9, 25.3, 38.4, 47.8, 51.4, 60.7, 74.3, 117.4, 121.9, 125.6, 125.7, 127.8, 128.9, 133.5, 137.1, 155.3, 164.9, 169.4, 172.9, 194.8; HRMS (ESI) calcd for $C_{24}H_{24}NO_6$ $[M+H]^+$ 422.1604, found 422.1608.

***trans*-Ethyl 3-chloro-6,11-dioxo-10a-phenyl-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4j):** Isolated yield = 63%; yellow solid; m.p. 130.8-131.6 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.98 (t, *J* = 7.2 Hz, 3 H), 1.73-1.77 (m, 2 H), 1.96-2.02 (m, 1 H), 2.26-2.32 (m, 1 H), 2.45-2.48 (m, 1 H), 2.60-2.64 (m, 1 H), 3.98-4.01 (m, 2 H), 4.29 (t, *J* = 4.2 Hz, 1 H), 7.21-7.22 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1 H), 7.26-7.28 (m, 2 H), 7.30-7.33 (m, 1 H), 7.36-7.37 (m, 2 H), 7.61 (d, *J* = 7.8 Hz, 1 H), 8.87 (d, *J* = 1.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.8, 19.9, 25.4, 38.4, 47.8, 60.7, 74.1, 118.2, 120.2, 124.53, 127.7, 128.9,

133.7, 142.4, 153.0, 169.5, 172.8, 194.5; HRMS (ESI) calcd for $C_{22}H_{21}ClNO_4$ $[M+H]^+$ 398.1159, found 398.1163.

***trans*-Ethyl 6,11-dioxo-10a-phenyl-3-(trifluoromethyl)-7,8,9,10,10a,11-hexahydro-6*H*-azepino [1,2-*a*]indole-10-carboxylate (4k):** Isolated yield = 52%; yellow solid; m.p. 140.8-141.6 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.98 (t, *J* = 7.2 Hz, 3 H), 1.74-1.78 (m, 2 H), 1.97-2.03 (m, 1 H), 2.28-2.33 (m, 1 H), 2.48-2.51 (m, 1 H), 2.63-2.67 (m, 1 H), 3.98-4.02 (m, 2 H), 4.34 (t, *J* = 4.2 Hz, 1 H), 7.21-7.26 (m, 2 H), 7.32-7.34 (m, 1 H), 7.37-7.39 (m, 2 H), 7.49 (d, *J* = 7.8 Hz, 1 H), 7.79 (d, *J* = 7.8 Hz, 1 H), 9.14 (s, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.8, 19.9, 25.4, 38.4, 48.2, 60.8, 74.2, 115.2 (d, *J* = 4.2 Hz), 120.6 (d, *J* = 3.4 Hz), 124.2, 124.3 (d, *J* = 164.4 Hz), 127.9, 129.0, 133.3, 135.3 (d, *J* = 31.5 Hz), 152.3, 169.5, 172.9, 195.1; HRMS (ESI) calcd for $C_{23}H_{21}F_3NO_4$ $[M+H]^+$ 432.1423, found 432.1428.

***trans*-Ethyl 6,11-dioxo-10a-(*p*-tolyl)-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*]indole-10- carboxylate (4l):** Isolated yield = 69%; yellow solid; m.p. 123.4-124.8 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.88 (t, *J* = 6.6 Hz, 3 H), 1.72-1.74 (m, 1 H), 1.77-1.84 (m, 1 H), 1.99-2.05 (m, 1 H), 2.30 (s, 3 H), 2.31-2.36 (m, 1 H), 2.43-2.46 (m, 1 H), 2.58-2.62 (m, 1 H), 3.91-3.97 (m, 2 H), 4.27 (t, *J* = 4.2 Hz, 1 H), 7.12-7.15 (m, 4 H), 7.21-7.23 (m, 1 H), 7.67-7.70 (m, 2 H), 8.79 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.6, 20.0, 20.1, 25.4, 38.5, 47.6, 60.5, 73.5, 117.8, 121.9, 123.7, 123.8, 129.5, 131.0, 135.9, 137.6, 152.7, 169.5, 172.8, 195.8; HRMS (ESI) calcd for $C_{23}H_{24}NO_4$ $[M+H]^+$ 378.1705, found 378.1709.

