JOC The Journal of Organic Chemistry

Article

TfOH catalyzed one-pot domino reaction for diastereoselective synthesis of poly substituted tetrahydrospiro[carbazole-1,3'-indolines]

Ren-Yin Yang, Jing Sun, Yao Tao, Qiu Sun, and Chao-Guo Yan

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b02397 • Publication Date (Web): 13 Nov 2017

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

TfOH Catalyzed One-pot Domino Reaction for Diastereoselective Synthesis of Polysubstituted Tetrahydrospiro[carbazole-1,3'-indolines]

Ren-Yin Yang, Jing Sun*, Yao Tao, Qiu Sun, Chao-Guo Yan*

College of Chemistry and Chemical Engineering, Yangzhou University, Yangzhou, 225002, China. E-mail: sunjing@yzu.edu.cn; cgyan@yzu.edu.cn

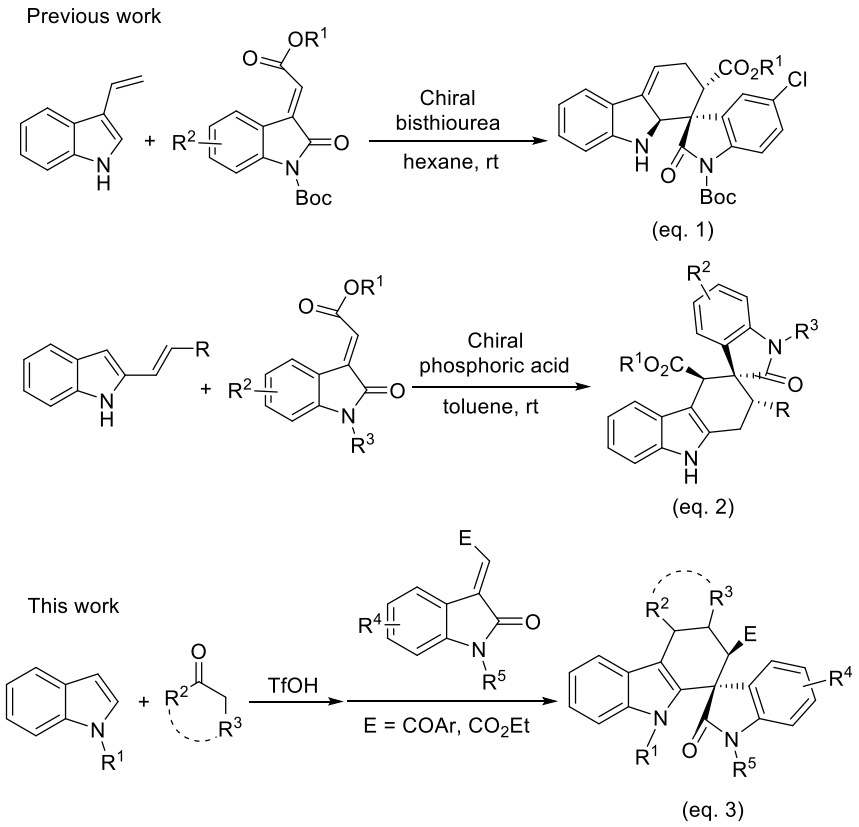
Abstract: TfOH catalyzed one-pot sequential reaction of indoles, acetophenones (cyclic ketones) and various 3-methyleneoxindolines in toluene afforded polysubstituted tetrahydrospiro[carbazole-1,3'-indolines] in satisfactory yields. ^{1}H NMR spectra and single crystal structures indicated that the obtained tetrahydrospiro[carbazole-1,3'-indolines] existing in unusual *trans*-configuration. The reaction mechanism was believed to proceed with domino acid catalyzed 3-alkenylation of indoles with acetophenones, Diels-Alder reaction of 3-alkyenylindoles with 3-methyleneoxindolines and acid catalyzed diastereoisomerization process.

Keywords: carbazole; 3-methyleneoxindoline; spiro[carbazole-1,3'-indoline]; Diels-Alder reaction; isomerization.

Introduction

The tetrahydrocarbazole architecture is a privileged heterocyclic ring system. It not only widely exists in various naturally occurring alkaloids and pharmacologically active compounds,[1] but also is featured in a large family of synthetic analogues exhibiting a wide spectrum of important bioactivities, such as anti-tumor activity, anti-protein kinase C

activity.[2] Additionally, the saturated carbazole derivatives are found potential applications in organic light-emitting diodes and other functional materials.[3] Therefore, many elegant methods for the preparation of various tetrahydrocarbazole derivatives have been developed in the past years,[4-6] Among the many efficient synthetic methodologies for tetrahydrocarbazoles, the [4+2] reaction of 3-vinylindolines or 2-vinylindolines with diverse dienophiles has proven to be the most attractive strategy for the synthesis of many carbazole derivatives.[7-10] Practically, as one of mostly common used dipolarophiles and dienophiles, 3-methyleneoxindolines were also employed in various cycloaddition reaction to construct potential bioactive spiro-carbazole-oxindoline skeleton.[11] Barbas and coworkers successfully developed an C2-symmetric bisthiourea organocatalytic reaction between 3-vinylindolines and methyleneindolinones for the direct construction of spiro-carbazole-oxindoline containing three or four stereocenters (eq. 1 in Scheme 1).[12] Melchiorre and coworkers also established a chiral amine-catalyzed asymmetric reaction of methyleneindolinones with indole-2,3-quinodimethanes generated from α,β-unsaturated aldehydes, which constructed a chiral spiro[tetrahydrocarbazole-3,3'-oxindoline] scaffold in a highly stereoselective fashion.[13] Feng's group also achieved a highly efficient catalytic asymmetric reaction between 3-vinylindoles and methyleneindolinones by using chiral N,N'-dioxide-Ni(II) complexes as the catalysts.[14] Shi and Tu reported chiral phosphoric acid catalyzed asymmetric reactions of 2-vinylindolines with methyleneindolinones to efficiently construct the spiro[tetrahydrocarbazole-3,3'-oxindoline] architecture with one quaternary and three contiguous stereogenic centers in high yields and excellent stereoselectivities (eq.



Scheme 1 Synthetic strategies for spiro-carbazole-oxindolines

2 in Scheme 1).[15] A similar cinchona-derived squaramide catalyzed asymmetric reaction of 2-vinylindoles with methyleneindolinones has also been disclosed.[16] Very recently, a AgOTf

catalyzed alkyne-annulation/Diels–Alder cascade for the construction of tetrahydrospiro[carbazole-4,3'-indoline] derivatives has been established from *N*-tosyl-2-(but-3-en-1-yn-1-yl)aniline with methyleneindolinones.[17] Against this background and in continuation of our aim to develop multicomponent reaction for construction of diverse spirooxindoline systems,[18] herein we wish to present TfOH catalyzed one-pot domino reaction of indoles, acetophenones (cyclic ketones) and various 3-methyleneoxindolines for the efficient synthesis of tetrahydrospiro[carbazole-1,3'-indolines] in good yields and with unexpected diastereoselectivity. The reaction process involved domino acid catalyzed 3-alkenylation of

indoles with acetophenones, Diels-Alder reaction of 3-alkyenylindoles with 3-methyleneoxindoles and acid mediated diastereoisomerization process.

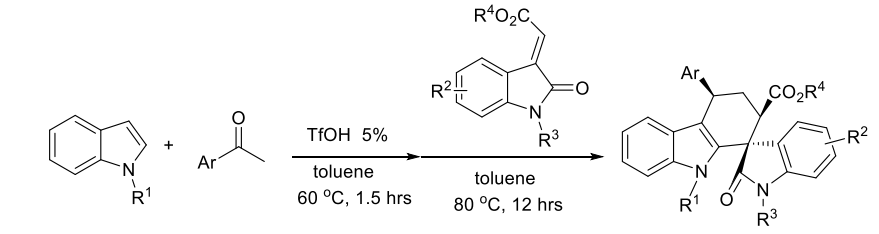
Results and Discussions

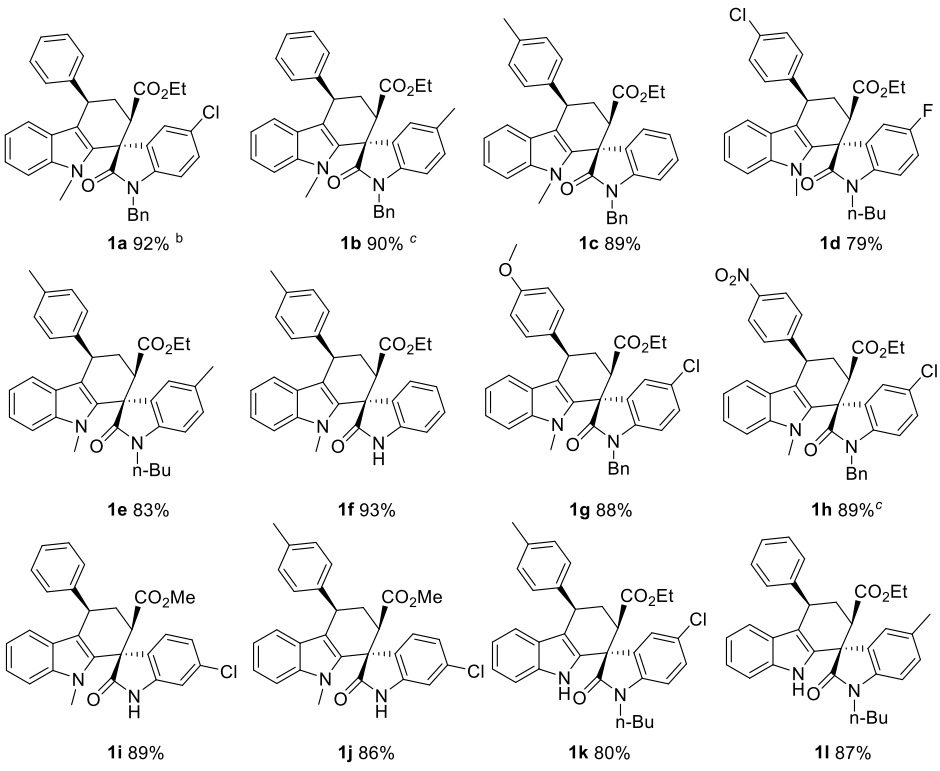
Initially, the reaction conditions were examined by using 1-methylindole, acetophenone and ethyl (*E*)-2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)acetate as standard.[9e] When the three-component reaction was carried out in the presence of TsOH and TfOH, 1-methylindole quickly added to 3-methyleneoxindoline to give the known Michael addition product in high yield.[19] In order to prevent the formation of this Michael addition product, 1-methylindole firstly reacted with acetophenone in toluene in the presence of TfOH. After TLC monitoring indicated that 1-methylindole has been completely consumed, ethyl (*E*)-2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)acetate was introduced in the reaction mixture. After workup, the expected tetrahydrospiro[carbazole-1,3'-indoline] **1a** was successfully obtained in moderate yield. Then, the amount of acid catalyst, molar ratio of the three substrates, reaction temperature, and reaction time of the one-pot two-step reaction procedure were carefully screened. At last, we were pleased to find the product **1a** can be obtained in 92% yield by carrying out the first-step reaction of 1-methylindole (0.5 mmol) and acetophenone (1.5 mmol) with TfOH (5 mol %) at 60 ^{o}C for half an hour, and the second-step reaction with ethyl (*E*)-2-(2-oxoindolin-3-ylidene)acetate (0.5 mmol) without further adding TfOH at 80 ^{o}C for twelve hours.

With the optimal reaction conditions in hand, we proceeded to explore the substrate scope of the reaction. Various ethyl or methyl (*E*)-2-(2-oxoindolin-3-ylidene)acetates and substituted acetophenones were employed in the one-pot two-step reaction. We were

pleased to find that the reaction proceeded smoothly to give the expected functionalized tetrahydrospiro[carbazole-1,3'-indolines] **1a-1j** in high yields. The results are summarized

Table 1. Synthesis of tetrahydrospiro[carbazole-1,3'-indolines] **1a**-**1l** via domino reaction [a]





[a] Reaction conditions: indole (0.5 mmol), acetophenone (1.5 mmol), TfOH (5 mol%), toluene (2.0 mL), 60 °C, 1.5 hrs; 3-methyleneoxindoline (0.5 mmol), 80 °C, 12 hrs; [b]Isolated yields. [c] TfOH (10 mol%) was used.

in Table 1. The substituted acetophenones with both electron-donating group and electron-withdrawing groups can be successfully employed in the reaction. The oxindoline scaffold with various substituents have marginal effect on the products. Besides 1-methylindole, indole itself also resulted in the products **1k** and **1l** in good yields. The structures of the obtained products **1a-1l** were established by the various spectroscopy.

