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TCCA-mediated oxidative rearrangement of tetrahydro-β-carbolines: facile access to spirooxindoles and the total synthesis of (±)-coerulescine and (±)-horsfiline†

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Multi-reactive centered reagents are beneficial in chemical synthesis due to their advantage of minimal material utilization and formation of less by-products. Trichloroisocyanuric acid (TCCA), a reagent with three reactive centers, was employed in the synthesis of spirooxindoles through the oxidative rearrangement of various *N*-protected tetrahydro-β-carbolines. In this protocol, low equivalents of TCCA were required to access spirooxindoles (up to 99% yield) with a wide substrate scope. Furthermore, the applicability and robustness of this protocol were proven for the gram-scale total synthesis of natural alkaloids such as (±)-coerulescine (**1**) and (±)-horsfiline (**2**) in excellent yields.

Introduction

Spirooxindoles are exceptional and versatile scaffolds, and thus have been extensively studied in the fields of synthetic and pharmaceutical chemistry.[1] The unique three-dimensional spiro system may be the main cause for the bioactivities of spirooxindoles.[1,2] Especially, spirooxindoles have been considered to exhibit antitumor,[3] antimicrobial,[4] antioxidant,[5] anti-inflammatory,[6] antiviral[1a] and other bioactivities. Moreover, many of their derivatives have been extensively used in clinical trials,[7] and some representative examples of bioactive spirooxindoles are depicted in Fig. 1. For example, horsfiline (2) is an intoxicating snuff,[8] rhynchophylline (4) is potent towards various cancer cell lines,[9] spirotryprostatin A prevents G_2M progression in mammalian tsFT210 cells,[10] and corynoxine and corynoxine B show potential for the treatment of Parkinson's disease.[11] Due to all these pharmaceutical potencies of spirooxindole derivatives, chemists have been inspired to establish various synthetic routes for this class of compounds.

Several approaches have been proposed in the literature to build spirooxindoles, which mainly involve two ways: (i) multistep synthesis[1d,8,12] and (ii) oxidative rearrangement.[13] However, oxidative rearrangement reaction is more beneficial than multistep synthesis, because it only involves a single step, avoids the use of various toxic reagents, and ultimately time saving. A few examples of oxidants have been reported previously to afford spirooxindoles, which involve the use of mild organic oxidants such as oxone (Fig. 2),[13f] *N*-bromosuccinimide (NBS),[13c] *t*-BuOCl[13a,13d] and transition metal oxidants such as $Pb(OAc)_4$,[13a] CrO_3 [13f] and OsO_4.[13b] However, the latter oxidants are more likely to produce highly toxic by-products. In continuation of our efforts in the development of new synthetic strategies,[14] we established a simple method employing the safer multi-reactive centered reagent (MRCR) trichloroisocyanuric acid (TCCA), a highly desirable catalyst that requires less equivalents, thereby reducing the by-products.

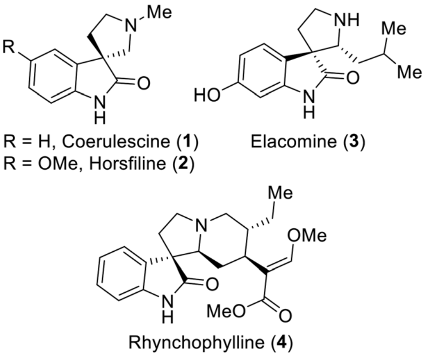

Fig. 1 Representative examples of bioactive spirooxindoles (**1–4**).

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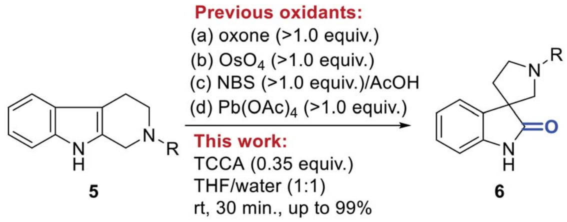


Fig. 2 Comparison of present work with previous methods.

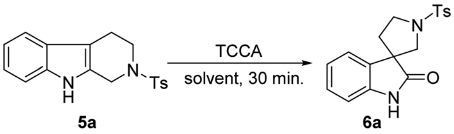
Particularly, TCCA is inexpensive and produces essentially the nontoxic cyanuric acid as a by-product, which can be easily separated from the reaction mixture.[15] TCCA is a versatile reagent with three reactive N–Cl centers, which helps to utilize only 0.33–0.5 equivalents in the reaction. In scaled-up reactions, it is also possible to re-generate TCCA by passing chlorine gas in the aqueous mixture of cyanuric acid.[16] Moreover, it is widely used in several applications such as chlorination and mild oxidation.[17] Studer and co-workers[18] utilized TCCA to obtain α-chloro aldehydes and α-chloro ketones from their corresponding 1° and 2° alcohols. Bathini and co-workers also reported the TCCA-mediated decarboxylative/dehydrogenative aromatization of tetrahydro-β-carbolines (THBCs), which was applied for the total synthesis of β-carboline alkaloids.[19] Veisi and co-workers developed a method to produce nitriles through the direct oxidation of the corresponding amines, alcohols, aldehydes, and benzyl halides using TCCA.[20] Thus, based on these significant findings such as bioactivity and research interest on the synthesis of spirooxindoles, we developed an efficient protocol to construct spirooxindole *via* oxidative rearrangement using TCCA, which is a cost effective and versatile reagent.

Results and discussion

All the key substrates **5a–z** were synthesized according to known reports.[21–23] Initially, we performed a model reaction with tetrahydro-β-carboline (**5a**) and TCCA (1 equiv.) in an acidic solvent mixture of THF/water/AcOH (1 : 1 : 1) for 4 h at 0 °C. The formation of spirooxindole **6a** was observed with 45% yield (entry 1, Table 1). Next, we considered to avoid the use of acidic solvents and executed another reaction without AcOH, which afforded spirooxindole **6a** with slightly improved yield (58%, entry 2, Table 1). We realized that the acidic nature of AcOH and HCl liberated from excess equivalents of TCCA may affect the yield of **6a**. Then, after reducing the TCCA equivalents to 0.33 at 0 °C for 2 h (entry 3, Table 1), we achieved 88% of **6a**. However, a slight improvement in the yield (90%) was seen after minimizing the reaction time to 30 min at room temperature (entry 4, Table 1). Considering our enthusiasm, another trial with similar reaction conditions was performed by taking 0.35 equiv. of TCCA, and surprisingly **6a** was isolated with excellent yield (99%, entry 5, Table 1). Hence, we established that 0.35 equiv. of TCCA is optimal for this oxidative rearrangement reaction. Further investigation using other immiscible solvent mixtures such as DCE/water, DCM/water, and EtOAc/water achieved poor isolated yields of **6a** (entries 6, 7 and 8, respectively, Table 1), thus showing the incompatibility of immiscible solvent mixtures for this reaction. However, considerable yields of **6a** were identified in the case of miscible solvent mixtures such as MeOH/water (82%) and MeCN/water (90%) (entries 9 and 10, respectively, Table 1).

Moreover, two reactions were tested in pure THF and distilled water as solvents, but only 40% of **6a** was isolated in the case of water (entry 11, Table 1) and no product (**6a**) was

Table 1 TCCA-mediated oxidative rearrangement[a]