***trans*-Methyl 6,11-dioxo-10a-(*p*-tolyl)-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*]indole-10- carboxylate (4m):** Isolated yield = 72%; yellow solid; m.p. 197.1-198.3 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.73-1.79 (m, 2 H), 1.99-2.05 (m, 1 H), 2.30 (s, 3 H), 2.32-2.35 (m, 1 H), 2.42-2.45 (dd, J_1 = 13.8 Hz, J_2 = 3.0 Hz, 1 H), 2.59-2.62 (m, 1 H), 3.50 (s, 3 H), 4.31 (t, *J* = 3.6 Hz, 1 H), 7.09-7.20 (m, 4 H), 7.21-7.24 (m, 1 H), 7.68-7.71 (m, 2 H), 8.80 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 20.1, 25.4, 38.5, 47.7, 51.4, 73.5, 117.7, 121.6, 123.7, 129.5, 130.8, 135.9, 137.6, 152.6, 170.1, 172.7, 195.9; HRMS (ESI) calcd for $C_{22}H_{22}NO_4$ $[M+H]^+$ 364.1549, found 364.1554.

***trans*-Ethyl 10a-(4-ethylphenyl)-6,11-dioxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4n):** Isolated yield = 72%; yellow solid; m.p. 159.8-161.1 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.88 (t, *J* = 7.2 Hz, 3 H), 1.94 (t, *J* = 7.8 Hz, 3 H), 1.71-1.75 (m, 1 H), 1.77-1.84 (m, 1 H), 1.99-2.05 (m, 1 H), 2.32-2.36 (m, 1 H), 2.43-2.46 (m, 1 H), 2.59-2.62 (m, 3 H), 3.90-3.99 (m, 2 H), 4.28 (t, *J* = 3.6 Hz, 1 H), 7.10-7.17 (m, 4 H), 7.20-7.23 (m, 1 H), 7.67-7.70 (m, 2 H), 8.80 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.6, 14.3, 20.0, 25.4, 27.4, 38.5, 47.6, 60.5, 73.5, 117.8, 121.9, 123.7, 123.8, 125.0, 128.3, 131.2, 135.9, 143.8, 152.7, 169.5, 172.8, 195.9; HRMS (ESI) calcd for $C_{24}H_{26}NO_4$ $[M+H]^+$ 392.1862, found 392.1868.

***trans*-Ethyl 10a-(4-methoxyphenyl)-6,11-dioxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4o):** Isolated yield = 77%; yellow solid; m.p. 143.3-144.6 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.88 (t, *J* = 7.2 Hz, 3 H), 1.71-1.83 (m, 2 H), 1.98-2.04 (m, 1 H), 2.32-2.37 (m, 1 H), 2.43-2.46 (m, 1 H), 2.59-2.62 (m, 1 H), 3.76 (s, 3 H), 3.91-3.97 (m, 2 H), 4.24 (t, *J* = 3.6 Hz, 1 H), 6.87 (d, *J* = 8.4 Hz, 2 H), 7.10-7.17 (m, 2 H), 7.21-7.24 (m, 1 H), 7.68-7.70 (m, 2 H), 8.79 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.6, 20.0, 25.3, 38.4, 47.5, 54.5, 60.5, 73.1, 114.2, 117.8, 121.8, 123.7, 125.6, 126.3, 135.9, 152.6, 158.8, 169.5, 172.8, 195.9; HRMS (ESI) calcd for $C_{23}H_{24}NO_5$ $[M+H]^+$ 394.1654, found 394.1659.

***trans*-Ethyl 10a-(4-chlorophenyl)-6,11-dioxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4p):** Isolated yield = 65%; yellow solid; m.p. 75.2-76.7 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.89 (t, *J* = 7.2 Hz, 3 H), 1.73-1.84 (m, 2 H), 1.91-1.97 (m, 1 H), 2.25-2.30 (m, 1 H), 2.45-2.48 (m, 1 H), 2.62-2.65 (m, 1 H), 3.92-3.98 (m, 2 H), 4.24 (t, *J* = 3.6 Hz, 1 H), 7.21-7.26 (m, 3 H), 7.33 (d, *J* = 7.8 Hz, 2 H), 7.68-7.72 (m, 2 H), 8.78 (d, *J* = 9 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.6, 19.9, 25.4, 38.5, 47.6, 60.7, 73.2, 117.9, 121.5, 123.8, 124.0, 128.9, 132.7, 133.8, 136.2, 152.6, 169.2, 172.5, 195.3; HRMS (ESI) calcd for $C_{22}H_{21}ClNO_4$ $[M+H]^+$ 398.1159, found 398.1164.