Because there are three chiral carbon atoms in the newly-formed cyclohexenyl ring, several diastereoisomers might be formed in the reaction. ^{1}H and ^{13}C NMR spectra clearly indicated that there is only one diastereoisomer in the obtained products. The single crystal structures of the compounds **1a (Fig. 1)**, **1f** and **1k** (Fig. s1-s2) were determined by X-ray diffraction method. It was pleased to find that they have same relative configuration, in which the aryl group, ethoxycarboxyl group exist in *cis*-position and the phenyl group of the oxindoline moiety stands at *trans*-configuration. It should be pointed out that the ethoxycarbonyl group and the phenyl group of the oxindoline moiety usually exist at *cis*-position in the starting ethyl (*E*)-2-(2-oxoindolin-3-ylidene)acetates.[19] Thus, the formation of a *trans*-configuration for these two groups in the obtained tetrahydrospiro[carbazole-1,3'-indolines] **1a-1l** suggested that the reaction contained a more complicated cyclization process rather than the expected concerted Diels-Alder reaction, which would afford the tetrahydrospiro[carbazole-1,3'-indolines] **1a-1l** with *cis*-configuration.[20]

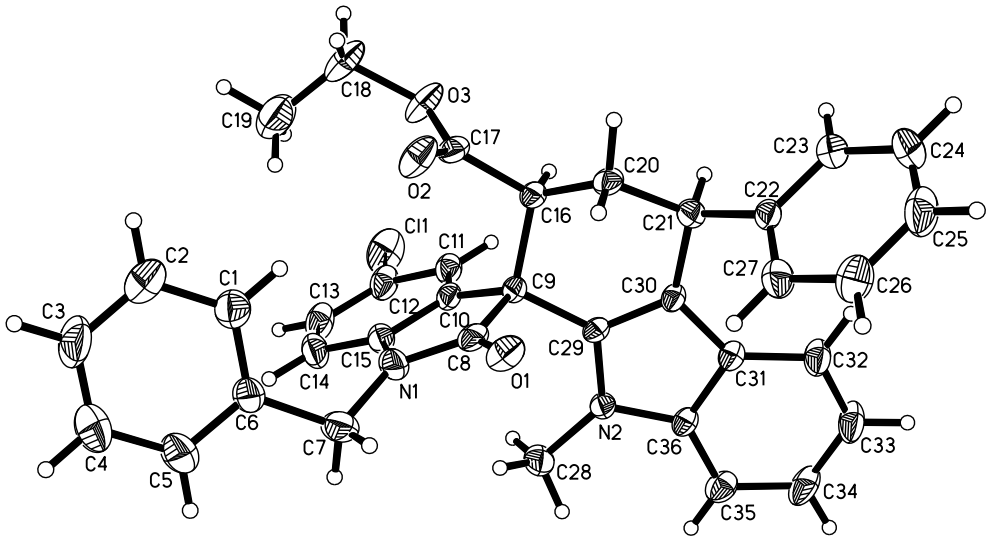
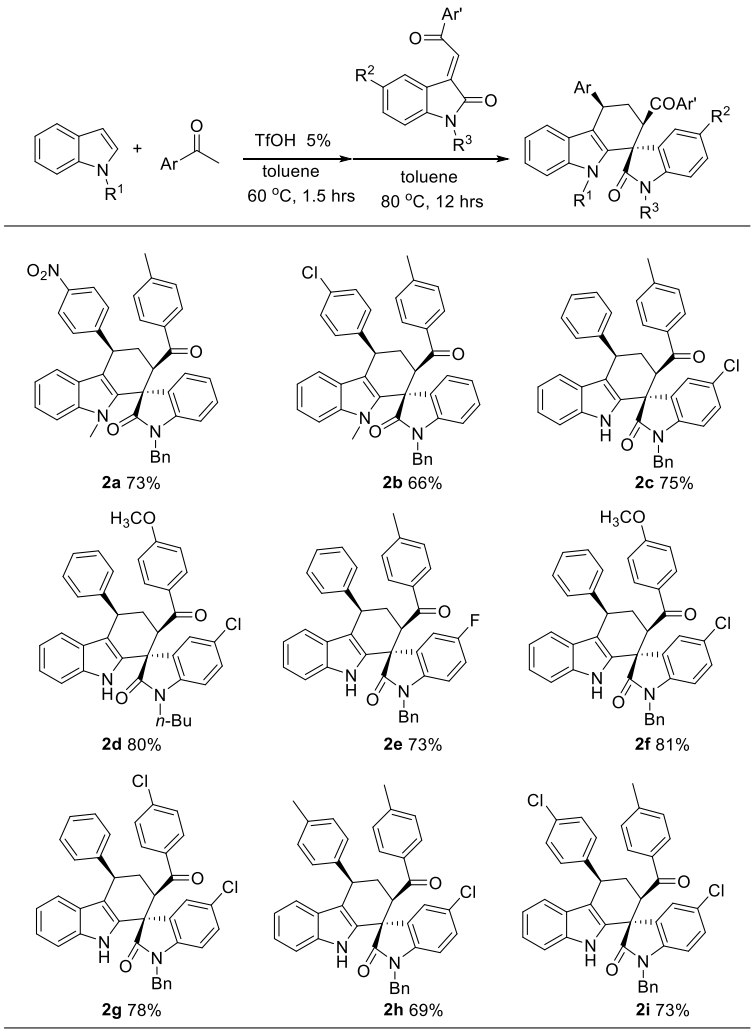


Fig. 1 ORTEP-drawing (30%) of the crystal structure of **1a**

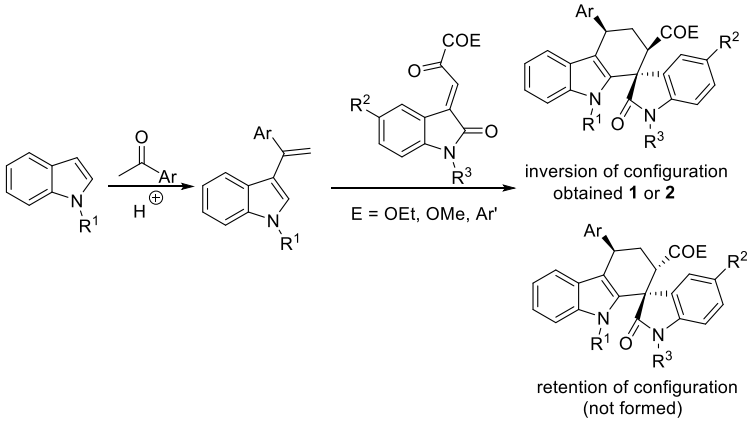
With the success in the reactions of ethyl (E)-2-(2-oxoindolin-3-ylidene)acetates, we turned our attention to another commonly used 3-methyleneoxindolines. Various 3-phenacylideneoxindolines were employed in the one-pot two-step reaction. The results are summarized in Table 2. Acetophenones with both electron-donating *p*-methyl group and electron-withdrawing *p*-chloro, *p*-nitro groups reacted smoothly to give the corresponding products **2a-2i** in good yields. It should be pointed out that indoles both with *N*-methyl group and without *N*-methyl group reacted well to afford the expected products. These results showed that this reaction has a wide variety of substrate scope. Besides characterizing the obtained products **2a-2i** with IR, HRMS, ^{1}H and ^{13}C spectroscopy, the structure of compounds **2a**, **2c** and **2d** were unambiguously confirmed by single crystal X-ray diffraction analysis. From the single crystal structure of **2a**, **2c** and **2d** (Fig. s3-s5), we have found that they have same relative configuration to that of the above obtained products **1a**, **1f** and **1k**, which indicated that the reaction has same

outcome of stereochemistry. It has been known that the phenacyl group or ethoxycarbonyl group usually exists at *cis*-position to the phenyl group of the oxindoline moiety in the starting 3-phenacylideneoxindoline or ethyl (*E*)-2-(2-oxoindolin-3-ylidene)acetates.[20] The previously reported [4+2] reactions of 2-vinyl and 3-vinylindolines with various 3-methyleneoxindolines also gave the spiro compounds with phenacyl group or ethoxycarbonyl group existing at *cis*-position to the phenyl group of the oxindoline.[12-17] If the *in situ* generated 3-alkenylindoles reacted with these two kinds of 3-methyleneoxindolines according to concerted Diels-Alder reaction process, the obtained tetrahydrospiro[carbazole-1,3'-indolines] **1** and **2** would have the *cis*-configuration for the phenacyl group or ethoxycarbonyl group to the phenyl group of the oxindoline (Scheme 2). Our obtained results clearly indicated that tetrahydrospiro[carbazole-1,3'-indolines] **1** and **2** have the *trans*-configuration for the phenacyl (ethoxycarbonyl) group and the phenyl group of the oxindoline. Thus, an unusual inversion of configuration was observed in the above reactions. A literature survey showed that some Lewis acid catalyzed [4+2] reactions of 2-alkenyl and 3-alkenylindoles with activated dienophiles might proceed with pure Diels–Alder mechanism or by asynchronous or stepwise mechanisms.[21] Herein, our experiments provided a new example of unusual cycloaddition reaction of 3-alkenylindolines with the cyclic dienophiles.

Table 2. Synthesis of tetrahydrospiro[carbazole-1,3'-indolines] **2a**-**2i** via domino reaction [a]



[a]Reaction conditions: indole (0.5 mmol), acetophenone (1.5 mmol), TfOH (5 mol%), toluene (2.0 mL), 60 °C, 1.5 hrs; 3-methyleneoxindoline (0.5 mmol), 80 °C, 12 hrs; [b]Isolated yields.

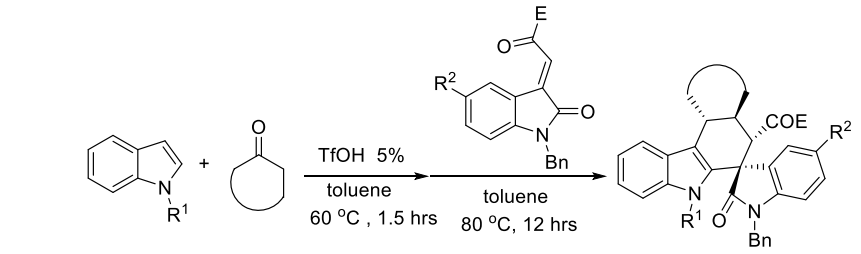


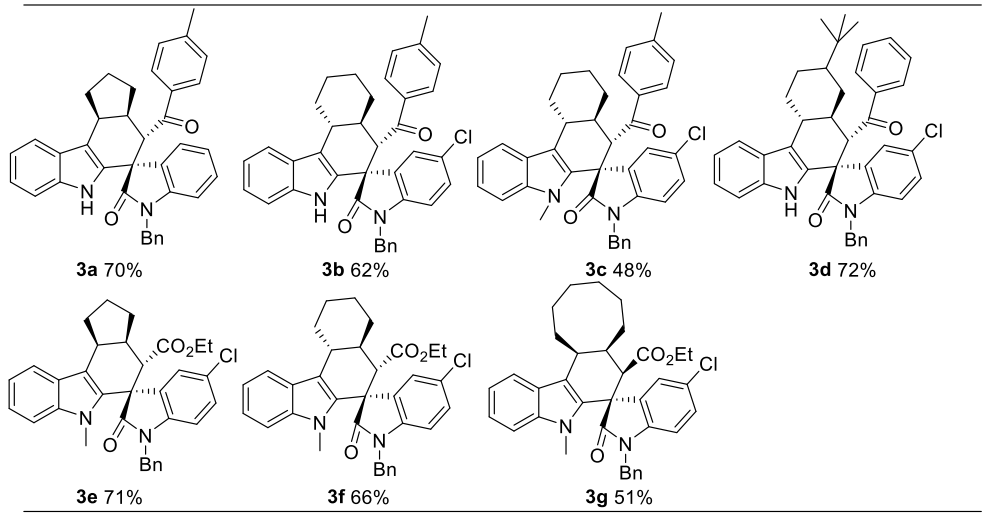
Scheme 2 stereochemistry of the domino reaction

For elucidating the stereochemistry of the reaction, various cyclic ketones were also employed in this one-pot two-step reaction procedure. The results are summarized in Table

3. Cyclopentanone, cyclohexanone, 4-*tert*-butylcyclohexane and cyclooctanone reacted smoothly to give the expected carbocyclic fused tetrahydrospiro[carbazole-1,3'-indolines] **3a-3g** in moderate to good yields. These results also showed that this reaction has a wide variety of substrate scope. The structures of the spiro compounds **3a-3g** were fully characterized by the spectroscopy. The single crystal structures of the compound **3c** (Fig. 2), **3e** (Fig. s6) and **3g** (Fig. s7) were also determined by X-ray diffraction method. They showed different configurations. From Fig. 2, it can be seen that the fused cyclohexyl ring has a *trans*-configuration and the benzoyl group and phenyl group of the oxindoline moiety exist on *cis*-position, which was different to that of the above spiro compounds **1** and **2**. In the single crystal structure of the compound **3e**, the fused cyclopentyl ring exists in *cis*-configuration. The benzoyl group and phenyl group of the oxindoline moiety also exist on *cis*-position. On the other hand, in the single crystal structure of the compound **3g** (Fig. s7), the fused cyclooctyl ring has a *cis*-configuration, while the ester group existing to the *trans*-position of phenyl group of the oxindoline moiety. It might be duo to the steric effect of the fused carbocyclic ring in the molecules, the most thermodynamically stable diastereoisomer would be predominately produced in the domino process. The unusual stereochemistry for the above obtained tetrahydrospiro[carbazole-1,3'-indolines] and the corresponding cyclic fused derivatives ambiguously showed that an acid catalyzed diastereoisomerization process was involved in the reaction.