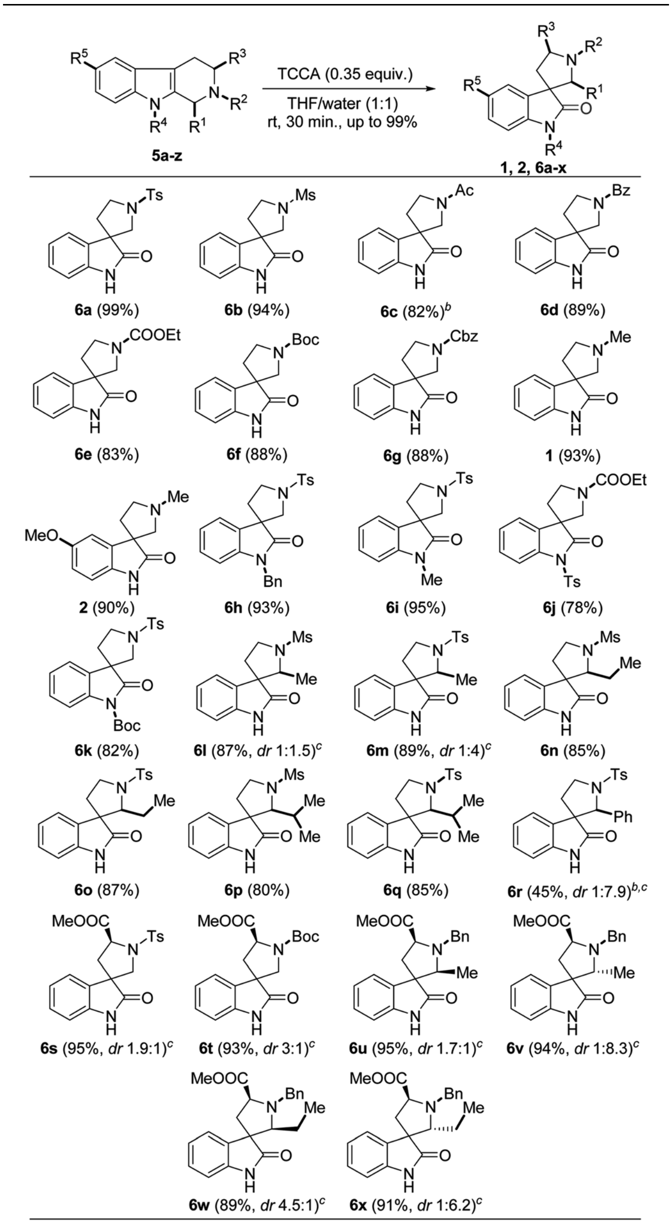


Entry	TCCA (equiv.)	Solvent	Temp. (°C)	Yield (%)
1	1	THF/water/AcOH (1 : 1 : 1)	0	45[b]
2	1	THF/water (1 : 1)	0	58[b]
3	0.33	THF/water (1 : 1)	0	88[b]
4	0.33	THF/water (1 : 1)	rt	90
5	**0.35**	**THF/water (1 : 1)**	**rt**	**99**
6	0.35	DCE/water (1 : 1)	rt	50
7	0.35	DCM/water (1 : 1)	rt	52
8	0.35	EtOAc/water (1 : 1)	rt	55
9	0.35	MeOH/water (1 : 1)	rt	82
10	0.35	MeCN/water (1 : 1)	rt	90
11	0.35	Water	rt	40[c]
12	0.35	THF	rt	—

[a] All reactions were performed using tetrahydro-β-carboline **5a** (1 equiv.) and TCCA for 30 min. [b] The reaction was stirred for 2 h. [c] The remaining starting material was recovered.

observed in THF (entry 12, Table 1). Based on all these observations, the optimized protocol for the oxidative rearrangement of tetrahydro-β-carbolines to spirooxindoles is 0.35 equiv. of TCCA and THF/water (1 : 1) as the solvent at room temperature for 30 min. During the reaction optimization, we identified that a homogenous reaction mixture is required before adding TCCA to achieve the complete conversion of the substrate. Accordingly, it is recommended to use 2 : 1 of THF/water if precipitation of tetrahydro-β-carbolines occurs in a 1 : 1 mixture of THF/water to ensure a homogeneous reaction mixture is obtained.

Table 2 Substrate scope of TCCA-mediated oxidative rearrangement of tetrahydro-β-carbolines[a]

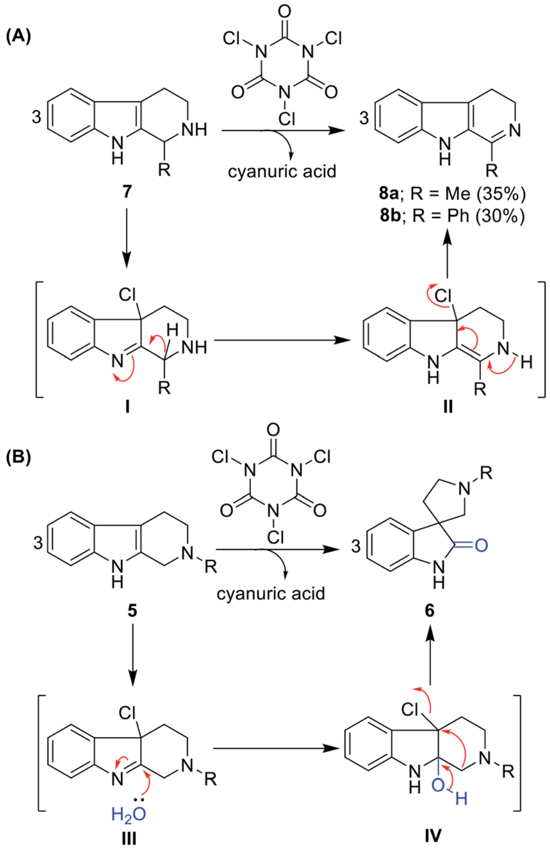


[a] All reactions were performed using tetrahydro-β-carboline **5** (1 equiv.) and TCCA (0.35 equiv.) for 30 min at room temperature. [b] The reaction was stirred at 0 °C. [c] The diastereomeric ratio (dr) measured by ^{1}H NMR analysis.

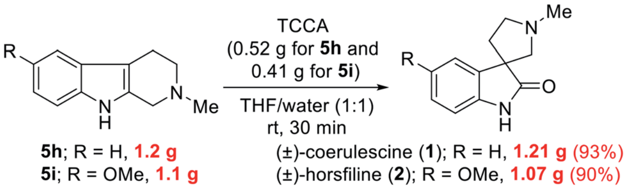
Having the optimized protocol in hand, we explored a sequential study on different substituted/protected THBCs **5a–z**, which delivered the corresponding spirooxindoles **6a–x**, **1** and **2** in good to excellent yields (78–99%). Totally, the protocol was executed on five types of THBC substrates based on their substitution/protection pattern as follows: (i) simple THBCs with N2-protection (**5a–i**); (ii) THBCs with N2-protection and N9-protection (**5j–m**); (iii) THBCs with C1-substitution and N2-protection (**5n–t**); (iv) THBCs with N2-protection and C3-substitutions (**5u** and **5v**); and (v) THBCs with C1-substitution, N2-protection and C3-substitutions (**5w–z**).

The sulfonyl groups (R^2 = tosyl and mesyl) on N2 of THBCs (**5a** and **5b**) smoothly underwent oxidative rearrangement to produce the corresponding spirooxindoles **6a** and **6b** with excellent yields (99% and 94%, Table 2), respectively. However, other electron-withdrawing groups (EWG) such as acetyl, benzoyl, CO_2Et, Boc and Cbz at N2-position of simple THBCs (**5c–g**) were only slightly affected to give lower yields (82%, 81%, 83%, 88% and 88%) of the corresponding spirooxindoles (**6c–g**, Table 2), respectively, which may be due to the acid sensitivity of the amide and carbamate functionalities. Furthermore, the reaction of **5c** with TCCA was performed at 0 °C, and a low yield (50%) was observed at room temperature, affording de-protected **5c**. However, an electron-donating group (EDG) such as methyl on N2 of THBC (**5h** and **5i**) gave good yields of natural spirooxindoles (±)-coerulescine (**1**, 93%) and (±)-horsfiline (**2**, 90%), respectively, as depicted in Table 2.

Further, our attempts on the oxidative rearrangement of THBCs **5k–m** with indole nitrogen protection succeeded and achieved the corresponding spirooxindoles **6h–k** in high yields, respectively. The EDGs (R^4 = benzyl and methyl) at the indole nitrogen of THBCs delivered **6h** and **6i** with satisfactory yields (93% and 95%), respectively. Interestingly, our protocol also worked well on EWG (R^4 = tosyl and Boc)-protected THBCs (**5l** and **5m**) to provide spirooxindoles **6j** (78%) and **6k** (82%) without affecting the protecting groups (Table 2), respectively. A recent report[13f] stated that the presence of EDGs such as hydrogen, alkyl and benzyl at the indolyl nitrogen (N–R^4) is essential to achieve oxidative rearrangement. It is noticeable that our protocol is very advantageous given that it works well on both EDGs and EWGs on the indole nitrogen. Next, we explored our protocol on C1 alkyl (R^1 = methyl, ethyl and isopropyl)- and phenyl-substituted THBCs **5n–t**, but only alkyl-substituted spirooxindoles **6l–q** were obtained in appreciable yields (80–89%, Table 2). A low yield was observed for **6r** (27%) at room temperature from 1-phenyl substituted THBC (**5t**), and interestingly another ring-opened side product (**6r′**, 64%) was isolated and confirmed by comparing its NMR data (for NMR and plausible mechanism see ESI†) with the available literature.[21] However, a slight improvement in yield (45%) was observed with good diastereoselectivity (**6r**, dr 1 : 7.9, Table 2) when the reaction was carried out at 0 °C and the yield of the ring-opened side product (**6r′**) decreased to 50%. The diastereomers of spirooxindoles **6l–q** could not be separated by column chromatography and the ratio was determined by ^{1}H



Scheme 1 (A) Imine formation of N2 unprotected THBCs. (B) Plausible reaction mechanism for the oxidative rearrangement of N2-protected THBCs.



Scheme 2 Gram-scale synthesis of (±)-coerulescine (**1**) and (±)-horsfiline (**2**).

NMR. Nevertheless, the THBCs **5u** and **5v** generated from L-tryptophan smoothly underwent oxidative rearrangement to produce spirooxindoles **6s** and **6t** in excellent yields and good diastereoselectivities (95%, dr 1.9 : 1 and 93%, dr 3 : 1 respectively, Table 2). Finally, the diastereomers of **5w–z** with C1 (R^1 = methyl or ethyl) and C3 ($R^3 = CO_2Me$) substitutions were easily separated by column chromatography and employed for oxidative rearrangement to afford spirooxindole products **6u–x** in good yields with prominent diastereomeric ratios (95%, dr 1.7 : 1, 94%, dr 1 : 8.3, 89%, dr 4.5 : 1 and 91%, dr 1 : 6.2, respectively) as shown in Table 2.

