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Rhodium(II)-Catalyzed [4+3] Cyclization of Triazoles with Indole Derivatives and Its Application in the Total Synthesis of (±)-Aurantioclavine

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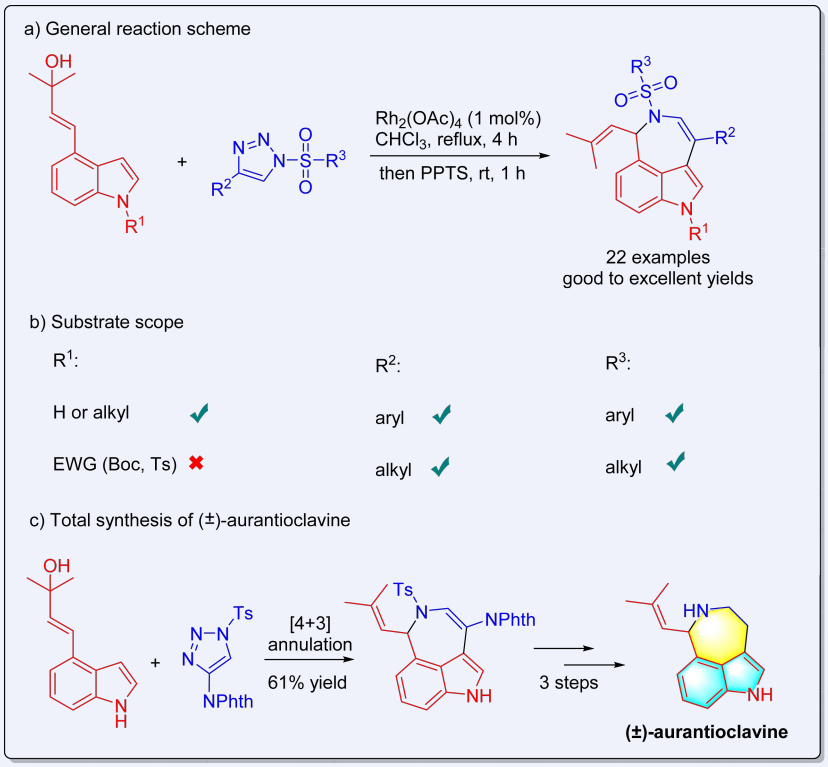
Keywords

Triazoles | Rhodium | Alkaloids | Cyclization | Aurantioclavine

Main observation and conclusion

An efficient rhodium(II)-catalyzed [4+3] cyclization reaction of 1-sulfonyl-1,2-3-triazoles and indoles was developed. Azepino[5,4,3-*cd*]indoles, which are widely distributed in ergot alkaloids with various biological activities, could be obtained in good to excellent yields. In addition, the total synthesis of (±)-aurantioclavine was completed in four steps from the known compound **1a** adopting this [4+3] cyclization as a key step.

Comprehensive Graphic Content



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Background and Originality Content

Azepino[5,4,3-*cd*]indole skeleton is mainly found in some indole alkaloids (Figure 1). This special unit consists of only three rings, but the related natural products exhibited a variety of important biological activities.[1a] For example, fargesine, which was isolated from *Evodia fargesii*, demonstrated inhibitory activity on monoamine oxidase-A;[1] hyrtinadine C, isolated from the marine sponge *Hyrtios* sp., showed antimicrobial activity.[2] In addition, communesin F, which has attracted much attention due to significant cytotoxicity and exquisite structural complexity, also contains an azepino[5,4,3-*cd*]indole core.[3] Aurantioclavine, the simplest azepinoindole alkaloid, which was isolated from *Penicillium aurantiovirens* by Kozlovskii and coworkers in 1981,[4] has been proven to be a biosynthetic intermediate of communesins alkaloids.[5] Thus, aurantioclavine was an attractive synthetic target for synthetic chemists.[6]

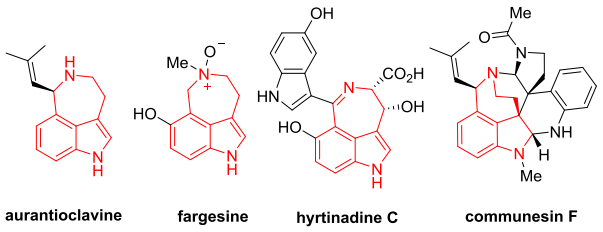


Figure 1 Representative natural products containing azepinoindole core.