Table 3 Synthesis of tetrahydrospiro[carbazole-1,3'-indolines] 3a-3g[a]





3a 70% **3b** 62% **3c** 48% **3d** 72%

3e 71% **3f** 66% **3g** 51%

a. Reaction conditions: indole (0.5 mmol), cyclic ketone (1.5 mmol), TfOH (5% mol), toluene (2.0 mL), 60°C, 1.5 hrs; 3-methyleneoxindoline (0.5 mmol), 80°C, 12 hrs; b. Isolated yields.

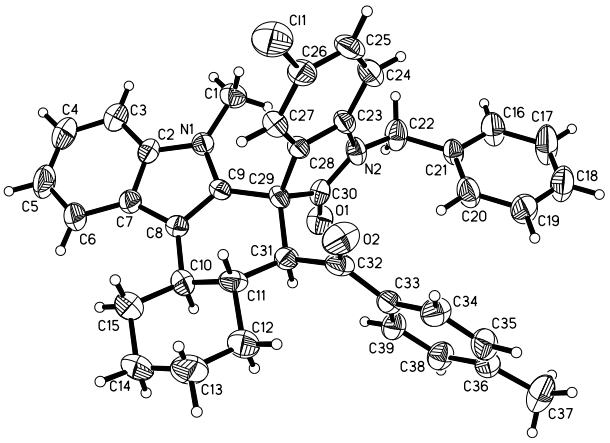
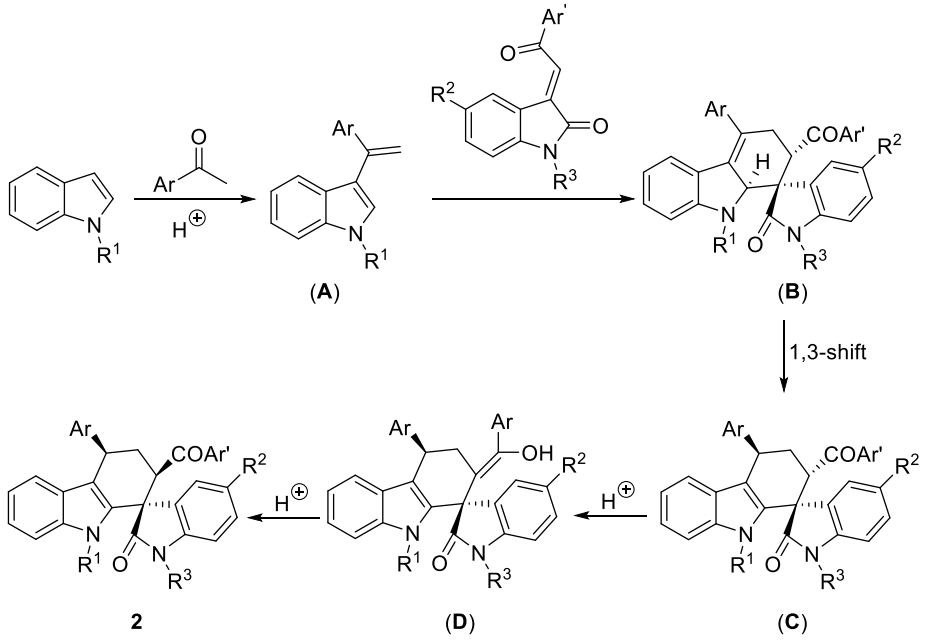


Fig. 2 ORTEP-drawing (30%) of the crystal structure of **3c**

On the basis of above results and the previously reported reactions,[7,21-23] a plausible domino reaction mechanism was relationally proposed in Scheme 3 by using 3-phenacylideneoxindoline as the substrate. At first, a 3-alkenylindole (**A**) was generated by the Friedel-Crafts reaction of indole and acetophenone with dehydration in the presence

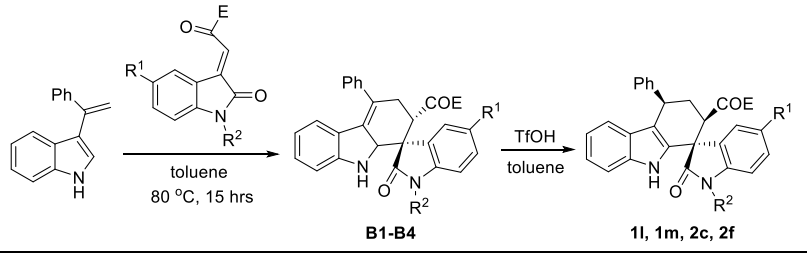
of triflic acid. Secondly, A Diels-Alder reaction of 3-alkenylindole (**A**) with 3-phenacylideneoxindolines directly afforded a 2,3,9,9*a*-tetrahydrocarbazole intermediate (**B**),[22] in which the benzoyl group and the phenyl group of oxindoline remained in *cis*-configuration. Thirdly, The intermediate (**B**) in turn converted to 2,3,4,9-tetrahydrocarbazole intermediate (**C**) by 1,3-H shift process. In the intermediate (B) and (C), the benzoyl group and phenyl group of oxindoline scaffold retained in the *cis*-configuration. Then, the final separated spiro compound **2** was formed by HOTf catalyzed keto-enol tautomerism through the intermediate (**D**), in which the configuration of benzoyl group was inverted to the *trans*-position of the phenyl group of oxindoline scaffold. In both 1,3-H shift and keto-enol tautomerism process, the configuration of the substituents can be changed. It might be due to the larger steric effect of the substituents in the newly-formed cyclohexenyl ring, the most thermodynamically stable *trans*-diastereoisomer was predominately formed in the acid-catalyzed heating reaction conditions.



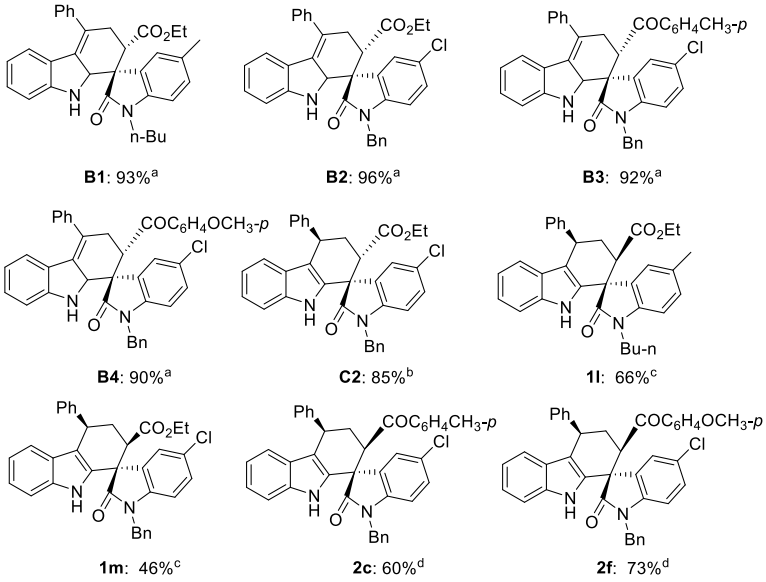
Scheme 3 Plausible reaction mechanism for domino three-component reaction

In order to shed more light on the proposed reaction mechanism, further control experiments were carried out. The Diels-Alder reaction of 3-methyleneoxindolines with 3-(1-phenylvinyl)indole, which was previously prepared from the reaction of 3-acetylindole with phenylmagnesium bromide according to the published method,[24] actually resulted in the intermediates (**B1**)-(**B4**) in very high yields (Table 4). The molecular structures (**B1**)-(**B4**) were established on the spectroscopy and determination of the single crystal structures of (**B2**) (Fig. s8) and (**B3**) (Fig. 3), in which the ethoxycarbonyl group or benzoyl group actually existing to the *cis*-position of the phenyl group of oxindoline scaffold. An *exo*-cyclic C=C double bond of the dihydroindoline was also observed in the molecule. When intermediates (**B3**) and (**B4**) were stirred in toluene in the presence of TfOH at room

Table 4. Acid catalyzed isomerization of tetrahydrospiro[carbazole-1,3'-indolines][a-d]



B1-B4 **1l, 1m, 2c, 2f**



B1: 93%[a] **B2**: 96%[a] **B3**: 92%[a]

B4: 90%[a] **C2**: 85%[b] **1l**: 66%[c]

1m: 46%[c] **2c**: 60%[d] **2f**: 73%[d]

[a] Reaction conditions: 3-(1-phenylvinyl)indole (0.5 mmol), 3-methyleneoxindoline (0.5 mmol), toluene (2.0 mL), 80 °C, 15 hrs; [b] TfOH (5 mol %), toluene (2.0 mL), rt, 5 hrs; [c] TfOH (5 mol%), toluene (2.0 mL), 50 °C 30 hrs; [d] TfOH (5 mol %), toluene (2.0 mL), rt, 5 hrs; [d] Isolated yields.

temperature for five hours, they completely converted to the above prepared spiro compounds **2c** and **2f** in good yields. If the product **B2** was were stirred in toluene in the presence of TfOH at room temperature for five hours, the intermediate **C2** was obtained in 96% yield, which was clearly formed by the 1,3-H shift, and the sequential diastereoisomerization of ethoxycarbonyl group has no finished. The single crystal structure of the intermediate **C2** was successfully determined by X-Ray diffraction method (Fig. s9). On the other hand, the products **B1** and **B2** in toluene in the presences of TfOH was heated to 50 °C for longer time, the expected isomerized products **1l** and **1m** could be formed in moderate yields. The single crystal structure of the compound **1m** (Fig. s10) also

showed that the ethoxycarbonyl group exists on the *trans*-position of phenyl group of the oxindoline scaffold. These experiments clearly indicated that the initially formed *cis*-isomer of tetrahydrospiro[carbazole-1,3'-indolines] actually isomerized to the more sable *trans*-isomer in acidic solution. Thus, only the *trans*-isomers were successfully synthesized in our acid catalyzed one-pot two-step reactions. These experiments not only provided stronger evidence to our proposed reaction mechanism, but also developed an efficient method for diastereoselective synthesis of the polysubstituted tetrahydrospiro[carbazole-1,3'-indolines].

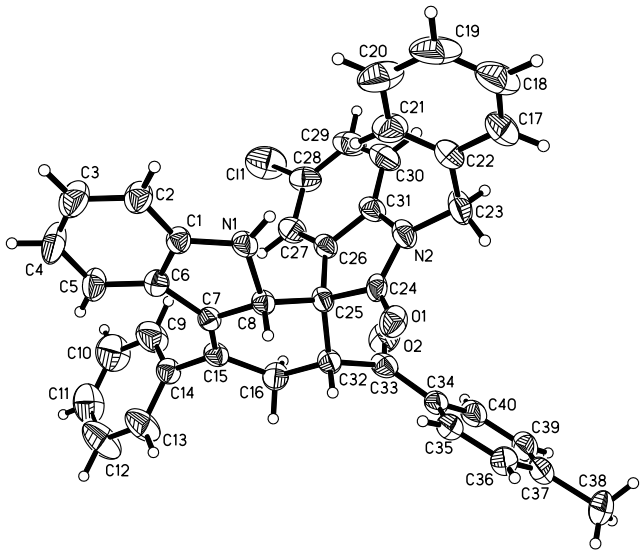


Fig. 3 ORTEP-drawing (30%) of the crystal structure of **B3**

Conclusion

In summary, we have successfully developed an acid catalyzed domino reaction of indole, acetophenones and 3-methyleneoxindolines for selective synthesis of biologically important carbazole derivatives. Importantly, the one-pot two-step reaction protocol afforded the functionalized tetrahydrospiro[carbazole-1,3'-indolines] with high

diastereoselectivity Furthermore, the unusual *trans*-configuration of the obtained tetrahydrospiro[carbazole-1,3'-indolines] clearly revealed a domino alkenylation/Diels-Alder reaction/isomerization process. Additionally, the advantages of this domino reaction included, readily available starting materials, simple reaction conditions, broad scope of substrates, satisfactory yields and high diastereoselectivity, which would be found potential applications in synthetic and medicinal chemistry.