Further, we tested this protocol on C1-substituted (R^1 = methyl and phenyl) and N2-unprotected (R^2 = hydrogen) THBCs **7a** and **7b** and isolated dihydro-β-carbolines **8a** and **8b**, albeit with very poor yields (35% and 30%, respectively) and no oxidative rearrangement product was observed. This can be attributed to dehydrohalogenation (**I** and **II**, Scheme 1A) instead of chlorohydrin formation, oxidative rearrangement, and thereby stabilization of the dihydro-β-carbolines by conjugation from imine, as shown in Scheme 1A.

Notably, in the reaction path of oxidative rearrangement, one mole of TCCA is sufficient to produce three moles of spirooxindoles. The reaction mechanism can be explained as initial TCCA chlorination of THBC to form Cl-THBC (**III**, Scheme 1B), formation of chlorohydrin (**IV**, Scheme 1B) and dehydrohalogenation followed by semi-pinacol-type rearrangement. The by-product cyanuric acid can be easily separated in the work-up given that it is soluble in water.

To highlight the utility of this protocol, we accomplished the gram-scale total synthesis of two bioactive spirooxindole natural products, (±)-coerulescine (**1**) and (±)-horsfiline (**2**) from **5h** and **5i** (Scheme 2), respectively. The gram-scale reaction of bioactive natural products is highly desirable from a commercial perspective. Specifically, **5h** (1.2 g) and **5i** (1.1 g) were reacted with TCCA to produce (±)-coerulescine (**1**) and (±)-horsfiline (**2**) in high yields (1.21 g, 93% and 1.07 g, 90%, respectively). It is important to highlight that the quantity of TCCA used for this gram-scale synthesis is very low (0.52 g for **5h** and 0.41 g for **5i**), whereas these reactions need large quantities of other earlier reported oxidants[13] when performing gram-scale synthesis (>1 g).

Conclusions

In conclusion, we developed an operationally simple and high yield protocol for the synthesis of spirooxindoles from the corresponding tetrahydro-β-carbolines (THBCs) using the inexpensive TCCA. The reaction proceeds *via* oxidative rearrangement and produced spirooxindoles in good to excellent yields (up to 99%). Diversely substituted spirooxindoles and naturally occurring (±)-coerulescine and (±)-horsfiline were furnished in excellent yields using the optimized reaction conditions. To demonstrate the commercial importance of this protocol, we also carried out gram-scale reactions to produce (±)-coerulescine (**1**) and (±)-horsfiline (**2**) with yields of 93% and 90%, respectively. In addition, this synthetic strategy is amenable for the generation of a library spiro-compounds and their derivatives, which can be further utilized in the drug discovery process.

Experimental

General

All solvents used for the reactions and purifications were of commercial grade or were purified prior to use when necessary. NMR spectral analyses were done on a Bruker 400 MHz or 500 MHz spectrometer for ^1H and 100 MHz or 125 MHz spectrometer for ^{13}C spectra, and calibrated to either TMS ($\delta = 0$ for ^1H) or residual DMSO ($\delta = 2.50$ for ^1H and $\delta = 39.51$ for ^{13}C) and residual $CHCl_3$ ($\delta = 7.26$ for ^1H and $\delta = 77.23$ for ^{13}C). Spin multiplicities are described as s (singlet), br s (broad singlet), d (doublet), t (triplet), dd (double doublet), td (triple doublet), q (quartet), and m (multiplet) and the coupling constants are reported in hertz (Hz). TLC analyses for the reactions and chromatography purifications were performed using silica gel plates (0.25 mm, E. Merck, 60 F254) with iodine and a UV lamp for visualization. Mass spectral measurements were recorded *via* electrospray ionization mass spectrometry (ESI-MS). HRMS was performed on a Varian QFT-ESI instrument. Melting points were measured on an electrothermal melting point apparatus and are uncorrected.

All the THBCs **5a**,[21a,22a] **5b**,[21b] **5c**,[21b] **5d**, **5e**,[21b] **5f**,[21b] **5g**,[21c] **5h**,[13e] **5i**,[13e] **5j**, **5k**,[21a] **5l**, **5m**, **5n**, **5o**,[22a] **5p**, **5q**,[21b] **5r**, **5s**,[22b] **5t**,[23] **5u**,[23a] **5v**,[23b] **5w**,[23c] **5x**,[23c] **5y** (ref. 23*d* and *e*) and **5z** (ref. 23*d* and *e*) were synthesized using known procedures in the literature from their corresponding starting materials such as tryptamine (**1a**), tryptophan methyl ester (**1b**) and 5-methoxy tryptamine (**1c**). For the preparation of **5a–i** and **5n–z**, initially we reacted **1** with the respective aldehydes to achieve Pictet-Spengler cyclized products (NH-THBCs). Later, N-protection of THBCs was performed with the corresponding protecting groups in the presence of bases such as triethylamine and *N*,*N*-diisopropylethylamine, as mentioned in the respective literature reports.[13e,21-23]

General procedure for N9-protection for the synthesis of 5j–m. Briefly, **5j**, **5k** and **5m** were synthesized from **5a**, whereas **5l** was synthesized from **5e** using protecting groups (PG) such as BnBr, MeI, TsCl and Boc_2O, respectively. To a stirred solution of **5a** (1 equiv.) in dry THF, 60% NaH (1.5 equiv.) was added at 0 °C. After stirring for 15 min at room temperature, the protecting group (1.1 equiv. of BnBr for **5j**, MeI for **5k** and TsCl for **5m**) was added at 0 °C and the reaction was stirred at room temperature for 8 h. The progress of the reaction was monitored by TLC analysis using EtOAc : hexane or MeOH : CH_2Cl_2 solvent systems and the ninhydrin charring technique. After completion, the reaction was quenched with saturated NH_4Cl solution and extracted with EtOAc and the combined organic phases were washed with water. The organic phase was evaporated *in vacuo* after drying over Na_2SO_4 to give the crude product, which was purified by silica gel column chromatography using 20–50% EtOAc/hexane to afford the pure products **5j**, **5k** and **5m**. The same procedure was used for the synthesis of **5l** from **5e** using Boc_2O as the protecting group.

2-Tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5a).[21b,22a] White solid (340 mg, 90% yield), mp: 110–115 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.75 (s, 1H), 7.71 (d, J = 8.3 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 7.8 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.03 (t, J = 8.0 Hz, 1H), 6.94 (t, J = 8.0 Hz, 1H), 4.27 (s, 2H), 3.39 (t, J = 5.7 Hz, 2H), 2.73 (t, J = 5.6 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6 + $CDCl_3$): δ 143.4, 135.9, 133.5, 129.7, 129.1, 127.1, 126.1, 120.9, 118.4, 117.5, 111.0, 106.1, 43.9, 43.3, 20.9, 20.9; HRMS (ESI) calcd for $C_{18}H_{19}N_2O_2S$ *m*/*z* 327.1162 $[M + H]^+$, found 327.1174.

2-(Methylsulfonyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5b).[21a] Light yellow solid (360 mg, 98% yield), mp: 200–202 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.1 Hz, 1H), 7.20 (t, J = 8.1 Hz, 1H), 7.13 (t, J = 8.1 Hz, 1H), 4.57 (s, 2H), 3.72 (t, J = 5.8 Hz, 2H), 2.93 (t, J = 5.8 Hz, 2H), 2.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.3, 128.6, 126.9, 122.5, 120.1, 118.3, 111.1, 108.5, 44.0, 43.4, 37.5, 21.2; HRMS (ESI) calcd for $C_{12}H_{15}N_2O_2S$ *m*/*z* 251.0849 $[M + H]^+$, found 251.0895.

Phenyl(1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indol-2-yl)methanone (5d). Light yellow solid (375 mg, 87% yield), mp: 153–155 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.37 (s, 0.76H), 7.80 (s, 0.24H), 7.50–7.44 (m, 6H), 7.31 (d, J = 7.3 Hz, 1H), 7.16 (t, J = 7.4 Hz, 1H), 7.11 (t, J = 7.3 Hz, 1H), 4.95 (s, 1.5H), 4.60 (s, 0.5H), 4.13 (s, 0.5H), 3.73 (s, 1.5H), 2.93 (s, 0.5H), 2.84 (s, 1.5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.7, 136.4, 136.2, 130.0, 128.7, 127.0, 127.0, 122.1, 122.0, 119.8, 118.0, 111.1, 108.1, 46.1, 41.2, 22.2; HRMS (ESI) calcd for $C_{15}H_{18}NOS_2$ *m*/*z* 277.1335 $[M + H]^+$, found 277.1350.

2-Methyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5h).[13e] Off-white solid (298 mg, 93% yield), mp: 207–212 °C; ^1H NMR (400 MHz, DMSO-d_6 + $CDCl_3$): δ 9.70 (s, 1H), 7.42 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 7.12–6.96 (m, 2H), 3.59 (s, 2H), 2.87–2.75 (m, 4H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6 + $CDCl_3$): δ 135.8, 132.0, 126.6, 120.2, 118.2, 117.1, 110.5, 106.5, 52.6, 52.0, 45.3, 21.1; HRMS (ESI): calcd for $C_{12}H_{15}N_2$ *m*/*z* 187.1230 $[M + H]^+$, found 187.1238.