***trans*-Methyl 10a-(4-chlorophenyl)-6,11-dioxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4q):** Isolated yield = 70%; yellow solid; m.p. 185.6-186.4 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.75-1.78 (m, 2 H), 1.93-1.98 (m, 1 H), 2.24-2.29 (m, 1 H), 2.44-2.47 (dd, J_1 = 14.4 Hz, J_2 = 3.0 Hz, 1 H), 2.62-2.66 (m, 1 H), 3.51 (s, 3 H), 4.27 (t, *J* = 3.6 Hz, 1 H), 7.21-7.26 (m, 3 H), 7.34 (d, *J* = 8.4 Hz, 2 H), 7.69-7.73 (m, 2 H), 8.80 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 20.0, 25.4, 38.5, 47.8, 51.5, 73.2, 117.8, 121.4, 123.8, 124.0, 129.0, 132.6, 133.9, 136.2, 152.6, 169.8, 172.4, 195.4; HRMS (ESI) calcd for $C_{21}H_{19}ClNO_4$ $[M+H]^+$ 384.1003, found 384.1009.

***trans*-Ethyl 10a-(3-fluorophenyl)-6,11-dioxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4r):** Isolated yield = 67%; yellow solid; m.p. 129.7-130.4 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.89 (t, *J* = 7.2 Hz, 3 H), 1.74-1.83 (m, 2 H), 1.95-2.01 (m, 1 H), 2.27-2.32 (m, 1 H), 2.47-2.49 (m, 1 H), 2.63-2.66 (m, 1 H), 3.92-3.98 (m, 2 H), 4.23 (t, *J* = 3.6 Hz, 1 H), 6.99-7.07 (m, 3 H), 7.24-7.26 (m, 1 H), 7.33-7.37 (m, 1 H), 7.69-7.73 (m, 2 H), 8.80 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.6, 19.9, 25.5, 38.5, 47.7, 60.7, 73.2, 114.6 (d, *J* = 21.3 Hz), 117.9, 121.5, 123.8, 123.9, 130.3, 136.2, 136.9 (d, *J* = 6.9 Hz), 152.6, 160.2 (d, *J* = 352.6 Hz), 169.1, 172.4, 195.1; HRMS (ESI) calcd for $C_{22}H_{21}FNO_4$ $[M+H]^+$ 382.1445, found 382.1450.

***trans*-Ethyl 3-chloro-6,11-dioxo-10a-(*p*-tolyl)-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4s):** Isolated yield = 62%; yellow solid; m.p. 209.2-210.7 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.97 (t, *J* = 7.2 Hz, 3 H), 1.72-1.76 (m, 2 H), 1.97-2.03 (m, 1 H), 2.29-2.33 (m, 4 H), 2.44-2.47 (m, 1 H), 2.59-2.63 (m, 1 H), 3.97-4.01 (m, 2 H), 4.26 (t, *J* = 3.6 Hz, 1 H), 7.08-7.17 (m, 4 H), 7.19-7.21 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1 H), 7.60 (d, *J* = 7.8 Hz, 1 H), 8.87 (d, *J* = 1.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.8, 19.9, 20.1, 25.4, 38.3, 47.7, 60.6, 73.9, 118.2, 120.3, 124.4, 124.5, 139.6, 130.6, 137.8, 142.3, 152.9, 169.5, 172.8, 194.6; HRMS (ESI) calcd for $C_{23}H_{23}ClNO_4$ $[M+H]^+$ 412.1316, found 412.1320.

***trans*-Ethyl 3-chloro-10a-(4-chlorophenyl)-6,11-dioxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino [1,2-*a*]indole-10-carboxylate (4t):** Isolated yield = 45%; yellow solid; m.p. 183.8-185.0 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.98 (t, *J* = 7.2 Hz, 3 H), 1.74-1.78 (m, 2 H), 1.90-1.96 (m, 1 H), 2.23-2.28 (m, 1 H), 2.45-2.48 (m, 1 H), 2.62-2.66 (m, 1 H), 3.97-4.01 (m, 2 H), 4.23 (t, *J* = 3.6 Hz, 1 H), 7.19-7.23 (m, 3 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 7.61 (d, *J* = 7.8 Hz, 1 H), 8.86 (d, *J* = 1.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.8, 19.9, 25.4, 38.3, 47.8, 60.8, 73.7, 118.2, 120.0, 124.5, 124.6, 129.1, 132.3, 134.0, 142.7, 152.9, 169.2, 172.5, 194.1; HRMS (ESI) calcd for $C_{22}H_{20}Cl_2NO_4$ $[M+H]^+$ 432.0769, found 432.0774.