Experimental section

Experimental section

1. General procedure for the synthesis of tetrahydrospiro[carbazole-1,3'-indoline] derivatives 1a-1l: In the nitrogen atmosphere, to a 10 mL Schlenk tube was added indole (0.5 mmol), substituted acetophenone (1.5 mmol), and TfOH (5% mol) and toluene (2.0 mL). The mixture was heated at 60^{o}C for 1.5 hours. Then, ethyl (*E*)-2-(2-oxoindolin-3-ylidene)acetate (0.5 mmol) was added. The solution was heated at 80^{o}C for about 12 hours. The solvent was removed at reduced pressure by rotator evaporation, the residue was subjected to preparative column chromatography with a mixture of light petroleum and ethyl acetate (V/V = 5:1) as eluent to give the pure product for analysis.

Ethyl

1'-benzyl-5'-chloro-9-methyl-2'-oxo-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1a): white solid, 92%, 0.264 g, m.p. 224-226℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.49-7.44 (m, 4H), 7.37-7.30 (m, 5H), 7.25-7.23 (m, 2H), 7.10-7.08 (m, 3H), 6.83-6.80 (m, 2H), 6.70 (d, J = 8.0 Hz, 1H), 5.23 (d, J = 15.2 Hz, 1H), 4.77 (d, J = 15.6 Hz, 1H), 4.41 (dd, J_1 = 11.6 Hz, J_2 = 5.6 Hz, 1H), 3.97-3.84 (m, 2H), 3.45 (d, J = 12.8 Hz, 1H), 3.18-3.08 (m, 1H), 2.83 (s,

3H), 2.44 (dd, J_1 = 13.2 Hz, J_2 = 5.6 Hz, 1H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.2, 171.2, 144.8, 142.7, 138.0, 135.7, 132.8, 131.9, 129.0, 128.8, 128.5, 128.4, 128.3, 128.2, 128.0, 126.6, 125.5, 124.0, 122.1, 120.3, 119.1, 116.5, 110.1, 108.7, 60.9, 52.8, 49.8, 45.0, 41.5, 33.1, 29.9, 13.9; IR (KBr) υ: 1720 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{36}H_{32}ClN_2O_3$ ($[M+H]^+$): 575.2101. Found: 575.2107.

Ethyl

1'-benzyl-5',9-dimethyl-2'-oxo-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1b): white solid, 90%, 0.100 g, m.p. 248-250℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, J = 6.4 Hz, 2H), 7.37-7.33 (m, 7H), 7.25 (brs, 1H), 7.17 (d, J = 8.0 Hz, 1H), 7.08-7.04 (m, 1H), 7.00-6.97 (m, 2H), 6.90 (d, J = 7.6 Hz, 1H), 6.69-6.65 (m, 1H), 6.56 (d, J = 7.6 Hz, 1H), 5.23 (d, J = 15.2 Hz, 1H), 4.82 (d, J = 14.8 Hz, 1H), 4.45-4.43 (m, 1H), 3.65-3.55 (m, 3H), 3.41 (s, 3H), 2.95-2.87 (m, 1H), 2.49 (d, J = 13.6 Hz, 1H), 2.15 (s, 3H), 0.67 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.3, 170.7, 140.5, 139.7, 136.4, 136.2, 135.2, 131.0, 130.4, 128.0, 127.8, 127.6, 127.6, 127.5, 126.8, 125.9, 124.4, 123.4, 120.5, 118.3, 117.6, 107.8, 107.2, 59.3, 49.9, 44.0, 42.4, 36.6, 31.0, 28.2, 20.0, 12.5; IR (KBr) υ: 1719 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{37}H_{35}N_2O_3$ ($[M+H]^+$): 555.2648. Found: 555.2643.

Ethyl

1'-benzyl-9-methyl-2'-oxo-4-(*p*-tolyl)-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1c): white solid, 89%, 0.247 g, m.p. 232-234℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 (d, J = 7.2 Hz, 2H), 7.36-7.33 (m, 4H), 7.31-7.26 (m, 2H), 7.14-7.10 (m, 3H), 7.06-7.01 (m, 3H), 6.90 (d, J = 8.0 Hz, 1H), 6.82-6.79 (m, 1H), 6.74 (d, J = 8.0 Hz, 1H), 5.24 (d, J = 15.2 Hz, 1H), 4.79 (d, J = 15.6 Hz, 1H), 4.38 (dd, J_1 = 11.6 Hz, J_2 = 5.6 Hz, 1H), 3.92-3.82 (m, 2H), 3.48 (d, J = 12.8 Hz,

1H), 3.19-3.10 (m, 1H), 2.79 (s, 3H), 2.40-2.35 (m, 4H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.6, 171.4, 144.0, 142.0, 137.9, 136.2, 135.9, 132.5, 130.9, 129.2, 129.0, 128.7, 128.3, 128.2, 127.8, 125.6, 123.6, 122.9, 121.8, 120.3, 118.9, 116.3, 109.2, 108.6, 60.6, 53.0, 49.7, 44.8, 41.2, 33.2, 29.8, 21.2, 13.8; IR (KBr) υ: 1722 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{37}H_{35}N_2O_3$ ($[M+H]^+$): 555.2648. Found: 555.2675.

Ethyl 1'-butyl-4-(4-chlorophenyl)-5'-fluoro-9-methyl-2'-oxo-2,3,4,9-tetrahydrospiro [carbazole-1,3'-indoline]-2-carboxylate (1d): white solid, 79%, 0.220 g, m.p. 239-241℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37 (d, J = 7.6 Hz, 2H), 7.27 (d, J = 7.6 Hz, 2H), 7.11-7.06 (m, 3H), 6.90-6.86 (m, 2H), 6.84-6.82 (m, 1H), 6.70 (d, J = 8.0 Hz, 1H), 4.38 (dd, J_1 = 11.2 Hz, J_2 = 5.6 Hz, 1H), 3.93-3.83 (m, 3H), 3.76-3.71 (m, 1H), 3.39 (d, J = 12.8 Hz, 1H), 3.10-3.00 (m, 1H), 2.96 (s, 3H), 2.36 (dd, J_1 = 13.6 Hz, J_2 = 5.6 Hz, 1H), 1.79-1.70 (m, 2H), 1.52-1.43 (m, 2H), 1.03-0.98 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.9, 170.9, 159.2 (d, J = 240.8 Hz), 143.6, 140.3, 140.2, 138.0, 132.6 (d, J = 7.6 Hz), 132.2, 132.1, 129.7, 128.6, 125.3, 122.1, 120.1, 119.1, 115.7, 115.5 (d, J = 23.2 Hz), 111.8 (d, J = 24.7 Hz), 109.0, 108.9, 108.8, 60.8, 52.6, 49.9, 40.7, 40.6, 32.8, 29.7, 29.3, 20.5, 13.9, 13.8; IR (KBr) υ: 1724 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{33}H_{33}ClFN_2O_3$ ($[M+H]^+$): 559.2164. Found: 559.2186.

Ethyl 1'-butyl-5',9-dimethyl-2'-oxo-4-(*p*-tolyl)-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1e): white solid, 83%, 0.222 g, m.p. 228-230℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32 (d, J = 7.2 Hz, 2H), 7.15-7.00 (m, 3H), 7.07-7.04 (m, 2H), 6.94 (s, 1H), 6.83-6.78 (m, 2H), 6.73 (d, J = 8.0 Hz, 1H), 4.35 (dd, J_1 = 11.2 Hz, J_2 = 5.6 Hz, 1H), 3.94-3.83 (m, 3H), 3.75-3.67 (m, 1H), 3.43 (d, J = 12.8 Hz, 1H), 3.14-3.04 (m, 1H), 2.92 (s, 3H), 2.37-2.34 (m, 4H), 2.29 (s, 3H),

1.79-1.71 (m, 2H), 1.52-1.43 (m, 2H), 1.01-0.97 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.3, 171.3, 142.0, 141.8, 137.9, 135.9, 132.8, 132.2, 131.0, 129.3, 129.1, 128.3, 125.6, 124.4, 121.7, 120.3, 118.8, 116.2, 108.5, 108.1, 60.5, 52.9, 49.7, 41.2, 40.5, 33.2, 29.6, 29.4, 21.2, 21.1, 20.5, 13.9, 13.8; IR (KBr) υ: 1724 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{35}H_{39}N_2O_3$ ($[M+H]^+$): 535.2961. Found: 535.2979.

Ethyl 9-methyl-2'-oxo-4-(*p*-tolyl)-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1f): white solid, 93%, 0.216 g, m.p. 219-221℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.47 (s, 1H), 7.33 (d, *J* = 7.2 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 2H), 7.10-7.02 (m, 4H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.83-6.80 (m, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 4.37 (dd, J_1 = 10.8 Hz, J_2 = 5.2 Hz, 1H), 3.97-3.88 (m, 2H), 3.47 (d, *J* = 13.2 Hz, 1H), 3.12-3.00 (m, 4H), 2.40-2.36 (m, 4H), 1.00 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.8, 171.5, 141.9, 141.8, 138.0, 135.9, 132.4, 131.4, 129.1, 129.1, 128.2, 125.5, 123.7, 122.8, 121.7, 120.3, 118.8, 116.1, 110.2, 108.7, 60.8, 53.0, 50.2, 41.1, 33.2, 29.6, 21.2, 13.7; IR (KBr) υ: 1728 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{30}H_{29}N_2O_3$ ($[M+H]^+$): 465.2178. Found: 465.2197.

Ethyl 1'-benzyl-5'-chloro-4-(4-methoxyphenyl)-9-methyl-2'-oxo-2,3,4,9-tetrahydrospiro [carbazole-1,3'-indoline]-2-carboxylate (1g): white solid, 88%, 0.266 g, m.p. 207-209℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47 (d, *J* = 7.2 Hz, 2H), 7.37-7.28 (m, 5H), 7.24 d, *J* = 8.0 Hz, 1H), 7.11-7.08 (m, 3H), 6.86 (d, *J* = 6.8 Hz, 2H), 6.84-6.80 (m, 2H), 6.75 (d, *J* = 7.6 Hz, 1H), 5.23 (d, *J* = 15.2 Hz, 1H), 4.77 (d, *J* = 14.8 Hz, 1H), 4.36 (dd, J_1 = 11.6 Hz, J_2 = 5.6 Hz, 1H), 3.98-3.83 (m, 2H), 3.81 (s, 3H), 3.44 (d, *J* = 12.8 Hz, 1H), 3.14-3.05 (m, 1H), 2.82 (s, 3H), 2.43-2.38 (m, 1H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.2, 171.2, 158.2, 142.6, 138.0, 137.0,

135.7, 132.8, 131.7, 129.3, 129.0, 128.8, 128.3, 128.2, 128.0, 125.5, 124.0, 122.0, 120.4, 119.0, 116.8, 113.8, 110.1, 108.7, 60.8, 55.2, 52.9, 49.8, 44.9, 40.7, 33.2, 29.9, 13.9; IR (KBr) υ: 1726 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{37}H_{34}ClN_2O_4$ ($[M+H]^+$): 605.2207. Found: 605.2222.

Ethyl 1'-benzyl-5'-chloro-9-methyl-4-(4-nitrophenyl)-2'-oxo-2,3,4,9-tetrahydrospiro [carbazole-1,3'-indoline]-2-carboxylate (1h): yellow solid, 89%, 0.276 g, m.p. 190-192℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.18 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.38-7.26 (m, 4H), 7.15-7.12 (m, 3H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.63 (d, *J* = 7.6 Hz, 1H), 5.11 (d, *J* = 15.2 Hz, 1H), 4.79 (d, *J* = 15.2 Hz, 1H), 4.58-4.54 (m, 1H), 3.96-3.86 (m, 2H), 3.47 (d, *J* = 12.0 Hz, 1H), 3.15-3.06 (m, 1H), 2.86 (m, 3H), 2.45 (dd, J_1 = 13.2 Hz, J_2 = 4.4 Hz, 1H), 1.00 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.0, 170.7, 152.9, 146.9, 142.6, 138.1, 135.5, 132.4, 132.3, 129.3, 129.2, 128.9, 128.5, 128.1, 128.1, 124.9, 124.0, 123.9, 122.4, 119.6, 119.5, 114.7, 110.3, 109.1, 61.0, 52.4, 49.7, 45.0, 41.1, 32.5, 30.0, 13.8; IR (KBr) υ: 1725(C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{36}H_{31}ClN_3O_5$ ($[M+H]^+$): 620.1952. Found: 620.1950.

Methyl 6'-chloro-9-methyl-2'-oxo-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1i): white solid, 89%, 0.209 g, m.p. 278-280℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.97 (s, 1H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.28 (d, *J* = 6.8 Hz, 1H), 7.13-7.07 (m, 2H), 7.04-6.99 (m, 3H), 6.81 (t, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 4.40 (dd, J_1 = 11.2 Hz, J_2 = 5.6 Hz, 1H), 3.52-3.47 (m, 4H), 3.12-3.03 (m, 4H), 2.46-2.41 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.0, 172.0, 144.7, 143.1, 138.1, 134.8, 131.8, 129.8, 128.5, 128.4, 126.7, 125.4, 124.5, 122.9, 122.1, 120.3, 119.0, 116.2, 111.1, 108.8, 52.8, 52.2, 49.9, 41.5, 33.3, 29.8; IR (KBr) υ:

1739 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{28}H_{24}ClN_2O_3$ ($[M+H]^+$): 471.1475. Found: 471.1493.