6-Methoxy-2-methyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5i).[13e] Pale yellow oil (302 mg, 91% yield); ^1H NMR (400 MHz, DMSO-d_6): δ 10.56 (s, 1H), 7.20 (d, J = 8.0 Hz, 1H), 6.90 (s, 1H), 6.69 (d, J = 8.0 Hz, 1H), 3.78 (s, 3H), 3.55 (s, 2H), 2.71 (s, 4H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.4, 133.0, 130.3, 126.4, 110.8, 109.2, 105.4, 99.2, 54.7, 52.1, 51.6, 44.9, 20.8; HRMS (ESI): calcd for $C_{13}H_{17}N_2O$ *m*/*z* 217.1335 $[M + H]^+$, found 217.1343.

9-Benzyl-2-tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5j). Pale yellow solid (210 mg, 83% yield); mp: 213–215 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 7.65 (d, J = 8.1 Hz, 2H), 7.38 (dd, J = 12.8, 8.2 Hz, 4H), 7.32–7.20 (m, 3H), 7.07 (t, J = 7.5 Hz, 1H), 7.02–6.97 (m, 3H), 5.36 (s, 2H), 4.27 (s, 2H), 3.38 (s, 2H), 2.73 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 143.5, 138.0, 136.5, 133.7, 130.3, 129.8, 128.6, 127.3, 127.2, 126.4, 125.9, 121.3, 119.0, 117.9, 109.7, 106.8, 45.8, 43.7, 42.7, 20.9, 20.8; HRMS (ESI): calcd for $C_{25}H_{25}N_2O_2S$ *m*/*z* 417.1631 $[M + H]^+$, found 417.1629.

Ethyl 9-tosyl-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate (5l). Brown oil (286 mg, 85% yield); ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 8.3 Hz, 1H), 7.71 (br s, 2H), 7.35 (d, J = 7.6 Hz, 1H), 7.33–7.27 (m, 1H), 7.24 (d, J = 7.4 Hz, 1H), 7.20 (d, J = 8.2 Hz, 2H), 4.95 (s, 2H), 4.20 (q, J = 7.1 Hz, 2H), 3.75 (s, 2H), 2.69 (s, 2H), 2.33 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.8, 145.0, 136.2, 136.1, 135.6, 130.0, 129.7, 129.6, 126.6, 124.7, 123.6, 118.4, 114.4, 61.8, 43.4, 41.1, 29.8, 21.6, 14.8; HRMS (ESI): calcd for $C_{21}H_{23}N_2O_4S$ *m*/*z* 399.1373 $[M + H]^+$, found 399.1381.

***tert*-Butyl 2-tosyl-1,2,3,4-tetrahydro-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (5m).** White solid (276 mg, 86% yield), mp: 223–228 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J = 8.1 Hz, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.34 (dd, J = 19.0, 7.8 Hz, 3H), 7.28–7.18 (m, 2H), 4.54 (s, 2H), 3.46 (t, J = 5.6 Hz, 2H), 2.80 (t, J = 5.3 Hz, 2H), 2.41 (s, 3H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 143.8, 135.8, 134.2, 130.0, 129.8, 128.6, 127.6, 124.4, 122.9, 117.9, 115.6, 114.8, 84.3, 45.8, 43.2, 28.3, 21.6, 21.6 HRMS (ESI): calcd for $C_{23}H_{26}N_2O_4S$ *m/z* 426.1613 [M + H]$^+$, found 426.1617.

1-Methyl-2-(methylsulfonyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5n). White solid (333 mg, 91% yield), mp: 176–178 °C; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.92 (s, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.1 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 5.09 (q, J = 6.7 Hz, 1H), 4.17 (dd, J = 14.5, 5.7 Hz, 1H), 3.49–3.40 (m, 1H), 2.96–2.87 (m, 1H), 2.82 (s, 3H), 2.79 (dd, J = 16.0, 4.3 Hz, 1H), 1.60 (d, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$): δ 135.9, 133.7, 126.6, 122.4, 119.8, 118.2, 111.0, 107.4, 48.6, 40.2, 39.0, 21.4, 20.8; HRMS (ESI) calcd for $C_{13}H_{17}N_2O_2S$ *m/z* 265.1005 [M + H]$^+$, found 265.0983.

1-Methyl-2-tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5o).[22a] Yellow solid (353 mg, 81% yield), mp: 206–207 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.94 (s, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 7.8 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.18–7.10 (m, 3H), 7.06 (t, J = 8.3 Hz, 1H), 5.26 (q, J = 6.6 Hz, 1H), 4.16–4.09 (dd, J = 16.0, 4.0 Hz, 1H), 3.42–3.34 (m, 1H), 2.63–2.45 (m, 2H), 2.31 (s, 3H), 1.54 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 143.3, 138.3, 136.0, 134.0, 129.7, 126.8, 126.7, 122.1, 119.6, 118.2, 111.0, 107.7, 48.9, 39.3, 21.5, 21.5, 20.7; HRMS (ESI) calcd for $C_{19}H_{21}N_2O_2S$ *m/z* 341.1318 [M + H]$^+$, found 341.1326.

1-Ethyl-2-(methylsulfonyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5p). White solid (301 mg, 78% yield), mp: 160–162 °C; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.91 (s, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.1 Hz, 1H), 7.21 (t, J = 8.1 Hz, 1H), 7.13 (t, J = 7.9 Hz, 1H), 4.81 (dd, J = 8.9, 5.1 Hz, 1H), 4.21 (dd, J = 14.9, 6.0 Hz, 1H), 3.50–3.42 (m, 1H), 2.99–2.90 (m, 1H), 2.82–2.75 (m, 1H), 2.76 (s, 3H), 1.97–1.83 (m, 2H), 1.14 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$): δ 135.9, 133.1, 126.7, 122.4, 119.9, 118.3, 111.0, 107.4, 54.3, 40.0, 39.4, 28.6, 20.2, 10.9; HRMS (ESI) calcd for $C_{14}H_{19}N_2O_2S$ *m/z* 279.1162 [M + H]$^+$, found 279.1132.

1-Ethyl-2-tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5q).[21b] Pale yellow solid (366 mg, 89% yield), mp: 68–70 °C; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.81 (s, 1H), 7.63 (d, J = 8.3 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.14 (t, J = 7.8 Hz, 1H), 7.09 (d, J = 8.2 Hz, 2H), 7.04 (t, J = 7.5 Hz, 1H), 5.06 (dd, J = 8.4, 5.1 Hz, 1H), 4.13 (dd, J = 14.7, 5.7 Hz, 1H), 3.45–3.34 (m, 1H), 2.49 (dd, J = 15.6, 4.1 Hz, 1H), 2.4–2.3 (m, 1H), 2.28 (s, 3H), 1.99–1.82 (m, 2H), 1.12 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$): δ 143.1, 138.2, 135.8, 133.0, 129.4, 126.7, 126.6, 121.9, 119.4, 118.1, 110.8, 107.8, 54.4, 39.7, 29.0, 21.4, 19.7, 10.8; HRMS (ESI) calcd for $C_{20}H_{23}N_2O_2S$ *m/z* 355.1475 [M + H]$^+$, found 355.1482.

1-Isopropyl-2-(methylsulfonyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5r). White solid (386 mg, 87% yield), mp: 128–129 °C; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.92 (s, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.21 (t, J = 8.1 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 4.51 (d, J = 8.3 Hz, 1H), 4.23 (dd, J = 15.1, 6.5 Hz, 1H), 3.59–3.50 (m, 1H), 3.04–2.92 (m, 1H), 2.79 (dd, J = 16.3, 5.2 Hz, 1H), 2.66 (s, 3H), 2.20–2.07 (m, 1H), 1.18 (d, J = 6.7 Hz, 3H), 1.12 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$): δ 135.9, 132.4, 126.7, 122.6, 120.0, 118.4, 111.1, 107.9, 58.8, 40.1, 39.9, 33.7, 20.3, 20.2, 20.1; HRMS (ESI) calcd for $C_{15}H_{21}N_2O_2S$ *m/z* 293.1318 [M + H]$^+$, found 293.1288.

1-Isopropyl-2-tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5s).[22b] White solid (363 mg, 91% yield), mp: 211–215 °C; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.77 (s, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.1 Hz, 1H), 7.24 (d, J = 7.9 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 6.97 (d, J = 8.2 Hz, 2H), 4.79 (d, J = 7.8 Hz, 1H), 4.13 (dd, J = 15.0, 6.5 Hz, 1H), 3.52–3.43 (m, 1H), 2.44 (dd, J = 15.9, 4.8 Hz, 1H), 2.32–2.23 (m, 1H), 2.19 (s, 3H), 2.17–2.08 (m, 1H), 1.17 (d, J = 6.7 Hz, 3H), 1.11 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$): δ 143.2, 138.0, 135.8, 132.3, 129.3, 126.8, 126.7, 122.1, 119.5, 118.1, 110.8, 108.2, 59.1, 40.2, 34.1, 21.4, 20.2, 20.1, 19.4; HRMS (ESI) calcd for $C_{21}H_{25}N_2O_2S$ *m/z* 369.1631 [M + H]$^+$, found 369.1647.