***trans*-Ethyl 6,11-dioxo-10a-(thiophen-2-yl)-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*] indole-10-carboxylate (4u):** Isolated yield = 66%; brown solid; m.p. 143.7-144.9 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.89 (t, *J* = 6.6 Hz, 3 H), 1.74-1.78 (m, 2 H), 1.99-2.05 (m, 1 H), 2.42-2.50 (m, 2 H), 2.64-2.68 (m, 1 H), 3.90-3.99 (m, 2 H), 4.18 (t, *J* = 3.6 Hz, 1 H), 6.98-6.99 (dd, J_1 = 4.8 Hz, J_2 = 0.6 Hz, 1 H), 7.08-7.09 (m, 1 H), 7.22-7.24 (m, 1 H), 7.35-7.36 (m, 1 H), 7.67-7.72 (m, 2 H), 8.76 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.6, 19.9, 26.0, 38.6, 48.3, 60.6, 72.3, 117.9, 121.5, 121.7, 123.8, 124.4, 127.1, 135.7, 135.9, 152.4, 169.2, 172.6, 195.0; HRMS (ESI) calcd for $C_{20}H_{20}NO_4S$ $[M+H]^+$ 370.1113, found 370.1117.

***trans*-Ethyl 10a-cyclopropyl-6,11-dioxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*]indole- 10-carboxylate (4v):** Isolated yield = 55%; brown solid; m.p. 139.5-141.2 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.24-0.28 (m, 1 H), 0.50-0.65 (m, 3 H), 0.88 (t, *J* = 6.6 Hz, 3 H), 1.51-1.55 (m,

1 H), 1.69-1.76 (m, 1 H), 1.91-1.94 (m, 1 H), 2.31-2.37 (m, 1 H), 2.51-2.54 (m, 1 H), 2.87-2.90 (m, 1 H), 2.95-3.00 (m, 1 H), 3.60 (t, *J* = 4.2 Hz, 1 H), 3.88-3.92 (m, 2 H), 7.18-7.20 (m, 1 H), 7.61-7.63 (m, 1 H), 7.70 (d, *J* = 7.2 Hz, 1 H), 8.63 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 0.7, 3.7, 13.4, 14.5, 20.9, 26.3, 40.1, 50.1, 61.1, 69.8, 119.2, 123.1, 124.1, 124.2, 136.5, 153.6, 170.5, 172.5, 198.0; HRMS (ESI) calcd for $C_{19}H_{22}NO_4$ $[M+H]^+$ 328.1549, found 328.1555.

***trans*-Ethyl 10a-butyl-6,11-dioxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-*a*]indole-10- carboxylate (4w):** Isolated yield = 45%; red solid; m.p. 177.2-178.4 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.77 (t, *J* = 7.2 Hz, 3 H), 0.83 (t, *J* = 7.2 Hz, 3 H), 0.86-0.89 (m, 1 H), 0.96-1.01 (m, 1 H), 1.17-1.25 (m, 4 H), 1.79-1.93 (m, 3 H), 2.14-2.20 (m, 1 H), 2.31-2.37 (m, 1 H), 2.42-2.46 (m, 1 H), 2.80-2.82 (m, 2 H), 3.42 (t, *J* = 3.6 Hz, 1 H), 3.83-3.87 (m, 2 H), 7.21-7.23 (m, 1 H), 7.63-7.66 (m, 1H), 7.76 (d, *J* = 7.8 Hz, 1 H), 8.66 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 12.6, 12.8, 20.0, 21.9, 23.2, 24.8, 34.7, 38.4, 48.4, 60.3, 70.4, 118.1, 122.1, 123.3, 124.3, 135.9, 153.0, 169.5, 171.7, 200.2; HRMS (ESI) calcd for $C_{20}H_{26}NO_4$ $[M+H]^+$ 344.1862, found 344.1866.