Methyl 6'-chloro-9-methyl-2'-oxo-4-(*p*-tolyl)-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1j): white solid, 86%, 0.208 g, m.p. over 300℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.74 (s, 1H), 7.30 (d, *J* = 7.6 Hz, 2H), 7.14-7.07 (m, 4H), 7.04-6.99 (m, 3H), 6.84-6.80 (m, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 4.36 (dd, J_1 = 10.8 Hz, J_2 = 5.6 Hz, 1H), 3.51 (s, 3H), 3.46 (d, *J* = 13.6 Hz, 1H), 3.09-2.99 (m, 4H), 2.40 (dd, J_1 = 13.2 Hz, J_2 = 5.6 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.9, 171.9, 143.1, 141.6, 138.0, 136.1, 134.8, 131.7, 129.9, 129.2, 128.1, 125.4, 124.5, 122.8, 122.0, 120.4, 119.0, 116.4, 111.0, 108.8, 52.9, 52.1, 49.9, 41.1, 33.3, 29.7, 21.2; IR (KBr) υ: 1735(C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{29}H_{26}ClN_2O_3$ ($[M+H]^+$): 485.1632. Found: 485.1645.

Ethyl 1'-butyl-5'-chloro-2'-oxo-4-(*p*-tolyl)-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1k): white solid, 80%, 0.216 g, m.p. 238-240℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.37-7.33 (m, 3H), 7.14-7.13 (m, 4H), 7.08 (s, 1H), 7.04 (t, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.82 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 4.37-4.33 (m, 1H), 4.04-3.90 (m, 2H), 3.78-3.74 (m, 2H), 3.47 (d, *J* = 13.2 Hz, 1H), 3.26-3.16 (m, 1H), 2.58-2.53 (m, 1H), 2.35 (s, 3H), 1.76-1.70 (m, 2H), 1.47-1.42 (m, 2H), 1.08 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.6, 171.3, 143.0, 141.5, 136.3, 136.0, 132.5, 131.2, 129.2, 129.1, 128.2, 127.7, 126.5, 124.0, 122.2, 120.2, 119.4, 115.8, 110.7, 109.4, 60.9, 50.3, 49.3, 40.5, 40.4, 33.3, 29.1, 21.1, 20.3, 13.9, 13.8; IR (KBr) υ: 1726 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{33}H_{34}ClN_2O_3$

$([M+H]^+)$: 541.2258. Found: 541.2264.

Ethyl

1'-butyl-5'-methyl-2'-oxo-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carboxylate (1l): white solid, 87%, 0.220 g, m.p. 227-229℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48 (d, *J* = 7.2 Hz, 2H), 7.35-7.31 (m, 2H), 7.27-7.24 (m, 1H), 7.19-7.17 (m, 2H), 7.11 (d, *J* = 8.4 Hz, 1H), 7.04-7.00 (m, 1H), 6.92 (brs, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.82-6.79 (m, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 4.41-4.37 (m, 1H), 4.02-3.88 (m, 2H), 3.79-3.73 (m, 2H), 3.51 (d, *J* = 12.8 Hz, 1H), 3.32-3.23 (m, 1H), 2.58-2.54 (m, 1H), 2.30 (s, 3H), 1.77-1.72 (m, 2H), 1.49-1.40 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.9, 171.4, 144.8, 141.9, 136.3, 132.4, 132.0, 130.6, 129.4, 128.4, 126.6, 126.5, 124.3, 122.1, 120.0, 119.3, 115.2, 110.7, 108.2, 60.7, 50.3, 49.2, 41.0, 40.3, 33.3, 29.3, 21.1, 20.3, 13.9, 13.8; IR (KBr) υ: 1725 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{33}H_{34}N_2NaO_3$ $([M+Na]^+)$: 529.2467. Found: 529.2475.

2. General procedure for the synthesis of tetrahydrospiro[carbazole-1,3'-indoline] derivatives 2a-2i and 3a-3g: In the nitrogen atmosphere, to a 10 mL Schlenk tube was added indole (0.5 mmol), substituted acetophenones or cyclohexanone (1.5 mmol), and TfOH (5% mol) and toluene (2.0 mL). The mixture was heated at 60^{o}C for 1.5 hours. Then, 3-phenacylideneoxindoline (0.5 mmol) was added. The solution was heated at 80^{o}C for about 12 hours. The solvent was removed at reduced pressure by rotator evaporation, the residue was subjected to preparative column chromatography with a mixture of light petroleum and ethyl acetate (V/V = 5:1) as eluent to give the pure product for analysis.

1'-Benzyl-9-methyl-2-(4-methylbenzoyl)-4-(4-nitrophenyl)-2,3,4,9-etrahydrospiro[carbazole-

1,3'-indolin]-2'-one (2a): yellow solid, 73%, 0.230 g, m.p. 220-222℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.15 (d, *J* = 9.0 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.39-7.37 (m, 2H), 7.33-7.30 (m, 1H), 7.20-7.16 (m, 4H), 7.14-7.11 (m, 3H), 6.94-6.91 (m, 1H), 6.85-6.84 (m, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 5.34 (d, *J* = 15.6 Hz, 1H), 4.91 (d, *J* = 15.6 Hz, 1H), 4.70-4.67 (m, 1H), 4.59 (dd, *J* = 7.6 Hz, 1H), 4.41-4.37 (m, 1H), 4.02-3.88 (m, 2H), 3.79-3.73 (m, 2H), 3.51 (d, J_1 = 12.6 Hz, J_2 = 1.2 Hz, 1H), 3.21-3.14 (m, 1H), 2.84 (s, 3H), 2.37 (s, 3H), 2.36-2.33 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 197.9, 176.3, 153.3, 146.8, 144.4, 138.2, 136.3, 134.0, 133.4, 130.4, 129.4, 129.3, 129.2, 128.8, 128.2, 128.1, 127.8, 125.2, 123.8, 123.0, 122.8, 122.2, 119.5, 119.4, 114.3, 109.6, 109.1, 54.3, 49.5, 45.1, 41.6, 32.9, 30.0, 21.6; IR (KBr) υ: 1716 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{41}H_{34}N_3O_4$ ($[M+H]^+$): 632.2549. Found: 632.2539.

1'-Benzyl-4-(4-chlorophenyl)-9-methyl-2-(4-methylbenzoyl)-2,3,4,9-tetrahydrospiro [carbazole-1,3'-indolin]-2'-one (2b): white solid, 66%, 0.205 g, m.p. 234-236℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 7.8 Hz, 2H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.38-7.36 (m, 2H), 7.32-7.29 (m, 2H), 7.24 (s, 1H), 7.19 (d, *J* = 9.0 Hz, 2H), 7.17-7.14 (m, 1H), 7.12-7.09 (m, 3H), 6.92-6.90 (m, 1H), 6.86-6.82 (m, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 5.35 (d, *J* = 15.6 Hz, 1H), 4.90 (d, *J* = 15.6 Hz, 1H), 4.56 (dd, J_1 = 12.0 Hz, J_1 = 1.2 Hz, 1H), 4.54-4.51 (m, 1H), 3.17-3.11 (m, 1H), 2.82 (s, 3H), 2.36 (s, 3H), 2.32-2.30 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 198.1, 176.4, 144.4, 144.1, 143.7, 138.1, 136.4, 133.6, 133.5, 132.1, 130.8, 129.8, 129.4, 129.0, 128.7, 128.6, 128.2, 128.1, 127.7, 125.5, 122.9, 122.6, 121.9, 119.9, 119.1, 115.4, 109.4, 108.8, 54.8, 49.5, 45.1, 41.3, 33.4, 29.8, 21.6; IR (KBr) υ: 1716 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{41}H_{34}ClN_2O_2$ ($[M+H]^+$): 621.2309. Found: 621.2309.

1'-Benzyl-5'-chloro-2-(4-methylbenzoyl)-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indolin]-2'-one (2c): white solid, 75%, 0.227 g, m.p. 262-264℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (d, *J* = 7.6 Hz, 2H), 7.52-7.48 (m, 4H), 7.42-7.36 (m, 3H), 7.33-7.29 (m, 3H), 7.26-7.23 (m, 3H), 7.16-7.14 (m, 2H), 6.87-6.83 (m, 1H), 6.79-6.74 (m, 2H), 5.28 (d, *J* = 15.6 Hz, 1H), 4.90 (d, *J* = 15.6 Hz, 1H), 4.58-4.54 (m, 2H), 3.41-3.12 (m, 1H), 2.58-2.53 (m, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.0, 176.7, 144.5, 142.8, 136.5, 136.0, 132.7, 132.2, 132.1, 129.5, 129.0, 128.9, 128.5, 128.4, 128.4, 127.8, 127.7, 127.7, 126.7, 126.6, 123.4, 122.3, 120.1, 119.6, 115.5, 110.9, 110.5, 53.8, 49.2, 44.5, 41.5, 34.0, 21.6; IR (KBr) υ: 1718 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{40}H_{31}ClN_2NaO_2$ ($[M+Na]^+$): 629.1972. Found: 629.1925.

1'-Butyl-5'-chloro-2-(4-methoxybenzoyl)-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indolin]-2'-one (2d): white solid, 80%, 0.235 g, m.p. 204-206℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.83 (d, *J* = 9.0 Hz, 2H), 7.47-7.46 (m, 2H), 7.30-7.27 (m, 3H), 7.23-7.20 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.08 (brs, 1H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.91-6.90 (m, 3H), 6.83 (t, *J* = 7.2 Hz, 1H), 6.77-6.76 (m, 1H), 4.53-4.50 (m, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 3.87-3.82 (m, 5H), 3.37-3.30 (m, 1H), 2.51-2.48 (m, 1H), 1.90-1.79 (m, 2H), 1.54-1.47 (m, 2H), 1.02 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 196.7, 176.4, 163.7, 144.6, 143.5, 136.4, 132.3, 132.2, 130.6, 129.1, 128.5, 128.4, 128.3, 127.4, 126.7, 126.6, 123.6, 122.2, 120.0, 119.5, 115.5, 114.0, 110.8, 109.5, 55.5, 53.7, 49.1, 41.5, 40.6, 33.9, 29.1, 20.4, 13.9; IR (KBr) υ: 1717 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{37}H_{34}ClN_2O_3$ ($[M+H]^+$): 589.2258. Found: 589.2268.

1'-Benzyl-5'-fluoro-2-(4-methylbenzoyl)-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indolin]-2'-one (2e): white solid, 73%, 0.215 g, m.p. 260-262℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.77 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 7.2 Hz, 2H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.39-7.37 (m, 2H),

7.32-7.29 (m, 3H), 7.24-7.21 (m, 3H), 7.17 (brs, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.07-7.04 (m, 1H), 6.91-6.87 (m, 1H), 6.86-6.83 (m, 2H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.75-6.73 (m, 1H), 5.26 (d, *J* = 15.6 Hz, 1H), 4.92 (d, *J* = 15.6 Hz, 1H), 4.57-4.54 (m, 2H), 3.42-3.36 (m, 1H), 2.56-2.53 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 197.9, 176.8, 159.1 (*J* = 240.2 Hz), 144.4, 140.3, 136.5, 136.2, 132.9, 132.3, 131.9 (*J* = 7.8 Hz), 129.5, 128.9, 128.9, 128.5, 128.4, 128.4, 127.7, 126.7, 126.7, 122.3, 120.1, 119.6, 115.6, 115.5 (*J* = 23.4 Hz), 111.1, 111.0, 110.8, 110.2, 110.1, 53.7, 49.5, 44.6, 41.6, 33.9, 21.6; IR (KBr) υ: 1713 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{40}H_{32}FN_2O_2$ ($[M+H]^+$): 591.2448. Found: 591.2456.

1'-Benzyl-5'-chloro-2-(4-methoxybenzoyl)-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indolin]-2'-one (2f): white solid, 81%, 0.252 g, m.p. 255-257℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.87-7.86 (m, 2H), 7.50 (d, *J* = 7.8 Hz, 4H), 7.38-7.36 (m, 2H), 7.31-7.29 (m, 3H), 7.24-7.22 (m, 1H), 7.20 (brs, 1H), 7.16-7.13 (m, 2H), 7.07-7.04 (m, 2H), 6.93-6.91 (m, 2H), 6.86-6.83 (m, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.73 (d, *J* = 9.0 Hz, 1H), 5.25 (d, *J* = 15.6 Hz, 1H), 4.91 (d, *J* = 15.6 Hz, 1H), 4.56-4.53 (m, 2H), 3.85 (s, 3H), 3.43-3.37 (m, 1H), 2.57-2.54 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 196.7, 176.7, 163.8, 144.5, 142.9, 136.5, 136.0, 132.3, 132.1, 130.7, 129.1, 128.9, 128.5, 128.4, 128.2, 127.8, 127.7, 127.7, 126.7, 126.7, 123.4, 122.3, 120.1, 119.6, 115.6, 114.0, 110.8, 110.5, 55.5, 53.6, 49.3, 44.6, 41.6, 34.1; IR (KBr) υ: 1718 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{40}H_{32}ClN_2O_3$ ($[M+H]^+$): 623.2101. Found: 623.2103.