1-Phenyl-2-tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5t).[22] White solid (393 mg, 93% yield), mp: 157–162 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.82 (s, 1H), 7.63 (d, J = 8.1 Hz, 2H), 7.38–7.13 (m, 9H), 7.05 (t, J = 7.5 Hz, 1H), 6.94 (t, J = 7.4 Hz, 1H), 6.24 (s, 1H), 3.95 (dd, J = 14.5, 5.6 Hz, 1H), 3.26–3.14 (m, 1H), 2.61 (dd, J = 15.7, 4.1 Hz, 1H), 2.48–2.35 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 143.0, 139.8, 137.6, 136.0, 130.6, 129.5, 128.4, 128.0, 128.0, 126.5, 126.0, 121.3, 118.5, 117.8, 111.2, 107.6, 55.3, 39.1, 20.8, 19.5; HRMS (ESI) calcd for $C_{24}H_{23}N_2O_2S$ *m/z* 403.1475 [M + H]$^+$, found 403.1489.

Methyl (*S*)-2-tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylate (5u).[23a] White solid (386 mg, 94% yield), mp: 138–143 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.06 (br s, 1H), 7.71 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 7.6 Hz, 1H), 7.28–7.22 (m, 3H), 7.16–7.04 (m, 2H), 5.15 (d, J = 6.4 Hz, 1H), 4.82 (d, J = 15.0 Hz, 1H), 4.64 (d, J = 15.1 Hz, 1H), 3.43 (s, 3H), 3.30 (d, J = 15.7 Hz, 1H), 3.06 (dd, J = 15.7, 6.6 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 171.0, 143.8, 136.3, 129.7, 128.4, 127.2, 126.7, 122.2, 119.7, 118.1, 111.1, 105.6, 54.1, 52.4, 41.0, 24.6, 21.6; HRMS (ESI) calcd for $C_{20}H_{21}N_2O_4S$ *m/z* 385.1217 [M + H]$^+$, found 385.1219.

General procedure for the synthesis of 5w, 5x, 5y and 5z. The diastereomeric mixtures of THBC esters (**5w** and **5x**) and (**5y** and **5z**) were synthesized according to the procedures given in previous literature reports.[23c–e] These diastereomeric mixtures were separated by silica gel column chromatography using EtOAc/hexane (20–30%) prior to use for TCCA-mediated oxidative rearrangement.

Methyl (1*R*,3*S*)-2-benzyl-1-methyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylate (5x)[22c]. Brown oil (312 mg, 92% yield); ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.70 (s, 1H), 7.51 (d, J = 7.3 Hz, 1H), 7.43 (d, J = 7.4 Hz, 2H), 7.34–7.25 (m, 3H), 7.23 (t, J = 7.3 Hz, 1H), 7.17–7.06 (m, 2H), 4.24 (q, J = 6.8 Hz, 1H), 4.01 (d, J = 4.5 Hz, 2H), 3.90 (t, J = 5.7 Hz, 1H), 3.62 (s, 3H), 3.26 (dd, J = 15.2, 6.1 Hz, 1H), 2.99 (dd, J = 17.2, 5.7 Hz, 1H), 1.34 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 174.2, 140.0, 136.1, 135.5, 128.6, 128.3, 127.2, 127.0, 121.7, 119.6, 118.3, 110.8, 106.6, 60.0, 54.9, 52.9, 51.8, 22.3, 18.3; HRMS (ESI) calcd for $C_{21}H_{23}N_2O_2$ *m/z* 335.1754 [M + H]$^+$, found 335.1762.

Methyl (1*R*,3*S*)-2-benzyl-1-ethyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylate (5z).[23d,23e] Brown oil (368 mg, 89% yield); ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.74 (s, 1H), 7.52 (d, J = 7.5 Hz, 1H), 7.44 (d, J = 7.3 Hz, 2H), 7.34–7.29 (m, 2H), 7.29–7.22 (m, 2H), 7.16–7.07 (m, 2H), 3.93 (d, J = 1.5 Hz, 2H), 3.86–3.80 (m, 2H), 3.60 (s, 3H), 3.23 (dd, J = 15.7, 4.5 Hz, 1H), 2.97 (dd, J = 15.7, 7.0 Hz, 1H), 1.71–1.61 (m, 2H), 1.00 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 174.2, 139.6, 136.1, 134.6, 128.9, 128.3, 127.2, 127.1, 121.6, 119.5, 118.3, 110.8, 106.5, 59.5, 59.1, 58.4, 51.7, 27.0, 20.4, 11.1; HRMS (ESI) calcd for $C_{22}H_{25}N_2O_2$ m/z 349.1911 $[M + H]^+$, found 349.1915.

General procedure for TCCA mediated oxidative rearrangement reaction. To a stirred homogeneous solution of THBCs (1.0 equiv.) in THF/H_2O (1 : 1), TCCA (0.35 equiv.) was added at room temperature in one batch. The resulting reaction mixture was stirred at room temperature for 30 min. After the reaction was completed, as monitored by TLC analysis (EtOAc : hexane or MeOH : CH_2Cl_2 solvent systems), it was quenched by addition of saturated $NaHCO_3$ and extracted with EtOAc three times. The combined organic phases were washed with water, dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The resulting crude product was purified by flash column chromatography (EtOAc/hexane = 1 : 10 to 1 : 1) to provide the pure spirooxindole. Note: This reaction was performed at 0 °C in the case of THBCs **5c** and **5t**.

1′-Tosylspiro[indoline-3,3′-pyrrolidin]-2-one (6a).[13f] White solid (98 mg, 99% yield), mp: 158–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (s, 1H), 7.77 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.21 (t, J = 7.7 Hz, 1H), 7.03 (d, J = 7.0 Hz, 1H), 6.96 (t, J = 7.4 Hz, 1H), 6.88 (d, J = 7.7 Hz, 1H), 3.74–3.68 (m, 1H), 3.57 (d, J = 9.6 Hz, 1H), 3.58–3.50 (m, 1H) 3.47 (d, J = 9.8 Hz, 1H), 2.46 (s, 3H), 2.35–2.24 (m, 1H), 2.10–2.00 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.3, 144.0, 139.9, 133.4, 132.8, 129.9, 128.6, 127.8, 123.2, 123.2, 110.1, 56.1, 53.0, 47.4, 36.4, 21.7; HRMS (ESI) calcd for $C_{18}H_{19}N_2O_3S$ m/z 343.1111 $[M + H]^+$, found 343.1123.

1′-(Methylsulfonyl)spiro[indoline-3,3′-pyrrolidin]-2-one (6b). White solid (90 mg, 94% yield), mp: 217–219 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.54 (s, 1H), 7.38 (d, J = 7.4 Hz, 1H), 7.23 (t, J = 7.7, 1H), 7.01 (t, J = 7.5 Hz, 1H), 6.88 (d, J = 7.7 Hz, 1H), 3.74–3.65 (m, 1H), 3.63–3.59 (m, 1H), 3.56 (d, J = 10.3 Hz, 1H), 3.44 (d, J = 10.3 Hz, 1H), 3.03 (s, 3H), 2.28–2.23 (m, 1H), 2.20–2.14 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 179.1, 141.5, 131.4, 128.4, 123.0, 121.87, 109.4, 54.9, 52.3, 47.0, 35.9, 34.3; HRMS (ESI) calcd for $C_{12}H_{15}N_2O_3S$ m/z 267.0798 $[M + H]^+$, found 267.0846.

1′-Acetylspiro[indoline-3,3′-pyrrolidin]-2-one (6c).[13f] This reaction was performed at 0 °C. Pale yellow solid (101 mg, 82% yield, found as 50 : 50 rotamers $CDCl_3$), mp: 75–78 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.38 and 9.22 (s, 1H), 7.29–7.20 (m, 1H), 7.19–7.10 (s, 1H), 7.09–7.00 (s, 1H), 6.95 (ddd, J = 21.6, 14.1, 8.0 Hz, 1H), 4.05–3.95 (m, 1H), 3.93–3.80 (m, 2H), 3.68 (dd, J = 65.0, 15.0 Hz, 1H), 2.54–2.40 (m, 1H), 2.29–2.21 (m, 1H), 2.19 and 2.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 180.5, 179.4, 169.7, 169.5, 140.7, 140.4, 132.5, 131.7, 128.8, 128.7, 123.1, 122.9, 122.7, 110.4, 110.3, 55.5, 53.9, 53.6, 51.9, 46.7, 45.2, 36.5, 35.1, 22.6, 22.4; HRMS (ESI) calcd for $C_{15}H_{15}N_2O_2$ m/z 231.1128 $[M + H]^+$, found 231.1108.

1′-Benzoylspiro[indoline-3,3′-pyrrolidin]-2-one (6d). White solid (95 mg, 89% yield, found as 62 : 38 rotamers in $CDCl_3$), mp: 83–85 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 and 8.03 (s, 1H), 7.63 (d, J = 7.0 Hz, 1H), 7.52 (d, J = 7.5 Hz, 1H), 7.47–7.43 (m, 1H), 7.41–7.32 (m, 2H), 7.27–7.20 (s, 2H), 7.17–7.01 (m, 1H), 6.91 (dd, J = 22.2, 7.7 Hz, 1H), 4.25–4.02 (m, 2H), 3.99–3.56 (m, 2H), 2.66–2.31 (m, 1H), 2.27–2.10 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 180.6, 178.8, 170.2, 170.1, 140.6, 140.1, 136.4, 132.4, 130.3, 128.8, 128.7, 128.5, 127.3, 123.2, 122.7, 110.3, 57.6, 54.2, 53.6, 51.9, 48.7, 45.6, 36.9, 35.0; HRMS (ESI) calcd for $C_{18}H_{17}N_2O_2S_2$ m/z 293.1285 $[M + H]^+$, found 293.1253.