2-(3-Oxo-2-phenylindolin-2-yl)-1*H*-indene-1,3(2*H*)-dione (5a): Isolated yield = 44%; brown solid; m.p. 157.2-158.6 ℃; ^{1}H NMR (DMSO-d_6, 600 MHz): δ = 4.81 (s, 1 H), 6.78-6.81 (m, 1 H), 6.86 (d, *J* = 7.8 Hz, 1 H), 7.32-7.34 (m, 1 H), 7.37-7.39 (m, 2 H), 7.44-7.48 (m, 2 H), 7.52-7.54 (m, 2 H), 7.90-7.92 (m, 1 H), 7.94-7.95 (m, 1 H), 7.98-8.02 (m, 3 H); ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 59.1, 71.3, 112.2, 118.8, 119.0, 123.2, 123.3, 125.0, 126.5, 127.8, 128.6, 136.5, 136.5, 137.1, 137.4, 142.1, 143.4, 161.6, 196.8, 197.6, 198.9; HRMS (ESI) calcd for $C_{23}H_{16}NO3$ $[M+H]^+$ 354.1130, found 354.1134.

2-(2-Butyl-3-oxoindolin-2-yl)-1*H*-indene-1,3(2*H*)-dione (5b): Isolated yield = 40%; red solid; m.p. 163.7-165.1 ℃; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.84 (t, *J* = 6.6 Hz, 3 H), 1.09-1.17 (m, 1 H), 1.23-1.31 (m, 3 H), 2.15-2.28 (m, 2 H), 3.59 (s, 1 H), 4.42 (s, 1 H), 6.73 (d, *J* = 7.8 Hz, 1 H), 6.87-6.89 (m, 1 H), 7.38-7.40 (m, 1 H), 7.70 (d, *J* = 7.8 Hz, 1 H), 7.78-7.82 (m, 2 H), 7.84-7.85 (m, 1 H), 7.94-7.95 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 13.0, 21.9, 23.8, 34.0, 57.1, 68.9, 111.8, 119.2, 121.7, 122.2, 122.5, 123.7, 134.7, 135.0, 136.0, 141.6, 142.2, 159.5, 195.3, 198.1, 200.8; HRMS (ESI) calcd for $C_{21}H_{20}NO_3$ $[M+H]^+$ 334.1443, found 334.1448.

Supporting Information

General information, and NMR are presented in the Supporting Information.

" CCDC for compound **4a**: 1942440 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via*. www.ccdc.cam.ac.uk/data_request/cif."

Acknowledgements

This work was supported by National Natural Science Foundation of China Grants (21302096), Natural Science Foundation of Jiangsu Province-Grants (BK20171449), Qing Lan Project, the National First-class Disciplines (PNFD), China, and the Priority Academic Program Development of Jiangsu Higher Education Insitutions (PAPD), China.

Keywords: indolin-3-ones • insertion reaction • *N*-fused seven-membered • one-pot • Palladium-catalyzed

[1] For selected recent examples, see: a) A. J. Kochanowska-Karamyan, M. T. Hamann, *Chem. Rev*. **2010**, *110*, 4489-4497; b) Y. Yang, Y. Bai, S. Sun, M. Dai, *Org. Lett.* **2014**, *16*, 6216-6219; c) K. Higuchi, S. Suzuki, R. Ueda, N. Oshima, E. Kobayashi, M. Tayu, T. Kawasaki, *Org. Lett.* **2015**, 17, 154-157; d) R. O. Torres-Ochoa, T. Buyck, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2018**, *57*, 5679-5683; e) Y. Liu, H. Wang, *Chem. Commun.* **2019**, *55*, 3544-3547; f) G. Li, C. Piemontesi, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed*. **2019**, *58*, 2870-2874.

[2] For first isolation and characterization of isatisine A, see: J. Liu, Z. Jiang, R. Wang, Y. Zheng, J. Chen, X. Zhang, Y. Ma, *Org. Lett.* **2007**, *9*, 4127-4129; For recent total syntheses of isatisine A**,** see: a) A. Karadeolian, M. A. Kerr, *Angew. Chem., Int. Ed.* **2010**, *49*, 1133-1135; b) P. Patel, C. V. Ramana, *J. Org. Chem.* **2012**, *77*, 10509-10515; c) J. Lee, J. S. Panek, *J. Org. Chem*. **2015**, *80*, 2959-2971; d) M. Xiao, W. Wu, L. Wei, X. Jin, X. Yao, Z. Xie, *Tetrahedron* **2015**, *71*, 3705-3714.