1'-Benzyl-5'-chloro-2-(4-chlorobenzoyl)-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indolin]-2'-one (2g): white solid, 78%, 0.244 g, m.p. 297-299℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (d, *J* = 8.4 Hz, 2H), 7.51-7.48 (m, 4H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.40-7.37 (m, 2H), 7.34-7.29 (m, 3H), 7.24-7.22 (m, 1H), 7.19-7.15 (m, 3H), 7.09-7.05 (m, 2H), 6.87-6.84 (m, 1H), 6.79-6.75 (m,

2H), 5.23 (d, *J* = 15.6 Hz, 1H), 4.94 (d, *J* = 15.6 Hz, 1H), 4.57-4.50 (m, 2H), 3.43-3.33 (m, 1H), 2.54-2.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.2, 176.3, 144.2, 142.8, 140.0, 136.4, 135.8, 133.5, 131.8, 131.8, 129.7, 129.2, 129.1, 128.9, 128.5, 128.3, 128.0, 127.8, 127.6, 126.8, 126.6, 123.3, 122.4, 120.1, 119.7, 115.5, 110.8, 110.6, 53.7, 49.1, 44.5, 41.4, 33.7; IR (KBr) υ: 1723 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{39}H_{29}Cl_2N_2O_2$ ($[M+H]^+$): 627.1606. Found: 627.1593.

1'-Benzyl-5'-chloro-2-(4-methylbenzoyl)-4-(p-tolyl)-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indolin]-2'-one (2h): white solid, 69%, 0.214 g, m.p. 259-261℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.77 (d, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.39-7.36 (m, 4H), 7.32-7.30 (m, 1H), 7.26-7.25 (m, 1H), 7.24 (brs, 1H), 7.17-7.13 (m, 3H), 7.10 (d, *J* = 7.8 Hz, 2H), 7.07-7.05 (m, 2H), 6.87-6.84 (m, 1H), 6.82-6.81 (m, 1H), 6.73 (d, *J* = 9.0 Hz, 1H), 5.25 (d, *J* = 15.6 Hz, 1H), 4.92 (d, *J* = 16.2 Hz, 1H), 4.55-4.50 (m, 2H), 3.38-3.31 (m, 1H), 2.54-2.50 (m, 1H), 2.39 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 198.0, 176.6, 144.4, 142.9, 141.3, 136.5, 136.1, 136.0, 132.8, 132.1, 132.1, 129.5, 129.2, 129.1, 128.9, 128.4, 128.2, 127.9, 127.7, 127.7, 126.8, 123.4, 122.3, 120.2, 119.6, 115.8, 110.8, 110.5, 53.9, 49.2, 44.6, 41.1, 34.0, 26.9, 21.6; IR (KBr) υ: 1719 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{41}H_{34}ClN_2O_2$ ($[M+H]^+$): 621.2309. Found: 621.2308.

1'-Benzyl-5'-chloro-4-(4-chlorophenyl)-2-(4-methylbenzoyl)-2,3,4,9-tetrahydrospiro [carbazole-1,3'-indolin]-2'-one (2i): white solid, 73%, 0.234 g, m.p. 247-249℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.77 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 7.2 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.39-7.37 (m, 2H), 7.33-7.31 (m, 1H), 7.28-7.26 (m, 4H), 7.20 (brs, 1H), 7.17-7.15 (m, 2H), 7.09-7.07 (m, 2H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.79-6.77 (m, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 5.24 (d, *J* = 15.6 Hz, 1H), 4.92 (d, *J* = 15.6 Hz, 1H), 4.56-4.52 (m, 2H), 3.35-3.29 (m, 1H), 2.54-2.50 (m,

1H), 2.40 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 197.7, 176.5, 144.5, 143.1, 142.8, 136.4, 135.9, 132.7, 132.3, 131.8, 129.7, 129.5, 129.2, 128.9, 128.7, 128.4, 127.9, 127.8, 127.6, 126.5, 123.4, 122.5, 119.9, 119.8, 115.0, 110.9, 110.6, 53.6, 49.2, 44.6, 40.8, 33.7, 21.6; IR (KBr) υ: 1718 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{40}H_{31}Cl_2N_2O_2$ ($[M+H]^+$): 641.1763. Found: 641.1752.

1'-Benzyl-4-(4-methylbenzoyl)-2,3,3*a*,4,6,10*c*-hexahydro-1*H*-spiro[cyclopenta[*c*]carbazole-5, 3'-indolin]-2'-one (3a): white solid, 70%, 0.187 g, m.p. 286-288℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 6.8 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.37-7.33 (m, 2H), 7.29 (d, *J* = 6.8 Hz, 1H), 7.25-7.23 (m, 2H), 7.16-7.10 (m, 4H), 7.03 (d, *J* = 7.2 Hz, 1H), 7.00 (s, 1H), 6.90-6.86 (m, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 5.27 (d, *J* = 15.2 Hz, 1H), 4.87 (d, *J* = 15.6 Hz, 1H), 4.72-4.71 (m, 1H), 3.86-3.81 (m, 1H), 3.08-3.00 (m, 1H), 2.68-2.61 (m, 1H), 2.39 (s, 3H), 2.08-2.01 (m, 1H), 1.92-1.90 (m, 1H), 1.48-1.39 (m, 2H), 1.26 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.7, 177.0, 143.9, 143.9, 136.7, 136.6, 133.9, 131.4, 130.9, 129.4, 128.9, 128.7, 128.2, 127.7, 127.5, 127.0, 122.8, 122.3, 122.2, 119.3, 119.2, 116.3, 110.9, 109.3, 49.6, 44.4, 41.2, 35.7, 34.1, 29.6, 28.1, 26.3, 21.6; IR (KBr) υ: 1716 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{37}H_{33}N_2O_2$ ($[M+H]^+$): 537.2542. Found: 537.2533.

1'-Benzyl-5'-chloro-5-(4-methylbenzoyl)-1,2,3,4,4a,5,6a,7,11*b*,11*c*-decahydrospiro [benzo[*c*]carbazole-6,3'-indolin]-2'-one (3b): white solid, 62%, 0.181 g, m.p. 259-261℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.79-7.64 (m, 3H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 2H), 7.35-7.33 (m, 1H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.13-7.06 (m, 5H), 6.91 (d, *J* = 1.8 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 5.31 (d, *J* = 15.0 Hz, 1H), 4.89 (d, *J* = 15.0 Hz, 1H), 4.48 (d, *J* = 1.8 Hz, 1H), 3.74 (brs, 1H), 3.04 (d, *J* = 13.8 Hz, 1H), 2.68-2.64 (m, 2H), 2.43 (s, 3H), 1.66 (d, *J* = 12.0 Hz, 1H),

1.51 (d, *J* = 12.0 Hz, 1H), 1.29 (m, 3H), 1.11-1.05 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 198.2, 176.8, 144.1, 141.6, 137.0, 136.5, 135.1, 133.4, 131.9, 129.5, 128.9, 128.7, 128.4, 128.0, 127.9, 127.7, 126.5, 123.5, 122.1, 120.4, 119.6, 112.8, 111.0, 110.2, 60.5, 50.1, 44.7, 41.8, 36.8, 30.0, 26.3, 23.9, 21.6, 21.2; IR (KBr) υ: 1719 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{38}H_{33}ClN_2NaO_2$ ($[M+Na]^+$): 607.2128. Found: 607.2114.

1'-Benzyl-5'-chloro-7-methyl-5-(4-methylbenzoyl)-1,2,3,4,4*a*,5,7,11*c*-octahydrospiro[benzo[*c*]carbazole-6,3'-indolin]-2'-one (3c): white solid, 48%, 0.143 g, m.p. 281-283℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.25-7.22 (m, 3H), 7.19-7.15 (m, 4H), 7.12-7.09 (m, 3H), 6.98 (d, *J* = 7.6 Hz, 2H), 6.67 (d, *J* = 7.6 Hz, 1H), 4.57 (d, *J* = 15.2 Hz, 1H), 4.49-4.41 (m, 2H), 3.07-2.98 (m, 2H), 2.90 (s, 3H), 2.39 (s, 3H), 2.33-2.25 (m, 1H), 1.97-1.94 (m, 1H), 1.77-1.74 (m, 1H), 1.65-1.59 (m, 2H), 1.54-1.47 (m, 2H), 1.15-1.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.4, 177.1, 144.3, 140.2, 137.9, 135.9, 134.7, 132.1, 130.2, 129.3, 128.6, 128.5, 128.4, 127.7, 127.6, 126.5, 125.5, 121.7, 120.6, 118.9, 116.3, 110.0, 108.9, 54.5, 53.7, 44.3, 42.1, 41.2, 32.0, 29.9, 29.1, 26.4, 26.2, 21.6; IR (KBr) υ: 1712 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{39}H_{35}ClN_2NaO_2$ ($[M+Na]^+$): 621.2285. Found: 621.2272.

5-Benzoyl-1'-benzyl-3-(*tert*-butyl)-5'-chloro-1,2,3,4,4*a*,5,7,11*c*-octahydrospiro[benzo[*c*]carbazole-6,3'-indolin]-2'-one (3d): white solid, 72%, 0.225 g, m.p. 249-251℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84-7.80 (m, 3H), 7.58-7.56 (m, 3H), 7.50-7.47 (m, 2H), 7.42-7.38 (m, 2H), 7.34-7.31 (m, 1H), 7.13-7.05 (m, 5H,), 6.91 (s, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 5.27 (d, *J* = 15.2 Hz, 1H), 4.97 (d, *J* = 15.6 Hz, 1H), 4.53 (s, 1H), 3.69 (s, 1H), 3.10 (d, *J* = 13.2 Hz, 1H), 2.69 (d, *J* = 11.2 Hz, 1H), 2.51-2.42 (m, 1H), 1.84-1.77 (m, 1H), 1.62-1.59 (m, 1H), 1.31-1.28 (m, 1H), 1.06-0.96 (m, 1H), 0.88-0.82 (m, 1H), 0.73 (s, 9H, 3CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 199.1,

176.3, 141.7, 137.0, 136.4, 136.3, 135.0, 132.9, 132.0, 128.9, 128.7, 128.6, 128.0, 127.8, 127.7, 127.6, 126.5, 123.3, 122.0, 120.3, 119.5, 112.7, 111.1, 110.3, 60.5, 50.0, 48.9, 44.7, 42.0, 36.2, 32.5, 30.0, 27.5, 25.5, 22.4; IR (KBr) υ: 1719 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{41}H_{40}ClN_2O_2$ ($[M+H]^+$): 627.2778. Found: 627.2769.

Ethyl 1'-benzyl-5'-chloro-6-methyl-2'-oxo-2,3,3a,4,6,10c-hexahydro-1*H*-spiro[cyclopenta[*c*] carbazole-5,3'-indoline]-4-carboxylate (3e): white solid, 71%, 0.191 g, m.p. 248-250℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.38-7.32 (m, 3H), 7.21-7.17 (m, 2H), 7.12-7.08 (m, 2H), 7.05 (s, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 4.99 (d, *J* = 15.2 Hz, 1H), 4.92 (d, *J* = 15.2 Hz, 1H), 3.81-3.77 (m, 1H), 3.72-3.68 (m, 1H), 3.50-3.41 (m, 2H), 3.06-2.99 (m, 1H), 2.95 (s, 3H), 2.52-2.45 (m, 2H), 2.17-2.09 (m, 1H), 1.98-1.92 (m, 1H), 1.85-1.77 (m, 1H), 1.71-1.63 (m, 1H), 1.47-1.39 (m, 1H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.8, 170.7, 140.7, 137.9, 135.1, 130.8, 129.6, 128.8, 128.7, 128.4, 128.3, 128.1, 126.3, 126.1, 122.2, 119.0, 119.0, 116.0, 109.9, 108.9, 60.5, 54.0, 52.3, 45.0, 37.2, 36.9, 32.7, 30.5, 29.4, 24.9, 13.8; IR (KBr) υ: 1720(C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{33}H_{32}ClN_2O_3$ ($[M+H]^+$): 539.2101. Found: 539.2088.