Ethyl 2-oxospiro[indoline-3,3′-pyrrolidine]-1′-carboxylate (6e). Colorless oil (85 mg, 83% yield, found as 56 : 44 rotamers in $CDCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.11 and 9.04 (s, 1H), 7.27–7.22 (m, 1H), 7.17 (t, J = 5.0 Hz, 1H), 7.05 (t, J = 7.4 Hz, 1H), 6.97–6.90 (m, 1H), 4.23–4.12 (m, 2H), 3.95–3.87 (m, 1H), 3.85–3.74 (m, 2H), 3.64 (dd, J = 18.0, 9.1 Hz, 1H), 2.48–2.40 (m, 1H), 2.16–2.07 (m, 1H), 1.32 (t, J = 7.0 Hz, 1.3H), 1.24 (t, J = 7.0 Hz, 1.7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 180.2, 179.9, 155.2, 155.1, 140.3, 140.2, 132.9, 132.5, 128.6, 123.4, 123.1, 123.1, 122.8, 111.2, 110.2, 61.6, 61.5, 54.3, 54.1, 53.4, 52.4, 45.7, 45.3, 36.5, 35.6, 14.9, 14.8; HRMS (ESI) calcd for $C_{14}H_{17}N_2O_3$ m/z 261.1234 $[M + H]^+$, found 269.1246.

***tert*-Butyl 2-oxospiro[indoline-3,3′-pyrrolidine]-1′-carboxylate (6f).**[13f] White solid (102 mg, 88% yield, found as 51 : 49 rotamers in DMSO-d_6), mp: 123–125 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.50 (s, 1H), 7.25–7.19 (m, 2H), 6.97 (t, J = 6.5 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 3.67–3.57 (m, 2H), 3.51–3.43 (m, 2H), 2.18–2.09 (m, 2H), 1.44 and 1.39 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 179.3, 153.5, 141.7, 131.8, 128.2, 122.8, 121.5, 109.4, 78.6, 53.8, 53.5, 52.2, 51.3, 45.0, 44.9, 35.5, 34.6, 28.1, 28.0; HRMS (ESI) calcd for $C_{16}H_{20}N_2O_3Na$ m/z 311.1366 $[M + Na]^+$, found 311.1416.

Benzyl 2-oxospiro[indoline-3,3′-pyrrolidine]-1′-carboxylate (6g). Colourless oil (75 mg, 88% yield, found as 52 : 48 rotamers in $CDCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.65 and 8.59 (s, 1H), 7.43–7.37 (m, 2H), 7.33–7.32 (m, 3H), 7.24 (t, J = 12.8 Hz, 1H), 7.15 (dd, J = 15.2, 7.4 Hz, 1H), 7.05–7.03 (m, 1H), 6.93 (d, J = 7.8 Hz, 1H), 5.21 (d, J = 2.8 Hz, 1H), 5.16 (s, 1H), 3.97–3.90 (m, 1H), 3.87–3.78 (m, 2H), 3.69 (dd, J = 23.0, 11.1 Hz, 1H), 2.47–2.41 (dt, J = 12.7, 8.1 Hz, 1H), 2.16–2.08 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.7, 154.8, 140.1, 136.9, 136.7, 132.7, 132.3, 128.6, 128.6, 128.1, 128.1, 128.0, 127.9, 123.1, 122.9, 110.1, 67.2, 54.5, 54.2, 53.3, 52.4, 45.8, 45.4, 36.5, 35.6; HRMS (ESI) calcd for $C_{19}H_{19}N_2O_3$ m/z 323.1390 $[M + H]^+$, found 323.1349.

(±)-Coerulescine (1).[13e,13f] Off-white solid (1.21 g, 93% yield), mp: 110–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.24 (s, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 7.06 (t, J = 8.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 3.06–3.00 (m, 1H), 2.92 (dd, J = 25.1, 9.3 Hz, 2H), 2.85 (dd, J = 15.1, 6.8 Hz, 1H), 2.50 (s, 3H), 2.49–2.41 (m, 1H), 2.19–2.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.5, 140.4, 136.3, 127.8, 123.3, 122.8, 109.8, 66.4, 56.9, 53.8, 41.9, 38.0; HRMS (ESI) calcd for $C_{12}H_{15}N_2O$ m/z 203.1179 $[M + H]^+$, found 203.1175.

(±)-Horsfiline (2).[13e,13f] White solid (69 mg, 90% yield), mp: 148–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (s, 1H), 7.01 (s, 1H), 6.75–6.66 (m, 2H), 3.77 (s, 3H), 3.05–2.95 (m, 1H), 2.88–2.80 (m, 2H), 2.71 (q, J = 8.4 Hz, 1H), 2.42 (s, 3H), 2.41–2.32 (m, 1H), 2.11–1.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.1, 156.1, 137.6, 133.6, 112.4, 110.2, 109.9, 66.3, 56.7, 55.8, 54.2, 41.8, 38.0; HRMS (ESI) calcd for $C_{13}H_{17}N_2O_2$ m/z 233.1285 $[M + H]^+$, found 233.1289.

1-Benzyl-1′-tosylspiro[indoline-3,3′-pyrrolidin]-2-one (6h).[23a] Colorless gummy oil (78 mg, 93% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.33–

7.25 (m, 3H), 7.24–7.08 (m, 4H), 6.97 (td, *J* = 7.6, 0.8 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 4.87 (d, *J* = 1.3 Hz, 2H), 3.81–3.72 (m, 1H), 3.63–3.47 (m, 3H), 2.47 (s, 3H), 2.39–2.30 (m, 1H), 2.13–2.01 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 144.0, 141.8, 135.6, 133.4, 132.5, 130.0, 128.9, 128.6, 127.8, 127.2, 123.3, 123.0, 109.3, 56.3, 52.6, 47.4, 44.0, 36.4, 21.7; HRMS (ESI) calcd for $C_{25}H_{25}N_2O_3S$ *m/z* 433.1580 [M + H]$^+$, found 433.1588.

1-Methyl-1′-tosylspiro[indoline-3,3′-pyrrolidin]-2-one (6i).[24a] Off-white solid (76 mg, 95% yield), 147–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.32–7.26 (m, 1H), 7.10 (d, *J* = 7.4 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 3.78–3.70 (m, 1H), 3.57–3.47 (m, 2H), 3.42 (d, *J* = 9.6 Hz, 1H), 3.18 (s, 3H), 2.47 (s, 3H), 2.33–2.23 (m, 1H), 2.05–1.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 143.9, 142.7, 133.4, 132.6, 129.9, 128.6, 127.8, 123.3, 122.9, 108.3, 56.2, 52.6, 47.4, 36.3, 26.5, 21.7; HRMS (ESI) calcd for $C_{19}H_{21}N_2O_3S$ *m/z* 357.1267 [M + H]$^+$, found 357.1273.

Ethyl 2-oxo-1-tosylspiro[indoline-3,3′-pyrrolidine]-1′-carboxylate (6j). Pale yellow oil (63 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 7.94 (d, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 7.7 Hz, 3H), 7.02 (t, *J* = 7.4 Hz, 1H), 4.20–4.10 (m, 3H), 3.98–3.51 (m, 2H), 3.03–2.99 (m, 1H), 2.37 (s, 3H), 2.27–1.99 (m, 2H), 1.30–1.24 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 173.0, 155.5, 143.2, 137.2, 129.7, 128.9, 127.7, 123.7, 123.0, 122.1, 113.2, 95.4, 75.7, 61.0, 60.8, 48.4, 32.4, 21.1, 14.3; HRMS (ESI) calcd for $C_{21}H_{22}N_2O_5S$ *m/z* 414.1249 [M]$^+$, found 414.1255.

***tert*-Butyl 2-oxo-1′-tosylspiro[indoline-3,3′-pyrrolidine]-1-carboxylate (6k).** Colorless oil (84 mg, 82% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.31–7.23 (m, 4H), 7.04 (t, *J* = 7.5 Hz, 1H), 3.92 (d, *J* = 13.3 Hz, 1H), 3.51–3.46 (m, 1H), 3.30 (d, *J* = 13.3 Hz, 1H), 2.80–2.72 (m, 1H), 2.40 (s, 3H), 2.26–2.14 (m, 2H), 1.63 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 152.9, 143.6, 140.3, 135.0, 130.6, 130.3, 129.8, 127.4, 123.7, 123.3, 115.3, 91.1, 83.8, 75.7, 50.0, 42.0, 32.2, 28.5, 21.6; HRMS (ESI) calcd for $C_{23}H_{27}N_2O_5S$ *m/z* 443.1635 [M + H]$^+$, found 443.1643.