[3] G. Cheng, D. Li, B. Hou, X. Li, L. Liu, Y. Chen, P. Lunga, A. Khan, Y. Liu, Z. Zuo, X. Luo, *J. Nat. Prod*. **2016**, *79*, 2158-2166.

[4] a) A. Rahman; M. Bashir, *Planta Med*. **1983**, *49*, 124; b) A. Rahman, A. Pervin, A. Muzaffar, K. T. D. De Silva, W. S. J. Silva. *Phytochemistry* **1989**, *28*, 3221-3225;

[5] For selected recent examples, see: For selected recent examples, see: a) Y. Zhao, Y. Wang, J. Cao, Y. Liang, P. Xu, *Org. Lett.* **2014**, *16*, 2438-2441; b) D. A. Petrone, A. Yen, N. Zeidan, M. Lautens, *Org. Lett*. **2015**, *17*, 4838-4841; c) B. Prasad, R. Adepu, A. K. Sharma, M. Pal, *Chem. Commun*. **2015**, *51*, 1259-1262; d) K. Higuchi, S. Suzuki, R. Ueda, N. Oshima, E. Kobayashi, M. Tayu, Tomomi Kawasaki, *Org. Lett*. **2015**, *17*, 154-157; e) A. V. Varlamov, N. I. Guranova, R. A. Novikov, V. V. Ilyushenkova, V. N. Khrustalev, N. S. Baleeva, T. N. Borisova, L. G. Voskressensky, *RSC Adv*. **2016**, *6*, 12642-12646; f) R. Liang, K. Wang, L. Song, W. Sheng. Y. Jia, *RSC Adv*. **2019**, *9*, 13959-13967; g) R. Kim, A. J. Ferreira, C. M. Beaudry, *Angew. Chem., Int. Ed*. **2019**, *58*, 12595-12598; h) A. D. Marchese, F. Lind, A. E. Mahon, H. Yoon, M. Lautens, *Angew. Chem., Int. Ed.* **2019**, *58*, 5095-5099.

[6] For selected syntheses of indolin-3-ones from 2-aryl-3*H*-indol-3-ones, see: a) M. Rueping, S. Raja, A. Núñez, *Adv. Synth. Catal.* **2011**, *353*, 563-568; b) C. V. S. Kumar, V. G. Puranik, C. V. Ramana, *Chem. Eur. J.* **2012**, *18*, 9601-9611; c) A. Parra, R. Alfaro, L. Marzo, A. Moreno-Carrasco, J. L.G. Ruano, J. Alemán, *Chem. Commun*. **2012**, *48*, 9759-9761; d) J. Huang, L. Qin, Y. Zhu, Q. Song, L. Dong, *Chem. Commun.* **2015**, *51*, 2844-2847; e) S.i Nakamura, N. Matsuda, M. Ohara, *Chem. Eur. J.* **2016**, *22*, 9478-9482; f) J. Li, Y. Liu, G. Zhang, J. Ma, *Org. Lett.* **2017**, *19*, 6364-6367; g) Y. Liu, X. Mao, X. Lin, G. Chen, *Org. Chem. Front.* **2018**, *5*, 2303-2307; h) J. Li, Y. Liu, S. Li, J. Ma, *Chem. Commun*. **2018**, *54*, 9151-9154; i) J. Xu, S. Hu, Y. Lu, Y. Dong, W. Tang, T. Lu, D. Du, *Adv. Synth. Catal.* **2015**, *357*, 923-927.

[7] X. Yuan, X. Wu, P. Zhang, F. Peng, C. Liu, H. Yang, C. Zhu, H. Fu, *Org. Lett.* **2019**, *21*, 2498-2503.

[8] S. Fang, S. Jin, R. Ma, T. Lu, D. Du, *Org. Lett*. **2019**, *21*, 5211-5214.

[9] S. Preciado, E. Vicente-García, S. Llabrés, F. J. Luque, R. Lavilla, *Angew. Chem., Int. Ed.* **2012**, *51*, 6874-6877.

[10] a) M. Rueping, S. Raja, *Beilstein J. Org. Chem*. **2012**, *8*, 1819-1824; b) S. Llabrés, E. Vicente-García, S. Preciado, C. Guiu, R. Pouplana, R. Lavilla, F. J. Luque, *Chem. Eur. J.* **2013**, *19*, 13355-13361; c) J. Liu, Q. Zhou, J. Deng, Y. Chen, *Org. Biomol. Chem.* **2013**, *11*, 8175-8178.