Ethyl 1'-benzyl-5'-chloro-7-methyl-2'-oxo-1,2,3,4,4a,5,7,11c-octahydrospiro[benzo[*c*] carbazole-6,3'-indoline]-5-carboxylate (3f): white solid, 66%, 0.182 g, m.p. 255-257℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.36-7.31 (m, 4H), 7.27-7.25 (m, 1H), 7.18-7.14 (m, 1H), 7.10-7.04 (m, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 5.04 (d, *J* = 14.8 Hz, 1H), 4.86 (d, *J* = 15.2 Hz, 1H), 3.79-3.70 (m, 3H), 3.53 (s, 1H), 3.04-2.96 (m, 1H), 2.77 (s, 3H), 2.63-2.57 (m, 1H), 2.09 (d, *J* = 10.0 Hz, 1H), 1.93-1.87 (m, 1H), 1.75-1.70 (m, 2H), 1.64-1.61 (m, 1H), 1.46-1.35 (m, 2H), 0.83 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:

177.7, 170.4, 143.1, 138.1, 135.3, 132.0, 128.8, 128.7, 128.5, 128.2, 128.1, 127.2, 125.8, 121.7, 120.6, 119.1, 109.6, 108.9, 60.3, 55.6, 52.0, 45.1, 36.5, 36.5, 29.5, 29.2, 26.0, 25.5, 22.1, 13.7; IR (KBr) υ: 1721(C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{34}H_{34}ClN_2O_3$ ($[M+H]^+$): 553.2258. Found: 553.2250.

Ethyl 1'-benzyl-5'-chloro-9-methyl-2'-oxo-1,2,3,4,5,6,6a,7,9,13c-decahydrospiro[cycloocta[*c*] carbazole-8,3'-indoline]-7-carboxylate (3g): white solid, 51%, 0.148 g, m.p. 261-263℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.38-7.34 (m, 2H), 7.32-7.29 (m, 1H), 7.19-7.15 (m, 2H), 7.12-7.06 (m, 2H), 6.83 (s, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.11 (d, *J* = 15.2 Hz, 1H), 4.91 (d, *J* = 15.2 Hz, 1H), 4.18-4.00 (m, 2H), 3.54-3.51 (m, 1H), 3.06 (s, 1H), 2.93 (s, 3H), 2.78-2.77 (m, 1H), 2.56-2.52 (m, 1H), 2.27-2.19 (m, 1H), 1.96-1.87 (m, 2H), 1.82-1.60 (m, 7H), 1.49-1.44 (m, 1H), 1.18 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.1, 170.7, 141.0, 138.2, 135.3, 134.4, 128.8, 128.7, 128.6, 128.3, 128.0, 128.0, 127.9, 127.8, 126.1, 124.6, 121.7, 120.2, 118.8, 110.0, 108.9, 60.7, 57.7, 51.2, 44.8, 38.1, 29.4, 29.3, 29.1, 28.4, 27.5, 26.4, 26.1, 14.1; IR (KBr) υ: 1738 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{36}H_{38}ClN_2O_3$ ($[M+H]^+$): 581.2571. Found: 581.2570.

3. General procedure for the synthesis of tetrahydrospiro[carbazole-1,3'-indoline] derivatives B1-B4: In the nitrogen atmosphere, to a 10 mL Shlenck tube was added 3-(1-phenylvinyl)-1*H*-indole (0.5 mmol), 3-methyleneoxindoline (0.5 mmol) and toluene (2 mL). The solution was heated at 80^oC for about 15 hours. The solvent was removed at reduced pressure by rotator evaporation, the residue was subjected to preparative column chromatography with a mixture of light petroleum and ethyl acetate (V/V = 5:1) as eluent to give the pure product for analysis.

ethyl

1'-butyl-5'-methyl-2'-oxo-4-phenyl-2,3,9,9a-tetrahydrospiro[carbazole-1,3'-indoline]-2-carbo

xylate (B1): white solid, 93 %, 0.235 g, m.p. 158-160℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50-7.45 (m, 4H), 7.42-7.38 (m, 1H), 7.12 (s, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.87 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.55 (d, *J* = 7.6 Hz, 1H), 6.44-6.38 (m, 2H), 5.02 (brs, 1H), 3.93-3.82 (m , 3H), 3.78-3.70 (m, 2H), 3.67-3.63 (m, 1H), 3.20-3.13 (m, 1H), 3.09-3.03 (m, 1H), 2.23 (s, 3H), 1.79-1.71 (m, 2H), 1.51-1.45 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.5, 171.0, 153.5, 141.7, 140.5, 132.6, 131.4, 129.0, 128.9, 128.3, 127.9, 127.6, 127.6, 127.5, 126.6, 125.8, 123.4, 118.6, 110.8, 107.7, 68.0, 60.7, 51.4, 44.7, 40.2, 33.5, 29.5, 21.4, 20.3, 13.8, 13.8; IR (KBr) υ: 1708 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{33}H_{35}N_2O_3$ ($[M+H]^+$): 507.2648. Found: 507.2668.

Ethyl

1'-benzyl-5'-chloro-2'-oxo-4-phenyl-2,3,9,9a-tetrahydrospiro[carbazole-1,3'-indoline]-2-carb

oxylate (B2): white solid, 96%, 0.268 g, m.p. 173-175℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52-7.46 (m, 4H), 7.45-7.30 (m, 7H), 7.29-7.27 (m, 1H), 7.12(dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H), 6.91 (t, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.55 (d, *J* = 7.6 Hz, 1H), 6.45-6.42 (m, 2H), 5.11 (d, *J* = 16.0 Hz, 1H), 5.05 (brs, 1H), 4.97 (d, *J* = 15.6 Hz, 1H), 3.96-3.84 (m, 2H), 3.69 (brs, 1H), 3.28-3.21 (m, 1H), 3.08-2.99 (m, 1H), 0.97 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.6, 170.8, 153.3, 142.6, 140.1, 135.6, 132.5, 129.4, 129.1, 129.1, 128.7, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.3, 125.9, 125.6, 123.5, 119.1, 110.9, 109.6, 68.3, 61.0, 51.8, 44.7, 44.3, 33.4, 13.8; IR (KBr) υ: 1716 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{35}H_{30}ClN_2O_3$ ($[M+H]^+$): 561.1945. Found: 561.1964.

1'-benzyl-5'-chloro-2-(4-methylbenzoyl)-4-phenyl-2,3,9,9a-tetrahydrospiro[carbazole-1,3'-indolin]-2'-one (B3): white solid, 92%, 0.278 g, m.p. 173-175℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76 (d, *J* = 8.0 Hz, 2H), 7.48-7.43 (m, 4H,), 7.39-7.36 (m, 1H), 7.33-7.30 (m, 2H), 7.29-7.26 (m, 4H), 7.23-7.21 (m, 2H), 7.12 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 6.91 (t, *J* = 7.6 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 6.46-6.42 (m, 2H), 5.19-5.18 (m, 1H), 4.96 (d, *J* = 16.0 Hz, 1H), 4.90 (d, *J* = 16.0 Hz, 1H), 4.67-4.62 (m, 1H), 3.73 (brs, 1H), 3.21-3.14 (m, 1H), 2.98-2.89 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.2, 178.3, 153.4, 144.1, 142.3, 140.0, 135.5, 133.7, 133.1, 130.4, 129.3, 129.2, 129.1, 128.7, 128.6, 127.9, 127.9, 127.8, 127.5, 127.5, 127.0, 125.9, 125.7, 123.6, 119.0, 111.0, 109.7, 68.4, 52.0, 47.9, 44.1, 35.3, 21.6; IR (KBr) υ: 1697 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{40}H_{32}ClN_2O_2$ ($[M+H]^+$): 607.2152. Found: 607.2176.

1'-benzyl-5'-chloro-2-(4-methoxybenzoyl)-4-phenyl-2,3,9,9a-tetrahydrospiro[carbazole-1,3'-indolin]-2'-one (B4): white solid, 90%, 0.280 g, m.p. 194-196℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, *J* = 8.8 Hz, 2H), 7.40-7.37 (m, 4H,), 7.31-7.27 (m, 2H), 7.23-7.14 (m, 5H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.85-6.80 (m, 3H), 6.56 (d, *J* = 8.4 Hz, 1H), 6.51 (d, *J* = 7.6 Hz, 1H), 6.38-6.34 (m, 2H), 4.88 (d, *J* = 16.0 Hz, 1H), 4.78 (d, *J* = 16.0 Hz, 1H), 4.57-4.52 (m, 1H), 3.75 (s, 3H), 3.71 (brs, 1H), 3.11-3.05 (m, 1H), 2.93-2.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.9, 178.3, 163.6, 153.5, 142.2, 140.0, 135.4, 133.0, 130.9, 130.4, 129.2, 129.1, 128.7, 128.0, 127.8, 127.5, 127.5, 127.0, 126.0, 125.7, 123.6, 119.0, 113.8, 111.0, 109.7, 68.4, 55.5, 55.4, 52.0, 47.5, 44.1, 35.5; IR (KBr) υ: 1700 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI-TOF) Calcd. for $C_{40}H_{32}ClN_2O_3$ ($[M+H]^+$): 623.2101. Found: 623.2098.

Ethyl

1'-benzyl-5'-chloro-2'-oxo-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carbo xylate (C2): white solid, 85%, 0.266 g, m.p. 186-188℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 6.8 Hz, 2H), 7.44-7.32 (m, 8H), 7.23-7.18 (m, 3H), 7.07-7.01 (m, 2H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.81-6.78 (m, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 5.14 (d, *J* = 15.2 Hz, 1H), 4.94 (d, *J* = 15.2 Hz, 1H), 4.39-4.35 (m , 1H), 3.88-3.81 (m, 2H), 3.77-3.72 (m, 1H), 2.83-2.78 (m, 1H), 2.39-2.29 (m, 1H), 0.80 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.2, 170.6, 144.1, 141.2, 136.8, 135.7, 132.6, 131.6, 129.0, 128.7, 128.7, 128.3, 128.2, 128.1, 126.8, 125.9, 124.8, 122.5, 120.7, 119.5, 115.4, 110.8, 110.4, 60.9, 51.3, 47.8, 44.8, 40.3, 34.5, 26.9, 13.6; IR (KBr) υ: 1737 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{35}H_{30}ClN_2O_3$ ($[M+H]^+$): 561.1945. Found: 561.1917.

Ethyl

1'-benzyl-5'-chloro-2'-oxo-4-phenyl-2,3,4,9-tetrahydrospiro[carbazole-1,3'-indoline]-2-carbo xylate (1m): white solid, 46 %, 0.129 g, m.p. 158-160℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, *J* = 7.6 Hz, 2H), 7.41(d, *J* = 7.6 Hz, 2H), 7.36-7.31 (m, 4H), 7.29-7.23 (m, 4H), 7.13-7.03 (m, 3H), 6.85-6.71 (m, 3H), 5.17 (d, *J* = 15.6 Hz, 1H), 4.78 (d, *J* = 15.6 Hz, 1H), 4.41 (dd, J_1 = 10.8 Hz, J_2 = 5.6 Hz, 1H), 4.04-3.88 (m , 2H), 3.54 (d, *J* = 13.2 Hz, 1H), 3.33-3.24 (m, 1H), 2.65-2.61 (m, 1H), 1.07 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.9, 171.3, 144.5, 142.5, 136.5, 135.7, 132.3, 131.4, 129.1, 129.0, 128.5, 128.3, 128.2, 127.8, 127.5, 126.5, 123.9, 123.8, 122.3, 120.2, 119.6, 115.7, 110.8, 110.4, 61.0, 50.2, 49.5, 44.4, 41.0, 18.4, 13.9; IR (KBr) υ: 1701 (C=O) cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{35}H_{30}ClN_2O_3$ ($[M+H]^+$): 561.1945. Found: 561.1936.

ASSOCIATED CONTENT

*S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

The copies of the ^{1}H, and ^{13}C NMR spectra for all new products (PDF). The tables of single crystal data. Single-crystal X-ray data for **1a** (CCDC 1542801), **1f** (CCDC 1542802), **1k** (CCDC1542803), **1m** (CCDC 1582188), **2a** (CCDC 1542804), **2c** (CCDC 1575723), **2d** (CCDC 1542805), **3c** (CCDC 1558240), **3e** (CCDC 1583716), **3g** (CCDC 1558541), **B2** (CCDC 1582190), **B3** (CCDC 1575724), and **C2** (CCDC 1582189).

AUTHOR INFORMATION

Corresponding Authors

*Fax: (+86) 514-87975531; E-mail: sunjing@yzu.edu.cn

*Fax: (+86) 514-87975590-9609; E-mail: cgyan@yzu.edu.cn

ORCID

Chao-Guo Yan: 0000-0002-2777-958

Notes

The authors declare no competing financial interest.

Acknowledgments: This work was financially supported by the National Natural Science Foundation of China (Grant No. 21572196) and the Priority Academic Program Development of Jiangsu Higher Education Institutions. We also thank Analysis and Test Center of Yangzhou University providing instruments for analysis.