2′-Methyl-1′-(methylsulfonyl)spiro[indoline-3,3′-pyrrolidin]-2-one (6l). White solid (58 mg, 87% yield, dr 1 : 1.6), mp: 140–142 °C; ^{1}H NMR (500 MHz, DMSO-d_6): major isomer: δ 10.52 (s, 1H), 7.43 (d, *J* = 7.4 Hz, 1H), 7.22 (t, *J* = 8.3 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 3.89–3.75 (m, 2H), 3.69–3.62 (m, 1H), 3.08 (s, 3H), 2.24–2.16 (m, 1H), 2.10 (dd, *J* = 6.4, 2.1 Hz, 1H), 1.07 (d, *J* = 6.4 Hz, 3H); minor isomer: δ 10.58 (s, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.22 (t, *J* = 8.3 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 3.77–3.70 (m, 2H), 3.60 (dd, *J* = 7.0, 3.1 Hz, 1H), 3.01 (s, 3H), 2.14 (dd, *J* = 12.9, 6.1 Hz, 1H), 2.07 (dd, *J* = 6.3, 1.9 Hz, 1H), 1.02 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 180.3, 178.9, 140.7, 130.0, 129.0, 128.7, 125.5, 123.2, 123.0, 122.8, 110.3, 110.0, 63.1, 61.4, 57.8, 57.4, 47.3, 47.2, 40.3, 35.1, 34.8, 34.3, 20.0, 15.8; HRMS (ESI) calcd for $C_{13}H_{17}N_2O_3S$ *m/z* 281.0954 [M + H]$^+$, found 281.0968.

2′-Methyl-1′-tosylspiro[indoline-3,3′-pyrrolidin]-2-one (6m). White solid (92 mg, 89% yield, dr 1 : 4), mp: 195–199 °C; ^{1}H NMR (400 MHz, $CDCl_3$): major isomer: δ 8.58 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.7 Hz, 1H), 6.95–6.85 (m, 2H), 6.57 (d, *J* = 7.4 Hz, 1H), 4.08–4.00 (m, 1H), 3.93–3.85 (m, 1H), 3.80–3.68 (m, 1H), 2.49 (s, 3H), 2.21–2.13 (m, 1H), 1.80–1.74 (m, 1H), 1.33 (d, *J* = 6.5 Hz, 3H); minor isomer: δ 8.44 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.95–6.85 (m, 2H), 6.57 (d, *J* = 7.4 Hz, 1H), 4.08–4.00 (m, 1H), 3.93–3.85 (m, 1H), 3.80–3.68 (m, 1H), 2.46 (s, 3H), 2.21–2.13 (m, 1H), 1.80–1.74 (m, 1H), 1.14 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.9, 178.5, 143.9, 143.8, 140.6, 140.2, 135.7, 133.5, 130.6, 129.9, 128.8, 127.9, 127.6, 125.2, 123.0, 122.9, 122.6, 110.2, 110.0, 63.7, 62.3, 58.4, 57.8, 48.4, 48.0, 34.8, 33.8, 23.9, 21.7, 17.5, 17.3; HRMS (ESI) calcd for $C_{19}H_{21}N_2O_3S$ *m/z* 357.1267 [M + H]$^+$, found 357.1269.

2′-Ethyl-1′-(methylsulfonyl)spiro[indoline-3,3′-pyrrolidin]-2-one (6n). White solid (82 mg, 85% yield), mp: 158–160 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.58 (s, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.19 (d, *J* = 7.7 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 3.83–3.76 (m, 2H), 3.69–3.63 (m, 1H), 3.12 (s, 3H), 2.18–2.09 (m, 1H), 2.09–2.02 (m, 1H), 2.00–1.88 (m, 1H), 1.83–1.72 (m, 1H), 0.39 (t, *J* = 7.6 Hz, 4H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 178.1, 141.2, 131.5, 128.2, 122.9, 121.8, 109.3, 67.7, 56.6, 47.4, 36.8, 34.8, 25.7, 10.1; HRMS (ESI) calcd for $C_{14}H_{19}N_2O_3S$ *m/z* 295.1111 [M + H]$^+$, found 295.1099.

2′-Ethyl-1′-tosylspiro[indoline-3,3′-pyrrolidin]-2-one (6o).[24b] White solid (74 mg, 87% yield), mp: 208–210 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.17 (t, *J* = 8.1 Hz, 1H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.56 (d, *J* = 7.4 Hz, 1H), 3.97 (ddd, *J* = 11.1, 10.1, 5.8 Hz, 1H), 3.86 (dd, *J* = 9.9, 4.4 Hz, 1H), 3.79–3.72 (m, 1H), 2.49 (s, 3H), 2.12–2.05 (m, 2H), 2.04–1.95 (m, 1H), 1.73–1.66 (s, 1H), 0.60 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.8, 143.9, 139.8, 135.9, 132.4, 130.0, 128.5, 127.8, 123.0, 122.6, 109.8, 69.4, 57.0, 48.1, 37.4, 26.3, 21.7, 10.8; HRMS (ESI) calcd for $C_{15}H_{18}NOS_2$ *m/z* 371.1424 [M + H]$^+$, found 371.1439.

2′-Isopropyl-1′-(methylsulfonyl)spiro[indoline-3,3′-pyrrolidin]-2-one (6p). Colourless oil (83 mg, 80% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 and 7.60 (d, *J* = 9.4 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 4.21 (d, *J* = 9.3 Hz, 1H), 3.91–3.84 (m, 1H), 3.81–3.73 (m, 1H), 3.08 (s, 3H), 3.92–3.84 (m, 1H), 2.35–2.21 (m, 2H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.69 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.3, 138.9, 133.7, 128.2, 123.4, 123.1, 109.4, 73.2, 56.4, 48.4, 41.0, 40.8, 30.4, 20.9, 19.7; HRMS (ESI) calcd for $C_{15}H_{21}N_2O_3S$ *m/z* 309.1267 [M + H]$^+$, found 309.1231.

2′-Isopropyl-1′-tosylspiro[indoline-3,3′-pyrrolidin]-2-one (6q). White solid (86 mg, 85% yield), mp: 216–219 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 6.8 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 4.72 (d, *J* = 11.3 Hz, 1H), 3.95 (dd, *J* = 15.4, 4.2 Hz, 1H), 3.73 (ddd, *J* = 15.1, 12.8, 2.1 Hz, 1H), 2.85–2.75 (m, 1H), 2.31 (d, *J* = 14.7 Hz, 1H), 2.20 (s, 3H), 1.25–1.16 (m, 1H), 1.15 (d, *J* = 6.6 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.6, 151.3, 143.4, 139.7, 137.3, 130.0, 129.4, 127.3, 127.0, 122.1, 121.3, 67.6, 65.7, 39.0, 37.7, 28.0, 21.2, 20.2, 19.3; HRMS (ESI) calcd for $C_{21}H_{25}N_2O_3S$ *m/z* 385.1580 [M + H]$^+$, found 385.1587.

2′-Phenyl-1′-tosylspiro[indoline-3,3′-pyrrolidin]-2-one (6r). This reaction was performed at 0 °C. White solid (52 mg, 45%

yield, dr 1 : 7.9), mp: 169–173 °C; ^{1}H NMR (400 MHz, DMSO-d_6): major isomer: δ 10.43 (s, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 7.9 Hz, 2H), 7.23–6.92 (m, 6H), 6.66 (dd, J = 14.1, 7.4 Hz, 2H), 6.55 (d, J = 7.4 Hz, 1H), 4.81 (s, 1H), 4.00–3.92 (m, 1H), 3.90–3.82 (m, 1H), 2.45 (s, 3H), 2.07–1.96 (m, 1H), 1.92–1.80 (m, 1H); minor isomer: δ 10.55 (s, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 7.9 Hz, 2H), 7.23–6.92 (m, 6H), 6.66 (dd, J = 14.1, 7.4 Hz, 2H), 6.55 (d, J = 7.4 Hz, 1H), 4.83 (s, 1H), 4.28–4.00 (m, 2H), 2.45 (s, 3H), 2.19–2.08 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.8, 143.5, 141.3, 138.7, 133.7, 129.7, 128.4, 128.1, 127.7, 127.4, 127.2, 126.8, 125.0, 121.0, 109.2, 69.1, 58.5, 47.9, 34.5, 21.1; HRMS (ESI) calcd for $C_{24}H_{23}N_2O_3S$ m/z 419.1424 [M + H]$^+$, found 419.1428.

***N*-(2-(2-Benzoyl-1*H*-indol-3-yl)ethyl)-4-methylbenzenesulfonamide (6r′)**.[24c] Yellow oil (110 mg, 50% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.45 (s, 1H), 7.75–7.56 (m, 9H), 7.43 (d, J = 8.1 Hz, 1H), 7.33–7.25 (m, 3H), 7.09 (t, J = 7.2 Hz, 1H), 2.96 (s, 4H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 188.4, 142.4, 138.7, 137.6, 136.7, 132.3, 131.4, 129.5, 128.9, 128.6, 127.2, 126.4, 125.3, 120.3, 120.0, 119.9, 112.8, 43.3, 25.3, 20.9; HRMS (ESI) calcd for $C_{24}H_{23}N_2O_3S$ m/z 419.1424 [M + H]$^+$, found 419.1432.