[11] a) H. Yoshida, M. Watanabe, J. Ohshita, A. Kunai, *Tetrahedron Lett*. **2005**, *46*, 6729-6731; b) T. Zhang, X. Huan, J. Xue, S. Sun, *Tetrahedron Lett*. **2009**, *50*, 1290-1294; c) Y. Liu, Y. Liang, S. Pi, J. Li, *J. Org. Chem*. **2009**, *74*, 5691-5694; d) Y. Tian, L. Tian, X. He, C. Li, X. Jia, J. Li, *Org. Lett*. **2015**, *17*, 4874-4877. e) B. Rao, J. Tang, X. Zeng, *Org. Lett.* **2016**, *18*, 1678-1681; f) A. C. Wright., C. K. Haley, G. Lapointe, B. M. Stoltz, *Org. Lett*. **2016**, *18*, 2793-2795; g) M. Asamdi, K. H. Chikhalia, *Asian J. Org. Chem*. **2017**, *6*, 1331-1348; h) M. M. Ahire, R. Khan, S. B. Mhaske, *Org. Lett.* **2017**, *19*, 2134-2137; i) U. K. Tambar, B. M. Stoltz, *J. Am. Chem. Soc*. **2005**, *127*, 5340-5341; j) Y. Kuninobu, H. Takata, A. Kawata, K. Takai, *Org. Lett.* **2008**, *10*, 3133-3135; k) P. M. Tadross, C. D. Gilmore, P. Bugga, S. C. Virgil, B. M. Stoltz, *Org. Lett.* **2010**, *12*, 1224-1227; l) X. Cheng, Y. Zhou, F. Zhang, K. Zhu, Y. Liu, Y. Li, *Chem. Eur. J*. **2016**, *22*, 1265512659;

[12] a) U. K. Tambar, B. M. Stoltz, *J. Am. Chem. Soc*. **2005**, *127*, 5340-5341; b) H. Yoshida, M. Watanabe, J. Ohshita, A. Kunai, *Chem. Commun.* **2005**, *26*, 3292-3294; c) Y. Kuninobu, A. Kawata, K. Takai, *J. Am. Chem. Soc*. **2006**, *128*, 11368-11369; d) Y. Zhou, X. Tao, Q. Yao, Y. Zhao, Y. Li, *Chem. Eur. J*. **2016**, *22*, 50, 17936-17939; e) Q. Yao, L. Kong, M. Wang, Y. Yuan, R. Sun, Y. Li, *Org. Lett*. **2018**, *20*, 1744-1747.

[13] a) X. Zhang, P. Li, C. Lyu, W. Yong, J. Li, X. Pan, X. Zhu, W. Rao, *Adv. Synth. Catal.* **2017**, *359*, 4147-4152; b) X. Zhang, P. Li, C. Lyu, W. Yong, J. Li, X. Zhu, W. Rao, *Org. Biomol. Chem.* **2017**, *15*, 6080-6083; c) P. Li, W. Yong, R. Sheng, W. Rao, X. Zhu, X. Zhang, *Adv. Synth. Catal.* **2019**, *361*, 201-207.

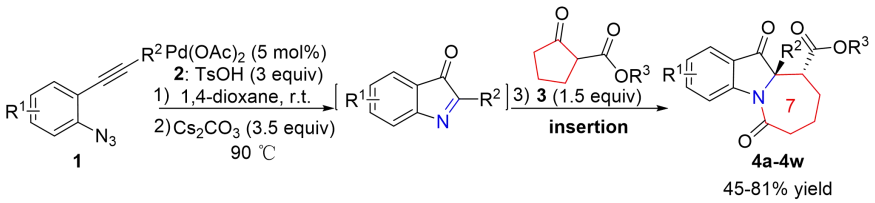
[14] For recent selected examples on the formation of metal carbenes: a) W. Rao, D. Susanti, B. J. Ayers, P. W. H. Chan, *J. Am. Chem. Soc.* **2015**, *137*, 6350-6355; b) W. Rao, M. J. Koh, D. Li, H. Hirao, P. W. H. Chan, *J. Am. Chem. Soc.* **2013**, *135*, 7926-7932; c) Y. Yu, Q. Lu, G. Chen, C. Li, X. Huang, *Angew. Chem. Int. Ed.* **2018**, *57*, 319-323; d) M. Lin, L. Zhu, J. Xia, Y. Yu, J. Chen, Z. Mao, X. Huang, *Adv. Synth. Catal*. **360**, 2280-2284; e) S. S. Giri, R. S. Liu, *Chem. Sci.* **2018**, *9*, 2991-2995; f) Y. Hsu, S. Hsieh, P. Li, R. S. Liu, *Chem. Commun*. **2018**, *54*, 2114-2117. For recent selected examples on the generation of α-imino palladium carbenes, see: a) Q. Zhou, Z. Zhang, Y. Zhou, S. Li, Y. Zhang, J. Wang, *J. Org. Chem.* **2017**, *82*, 48-56; b) H. Ding, S. Bai, P. Lu, Y. Wang, *Org. Lett.* **2017**, *19*, 4604-4607. For recent selected examples on the generation of palladium carbenes, see: a) Z. Shao, H. Zhang, *Chem. Soc. Rev.* **2012**, *41*, 560-572; b) Q. Xiao, Y. Zhang, J. Wang, *Acc. Chem. Res*. **2013**, *46*, 236-247; c) Y. Xia, Y. Zhang, J. Wang, *ACS Catal*. **2013**, *3*, 2586-2598; d) Z. Liu, H. Tan, T. Fu, Y. Xia, D. Qiu, Y. Zhang, J. Wang, *J. Am. Chem. Soc*. **2015**, *137*, 12800-12803.