RRFERENCES

(1) (a) Ito, C.; Katsuno, S.; Ohta, H.; Omura, M.; Kajura, I.; Furukawa, H. *Chem. Pharm. Bull.* **1997**, *45*, 48-52. (b) Chakravarty, A. K.; Sarkar, T.; Masuda, K.; Shiojima, K. *Phytochemistry* **1999**, *50*, 1263-1266. (c) Ito, C.; Katsuno, S.; Itoigawa, M.; Ruangrungsi, N.; Mukainaka, T.; Okuda, M.; Kitagawa, Y.; Tokuda, H.; Nishino, H.; Furukawa, H. *J. Nat. Prod.* **2000**, *63*, 125-128. (d) Wang, Y.-S.; He, H.-P.; Shen, Y.-M.; Hong, X.; Hao, X.-J. *J. Nat. Prod.* **2003**, *66*, 416-418. (e) Thevissen, K.; Marchand, A.;

Chaltin, P.; Meert, E. M. K.; Cammue, B. P. A. *Curr. Med. Chem.* **2009**, *16*, 2205-2211. (f) Dhara, K.; Mandal, T.; Das, J.; Dash, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 15831-15835.

(2) (a) Rajasekaran, A.; Thampi, P. P. *Eur. J. Med. Chem.* **2005**, *40*, 1359-1364. (b) Maertens, F.; Toppet, S.; Hoornaert, G. J.; Compernolle, F. *Tetrahedron* **2005**; *61*; 1715-1722. (c) DiFabio, R.; Giovannini, R.; Bertani, B.; Borriello, M.; Bozzoli, A.; Donati, D.; Falchi, A.; Ghirlanda, D.; Leslie, C. P.; Pecunioso, A.; Rumboldt, G.; Spada, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1749-1752. (d) Nikitenko, A.; Evrard, D.; Sabb, A. L.; Vogel, R. L.; Stack, G.; Young, M.; Lin, M.; Harrison, B. L.; Potoski, J. R. *Org. Process Res. Dev.* **2008**, *12*, 76-80. (e) Hesse, R.; Kataeva, O.; Schmidt, A. W.; Knolker, H. J. *Chem.-Eur. J.* **2014**, *20*, 9504-9509. (f) Shaikh, M. S.; Karpoormath, R.; Thapliyal, N.; Rane, R. A.; Palkar, M. B.; Faya, A. M.; Patel, H. M.; Alwan, W. S.; Jain, K.; Hampannavar, G. A. *Anti-Cancer Agents Med. Chem.* **2015**, *15*, 1049-1065.

(3) (a) Zhang, Y. D.; Wada, T.; Sasabe, H.; *J. Mater. Chem.,* **1998**, *8*, 809-828. (b) Jiang, H. J.; Sun, J.; Zhang, J. L. *Curr. Org. Chem.* **2012**, *16*, 2014-2025. (c) Kamtekar, K. T.; Monkman, A. P.; Bryce, M. R. *Adv. Mater.* **2010**, *22*, 572-582. (d) Hong, M. K.; Ravva, M. K.; Winget, P.; Bredas, J. L. *Chem. Mater.* **2016**, *28*, 5791-5798.

(4) (a) Knolker, H.-J.; Kethiri, R. R. *Chem. Rev.* **2002**, *102*, 4303-4427. (b) Schmidt, A. W.; Reddy, K. R.; Knlker, H. J. *Chem. Rev.* **2012**, *112*, 3193-3328. (c) Lancianesi, S.; Palmieri, A.; Petrini, M. *Chem. Rev.* **2014**, *114*, 7108-7149. (d) Zhao, S. Z.; Andrade, R. B. *J. Am. Chem. Soc.* **2013**, *135*, 13334-13337.

(5) (a) Kumar, V. P.; Gruner, K. K.; Kataeva, O.; Knolker, H. J. *Angew. Chem., Int. Ed.* **2013**, *52*, 11073-11077. (b) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996-6005. (c) Hernandez-Perez, A. C.; Collins, S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 12696-12700. (d) Gao, H.; Xu, Q. L.; Yousufuddin, M.; Ess, D. H.; Kurti, L. *Angew. Chem., Int. Ed.* **2014**, *53*, 2701-2705.

(6) (a) Liu, C.; Han, X. Q.; Wang, X.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 3700-3701. (b) Kuroda, N.; Takahashi, Y.; Yoshinaga, K.; Mukai, C. *Org. Lett.* **2006**, *8*, 1843-1845. (c) Liu, C.; Widenhoefer, R. A. *Org. Lett.* **2007**, *9*, 1935-1938. (d) Anderson, L. L.; Kroc, M. A.; Reidl, T. W.; Son, J. W. *J. Org. Chem.* **2016**, *81*,

9521-9529. (e) Zhao, F.; Li, N.; Zhu, Y. F.; Han, Z. Y. *Org. Lett.* **2016**, *18*, 1506-1509. (f) Zhao, S. Z.; Andrade, R. B. *J. Org. Chem.* **2017**, *82*, 521-531.

(7) (a) Pindur, U. *Heterocycles* **1988**, *27*, 1253-1268. (b) Kester, R. F.; Berthel, S. J.; Firooznia, F. *Top. Heterocycl. Chem.* **2010**, *26*, 327-396. (c) Rossi, E.; Abbiati, G.; Pirovano, V. *Eur. J. Org. Chem.* **2017**, 4512-4529.

(8) (a) Sengul, I. F.; Somphol, K.; Kandemir, H.; Kumar, N.; Black, D. *Tetrahedron* **2014**, *70,* 9601-9614. (b) Abualnaja, M.; Waddell, P. G.; Clegg, W.; Hall, M. J. *Tetrahedron* **2016**, *72*, 5798-5806. (c) Gioia, C., Hauville, A.; Bernardi, L.; Fini, F.; Ricci, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 9236-9239. (d) Tao, Y.; Zhang, F.; Tang, C. Y.; Wu, X. Y.; Sha, F. *Asian J. Org. Chem.* **2014**, *3*, 1292-1301. (e) Zhou, L. J.; Xu, B.; Zhang, J. L. *Angew. Chem., Int. Ed.* **2015**, *54*, 9092-9096. (f) Ren, J. W.; Zhou, Z. F.; Xiao, J. A.; Chen, X. Q.; Yang, H. *Eur. J. Org. Chem.* **2016**, 1264-1268.

(9) (a) Cowell, J.; Abualnaja, M.; Morton, S.; Linder, R.; Buckingham, F.; Waddell, P. G.; Probert, M. R.; Hall, M. J. *RSC Adv.* **2015**, *5*, 16125-16152. (b) Wu, L. J.; Huang, H.; Dang, P.; Liang, Y.; Pi, S. F. *RSC Adv.* **2015**, *5*, 64354-64357. (c) Kuo, C. W.; Konala, A.; Lin L.; Chiang, T. T.; Huang, C. Y.; Yang, T. H.; Kavala, V.; Yao, C. F. *Chem. Commun.* **2016**, *52*, 7870-7873. (d) Rathore, K. S.; Lad, B. S.; Chennamsetti, H.; Katukojvala, S. *Chem. Commun.* **2016**, *52*, 5812-5815. (e) Sharma, P.; Kumar, N. P.; Krishna, N. H.; Prasanna B. S. D.; Shankaraiah, N.; *Org. Chem. Front.* **2016**, *3*, 1503-1508.

(10) (a) Wang, T.; Hoye, T. R. *J. Am. Chem. Soc.* **2016**, *138*, 13870-13873. (b) Sha, F.; Tao Y.; Tang, C. Y.; Zhang, F.; Wu, X. Y. *J. Org. Chem.* **2015**, *80*, 8122-8133. (c) Dai, W.; Jiang, X. L.; Tao, J. Y.; Shi, F. *J. Org. Chem.,* **2016**, *81*, 185-192. (d) Chen, S.; Li, Y.; Ni, P.; Huang, H.; Deng, G. J. *Org. Lett.* **2016**, *18*, 5384-5387. (e) Chen, S. P.; Li, Y. X.; Ni, P. H.; Yang, B. C.; Huang, H. W.; Deng, G. J. *J. Org. Chem.* **2017**, *82*, 2935-2942.

(11) (a) Singh, G. S.; Desta, Z. Y. *Chem. Rev.* **2012**, *112*, 6104-6155. (b) Hong, L.; Wang, R. *Adv. Synth. Catal.* **2013**, *355*, 1023-1052. (c) Cao, Z. Y.; Wang, Y. H.; Zeng, X. P.; Zhou, J. *Tetrahedron* **2014**, *70*, 2406-2415; (d) Cheng, D. Q.; Ishihara, Y.; Tan, B.; Barbas III, C. B. *ACS Catalysis* **2014**, *4*, 743-762.

(12) Tan, B.; Torres, G. H.; Barbas III, C. F. *J. Am. Chem. Soc.* **2011**, *133*, 12354-12357.

(13) Liu, Y. K.; Nappi, M.; Arceo, E.; Vera, S.; Melchiorre, P. *J. Am. Chem. Soc.* **2011**, *133*, 15212-15218.

(14) Zheng, H. F.; He, P.; Liu, Y. B.; Zhang, Y. L.; Liu, X. H.; Lin, L. L.; Feng, X. M. *Chem. Commun.* **2014**, *50*, 8794-8796.

(15) Wang, Y.; Tu, M. S.; Yin, L.; Sun, M.; Shi, F. *J. Org. Chem.* **2015**, *80*, 3223-3232.

(16) Huang, L. J.; Weng, J.; Wang, S.; Lu, G. *Adv. Synth. Catal.* **2015**, *357*, 993-1003.

(17) Sharma, P.; Kumar, N. P.; Krishna, N. H.; Prasanna, D.; Sridhar, B.; Shankaraiah, N. *Org. Chem. Front.* **2016**, *3*, 1503-1508.

(18) (a) Sun, J.; Sun, Y.; Gong, H.; Xie, Y. J.; Yan, C. G. *Org. Lett.* **2012**, *14*, 5172-5175. (b) Sun, J.; Xie, Y. J.; Yan, C. G. *J. Org. Chem.* **2013**, *78,* 8354-8365. (c) Gao, H.; Sun, J.; Yan, C. G. *J. Org. Chem.* **2014**, *79*, 4131-4136; (d) Han, Y.; Sheng, Y. J.; Yan, C. G. *Org. Lett.* **2014**, *16*, 2654-2657. (e) Sun, J.; Chen, L.; Gong, H.; Yan, C. G. *Org. Biomol. Chem.* **2015**, *13*, 5905-5917. (f) Chen, L.; Sun, J.; Xie, J.; Yan, C. G. *Org. Biomol. Chem.* **2016**, *14*, 6497-6507.

(19) Reddy, B. V. S.; Rajeswari, N.; Sarangapani, M.; Reddy, G. R.; Madan, C.; Kumar, K. P.; Rao, M. S. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 6510-6514.

(20) (a) Reddy, C. N.; Nayak, V. L.; Mani, G. S.; Kapure, J. S.; Adiyala, P. R.; Maurya, R. A.; Kamal, A. *Bioorg. Med. Chem. Lett.* **2015**, *25*, 4580-4586. (b) Edeson, S. J.; Jiang, J. L.; Swanson, S.; Procopiou, P. A.; Adams, H.; Meijer, A.; Harrity, J. *Org. Biomol. Chem.* **2014**, *12*, 3201-3210.

(21) (a) Eitel, M.; Pindur, U. *J. Org. Chem.* **1990**, *55*, 5368-5374. (b) Pfeuffer, L.; Pindur, U. *Helv. Chim. Acta.* **1987**, *70*, 1419-1428. (c) Abbiati, G.; Canevari, V.; Facoetti, D.; Rossi, E. *Eur. J. Org. Chem.* **2007**, 517-525; (d) Pirovano, V.; Dell'Acqua, M.; Facoetti, D.; Rizzato, S.; Abbiati, G.; Rossi, E. *Eur. J. Org. Chem.* **2013**, 6267-6279.

(22) (a) Rehn, S.; Bergman, J. *Tetrahedron* **2005**, *61,* 3115-3123. (b) Han, Y.; Sun, Y.; Sun, J.; Yan, C. G. *Tetrahedron* **2012**, *68*, 8256-8260. (c) Jiang, Y. H.; Yan, C. G. *Synthesis* **2016**, *48*, 3057-3064.

(23) (a) Taheri, A.; Liu, C. H.; Lai, B. B.; Cheng, C.; Pan, X. J.; Gu, Y. L. *Green. Chem*. **2014**, *16*, 3715-3719. (b) Xue, J. H.; Shi, M.; Yu, F.; Li, X. Y.; Ren, W.; Fu, L. N., Guo, Q. X. *Org. Lett.* **2016**, *18*, 3874-3877. (c) Huang Y. W.; Li, X. Y.; Fu, L. N.; Guo, Q. X. *Org. Lett.* **2016**, *18*, 6200-6203. (d) Yan, C. X.; Yang, F.; Yang, X.; Zhou, D. G.; Zhou, P. P. *J. Org. Chem.* **2017**, *82*, 3046-3061.

(24) Wang, Z. B.; Ai, F. J.; Wang, Z.; Zhao, W. X.; Zhu, G. Y.; Lin, Z. Y.; Sun, J. W. *J. Am. Chem. Soc*. **2015**, *137*, 383-389.

Table of contents