Methyl 2-oxo-1′-tosylspiro[indoline-3,3′-pyrrolidine]-5′-carboxylate (6s). Light brown oil (87 mg, 95% yield, dr 1 : 1.9); ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.62 and 8.40 (s, 1H), 7.81 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 7.4 Hz, 0.5H), 7.34 (d, J = 8.0 Hz, 2H), 7.26–7.18 (m, 1H), 7.06 (t, J = 7.6 Hz, 0.5H), 6.92–6.85 (m, 1.5H), 6.77 (d, J = 7.5 Hz, 0.5H), 4.79 (t, J = 8.1 Hz, 0.66H), 4.57 (t, J = 7.9 Hz, 0.34H), 3.83 and 3.72 (s, 3H), 3.82–3.57 (m, 2H), 2.68–2.60 (m, 1H), 2.46 and 2.43 (s, 3H), 2.42–2.34 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 179.4, 177.6, 172.0, 171.5, 144.2, 144.0, 140.2, 139.8, 136.1, 133.9, 132.3, 130.5, 129.8, 129.8, 129.0, 128.8, 128.2, 127.6, 124.1, 123.4, 123.2, 123.0, 110.3, 110.1, 60.9, 60.5, 56.8, 56.5, 53.0, 52.8, 52.7, 52.1, 41.5, 40.6, 21.7, 21.7; HRMS (ESI) calcd for $C_{20}H_{21}N_2O_5S$ m/z 401.1166 [M + H]$^+$, found 401.1172.

1′-(*tert*-Butyl) 5′-methyl 2-oxospiro[indoline-3,3′-pyrrolidine]-1′,5′-dicarboxylate (6t).[23b] Colorless oil (98 mg, 93% yield, dr 1 : 3); ^{1}H NMR (400 MHz, CDCl$_3$) Major isomer: δ 8.71 (m, 1H), 7.35–7.21 (m, 1H), 7.16–7.02 (m, 2H), 6.99–6.88 (m, 1H), 4.88–4.71 (m, 1H), 3.94–3.68 (m, 2H), 3.79 (s, 3H), 2.74–2.48 (m, 2H), 1.46 (s, 9H); minor isomer: δ 7.63 (m, 1H), 7.35–7.21 (m, 1H), 7.16–7.02 (m, 2H), 6.99–6.88 (m, 1H), 4.66–4.59 (m, 1H), 3.94–3.68 (m, 2H), 3.80 (s, 3H), 2.45–2.26 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 178.0, 173.4, 172.5, 172.2, 154.4, 153.5, 140.8, 139.8, 133.3, 133.1, 129.4, 129.0, 128.8, 123.4, 123.2, 123.1, 122.5, 110.4, 110.1, 81.0, 80.7, 59.1, 58.7, 55.4, 54.9, 54.5, 52.4, 52.3, 41.0, 40.6, 40.3, 39.7, 28.4, 28.3; HRMS (ESI) calcd for $C_{18}H_{23}N_2O_5$ m/z 347.1601 [M + H]$^+$, found 347.1613.

Methyl 1′-benzyl-2′-methyl-2-oxospiro[indoline-3,3′-pyrrolidine]-5′-carboxylate (6u). Pale yellow oil (93 mg, 95% yield, dr 1.7 : 1); ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.96–8.73 (m, 1H), 7.80 (d, J = 7.4 Hz, 1H), 7.41–7.29 (m, 4H), 7.28–7.18 (m, 2H), 7.14–7.03 (m, 1H), 6.95–6.88 (m, 1H), 4.03–3.80 (m, 1H), 3.79–3.60 (m, 3H), 3.50 (s, 2H), 3.17 (dd, J = 12.1, 6.0 Hz, 1H), 2.76–2.66 (m, 0.6H), 2.51–2.45 (m, 0.4H), 2.30 (dd, J = 13.3, 9.2 Hz, 0.4H), 2.11 (dd, J = 13.4, 6.0 Hz, 0.6H), 0.75 and 0.73 (d, J = 10.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 180.9, 180.3, 174.3, 174.0, 140.6, 140.3, 139.2, 137.4, 132.8, 132.5, 129.5, 128.7, 128.4, 128.2, 128.0, 127.9, 127.2, 126.3, 125.0, 122.8, 122.5, 109.8, 109.6, 67.0, 64.5, 64.2, 60.4, 57.9, 57.3, 55.8, 51.8, 51.5, 50.9, 38.6, 38.2, 14.5, 14.3; HRMS (ESI) calcd for $C_{21}H_{23}N_2O_3$ m/z 351.1703 [M + H]$^+$, found 351.1711.

Methyl 1′-benzyl-2′-methyl-2-oxospiro[indoline-3,3′-pyrrolidine]-5′-carboxylate (6v). Pale yellow oil (87 mg, 94% yield, dr 1 : 8.3); ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.28 (s, 1H), 7.51 (d, J = 7.4 Hz, 1H), 7.44 (d, J = 7.3 Hz, 2H), 7.37–7.31 (m, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.25–7.16 (m, 2H), 7.06 (td, J = 7.6, 0.9 Hz, 1H), 6.87 (d, J = 7.7 Hz, 1H), 4.06–3.98 (m, 2H), 3.78–3.70 (m, 2H), 3.69 (s, 3H), 2.76 (dd, J = 13.7, 9.3 Hz, 1H), 2.17 (dd, J = 13.7, 3.6 Hz, 1H), 1.01 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 180.8, 175.0, 140.6, 139.3, 133.3, 128.5, 128.3, 128.1, 127.0, 124.2, 122.9, 109.3, 66.1, 62.3, 57.3, 51.8, 51.5, 38.3, 12.9; HRMS (ESI) calcd for $C_{21}H_{23}N_2O_3$ m/z 351.1703 [M + H]$^+$, found 351.1711.

Methyl 1′-benzyl-2′-ethyl-2-oxospiro[indoline-3,3′-pyrrolidine]-5′-carboxylate (6w). Yellow oil (96 mg, 89% yield, dr 4.5 : 1); ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.58 and 8.41 (s, 1H), 7.48–7.42 (m, 3H), 7.31 (t, J = 7.4 Hz, 2H), 7.26–7.15 (m, 2H), 7.05 (td, J = 7.6, 0.8 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 4.09 (d, J = 14.2 Hz, 1H), 3.99 (dd, J = 9.1, 3.3 Hz, 1H), 3.88 (d, J = 14.2 Hz, 1H), 3.68 (s, 3H), 2.75 (dd, J = 13.6, 9.1 Hz, 1H), 2.16 (dd, J = 13.6, 3.3 Hz, 1H), 1.78–1.65 (m, 1H), 1.63–1.50 (m, 2H), 0.59 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 181.3, 175.1, 140.4, 139.8, 134.4, 128.4, 128.3, 127.9, 126.9, 124.0, 122.9, 109.4, 73.0, 63.1, 57.1, 52.0, 51.5, 40.0, 21.2, 11.1; HRMS (ESI) calcd for $C_{22}H_{25}N_2O_3$ m/z 365.1860 [M + H]$^+$, found 365.1866.

Methyl 1′-benzyl-2′-ethyl-2-oxospiro[indoline-3,3′-pyrrolidine]-5′-carboxylate (6x). Pale yellow oil (98 mg, 91% yield, dr 1 : 6.2); ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.74 (d, J = 48.5 Hz, 1H), 7.80 (d, J = 7.4 Hz, 1H), 7.39 (d, J = 7.2 Hz, 2H), 7.32 (t, J = 10.1 Hz, 2H), 7.27–7.19 (m, 2H), 7.12–7.06 (m, 1H), 6.91 (d, J = 7.7 Hz, 1H), 4.01 (d, J = 14.3 Hz, 1H), 3.80 (d, J = 14.3 Hz, 1H), 3.69 (dd, J = 10.2, 6.3 Hz, 1H), 3.47 (s, 3H), 3.11 (dd, J = 10.1, 3.7 Hz, 1H), 2.66 (dd, J = 13.3, 10.5 Hz, 1H), 2.09 (dd, J = 13.3, 6.0 Hz, 1H), 1.69–1.54 (m, 2H), 0.51 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 181.6, 174.0, 140.3, 138.0, 132.3, 129.3, 128.2, 127.9, 127.1, 126.5, 122.8, 109.7, 73.0, 64.8, 56.6, 56.1, 51.8, 40.1, 23.3, 9.8; HRMS (ESI) calcd for $C_{22}H_{25}N_2O_3$ m/z 365.1860 [M + H]$^+$, found 365.1866.

1-Methyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (8a).[13e] Yellow solid (22 mg, 35% yield), mp: 181–184 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 9.38 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 3.77 (t, J = 8.3 Hz, 2H), 2.82 (t, J = 8.4 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 159.2, 137.5, 128.6, 125.1, 125.0, 120.4, 120.1, 117.4, 112.2, 47.0, 21.4, 19.2; HRMS (ESI) calcd for $C_{12}H_{13}N_2$ m/z 185.1073 [M + H]$^+$, found 185.1077.

1-Phenyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (8b).[13e] Pale yellow solid (28 mg, 30%), mp: 219–223 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.35 (br s, 1H), 7.85–7.60 (m, 3H), 7.57–7.45 (m, 3H), 7.43–7.15 (m, 3H), 4.06 (s, 2H), 3.01 (s, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 159.4, 137.7, 136.6, 130.0, 128.9, 127.9, 127.9, 125.6, 124.6, 120.5, 120.1, 117.9, 112.1, 48.9, 19.3; HRMS (ESI) calcd for $C_{17}H_{15}N_2$ m/z 247.1230 [M + H]$^+$, found 247.1226.

Conflicts of interest

There are no conflicts to declare.

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