[15] For the preparation of key intermediate 2-phenyl-3*H*-indol-3-one **G**, see: a) R. Balickia, M. Cybulskia, G. Maciejewskia, *Synth. Commun.* **2003**, *33*, 4137-4141; b)F. Nepveu, S. Kim, J. Boyer, O. Chatriant, H. Ibrahim, K. Reybier, M. C. Monje, S. Chevalley, P. Perio, B. H. Lajoie, J. Bouajila, E. Deharo, M. Sauvain, R. Tahar, L. Basco, A. Pantaleo, F. Turini, P. Arese, A. Valentin, E. Thompson, L. Vivas, S. Petit, J. P. J. Nallet, *Med. Chem.* **2010**, *53*, 699-714; c) R. O. Torres-Ochoa, T. Buyck, Q. Wang, J. Zhu, *Angew. Chem., Int. Ed*. **2018**, *57*, 5679-5683.

[16] For selected examples of sulfonyl group migrations, see: a) R. A. Weatherheadloster, E. J. Corey, *Org. Lett*. **2006**, *8*, 171-174; b) I. Nakamura, U. Yamagishi, D. Song, S. Konta, Y. Yamamoto, *Angew. Chem., Int. Ed.* **2007**, *46*, 2284-2287; c) X. Xin, D. Wang, X. Li, B. Wan, *Angew. Chem., Int. Ed.* **2012**, *51*, 1693-1697; d) B. Prasad, R. Adepu, S. andra, D. Rambabu, G. R. Krishna, C. M. Reddy, G. S. Deora, P. Misra, M. Pal, *Chem. Commun*. **2012**, *48*, 10434-10436; e) X. Xu, M. Taniguchi, A. Azuma, G. Liu, E. Tokunaga, N. Shibata, *Org. Lett*. **2013**, *15*, 686-689; f) W. T. Teo, W. Rao, M. J. Koh, P. W. H. Chan, *J. Org. Chem*. **2013**, *78*, 7508-7517; g) X. Yu, X. Xin, B. Wan, X. Li, *J. Org. Chem.* **2013**, *78*, 4895-4904.

[17] For base-mediated reductive desulfonylation of α-amino sulfons, see:a) A. M. Kanazawa, J. N. Denis, A. E. Greene, *J. Org. Chem*. **1994**, *59*, 1238-1240; b) T. Mecozzi, M. Petrini, *J. Org. Chem.* **1999**, *64*, 8970-8972; c) J. N. Desrosiers, A. Côté, A. A. Boezio, A. B. Charette, *Org. Synth.* **2006**, *83*, 5-17; d) T. Mita, J. Chen, M. Sugawara, Y. Sato, *Angew. Chem., Int. Ed*. **2011**, *50*, 1393-1396.

Entry for the Table of Contents



Heterocycles Synthesis:

A novel insertion reaction of cyclic *C*-acylimines into cyclic *β*-diketones to construct *N*-fused seven-membered multifunctional polycyclic indoline-3-one derivatives has been described, which has shown good tolerance of various functional groups. The corresponding products were obtained in moderate to good yields under mild reaction conditions.