In 2008, Gevorgyan and Fokin reported a rhodium(II)-catalyzed denitrogenative transannulation reaction by converting 1-sulfonyl-1,2,3-triazoles to imidazoles *via* α-imino rhodium(II) carbene intermediates (Scheme 1a).[7] On the basis of this seminal work, α-imino carbene became one of the most important intermediates, especially in the synthesis of nitrogen-containing heterocycles.[8] Due to the high electrophilic nature of the rhodium(II) carbene and the nucleophilic sulfonylimine moiety, α-imino carbene often acts as an aza-[3C] synthon in cyclization reaction. Meanwhile, as an excellent nucleophile, indole was used in several reactions with 1-sulfonyl-1,2,3-triazoles.[9-10] Accordingly, a retrosynthesis of azepino[5,4,3-*cd*]indole would lead to a triazole-derived α-imino carbene and a suitable [4C] synthon containing indole (Scheme 1b). Herein, we report facile synthesis of azepino-[5,4,3-*cd*]indoles through rhodium(II)-catalyzed [4+3] cyclization of 1-sulfonyl-1,2,3-triazoles and indole derivatives. Furthermore, the total synthesis of (±)-aurantioclavine was completed in four steps adopting this [4+3] cyclization as a key step.

To simulate the substituents in the natural product, a tertiary allyl alcohol was introduced at the 4-position of indole (Scheme 1c, compounds **1a** and **1b**). It is worth noting that there are three potential nucleophilic sites in this compound, including oxygen, nitrogen and the C3 position of indole. From our initial hypothesis, we thought the steric hindrance of the tertiary alcohol would reduce the reaction of the hydroxyl attacking the rhodium carbene and by protecting the nitrogen with methyl would facilitate the reaction between the C3 position of indole and carbene. If intermediate **3aa** or **3ba** could be obtained, an appropriate acid would promote the formation of a 7-membered ring in spite of higher ring strain.

Results and Discussion

We started our investigation with the reaction of readily available indole **1a** and triazole **2a** in the presence of $Rh_2(OAc)_4$. The reaction mixture was complicated and the uncyclized product

Scheme 1 Previous work and our proposal

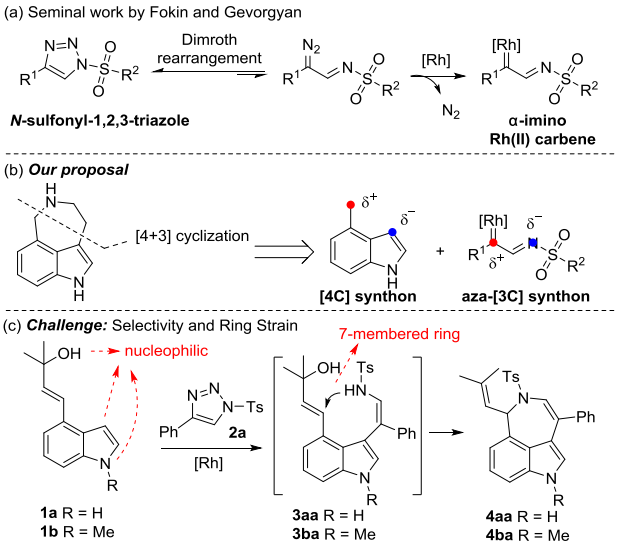
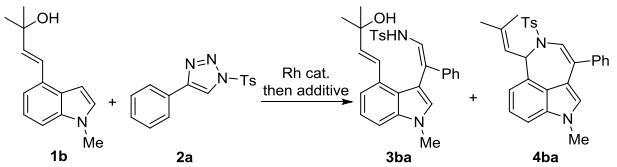


Table 1 Optimization of reaction conditions[a]



entry	[Rh]	additive	solvent	**3ba**/**4ba**[b] (%)
1	$Rh_2(OAc)_4$	—	DCE	74/9
2	$Rh_2(piv)_4$	—	DCE	5/23
3	$Rh_2(oct)_4$	—	DCE	15/40
4	$Rh_2(adc)_4$	—	DCE	13/37
5	$Rh_2(OAc)_4$	$TsOH·H_2O$	DCE	0/0
6	$Rh_2(OAc)_4$	PPTS	DCE	0/0
7	$Rh_2(OAc)_4$	$TsOH·H_2O$[c]	DCE	0/50
8	$Rh_2(OAc)_4$	PPTS[c]	DCE	0/85
9	$Rh_2(piv)_4$	PPTS[c]	DCE	0/32
10	$Rh_2(oct)_4$	PPTS[c]	DCE	0/59
11	$Rh_2(esp)_4$	PPTS[c]	DCE	0/83
12	$Rh_2(adc)_4$	PPTS[c]	DCE	0/60
13	$Rh_2(dpf)_4$	PPTS[c]	DCE	0/0
14[d]	$Rh_2(OAc)_4$	PPTS[c]	DCE	0/89
15[d]	$Rh_2(OAc)_4$	PPTS[c]	toluene	0/71
16[d]	$Rh_2(OAc)_4$	PPTS[c]	PhCl	0/77
17[d]	$Rh_2(OAc)_4$	PPTS[c]	$CHCl_3$	0/93
18[d]	$Rh_2(OAc)_4$	PPTS[c]	CH_2Cl_2	0/88
19[d,e]	$Rh_2(OAc)_4$	PPTS[c]	$CHCl_3$	0/97

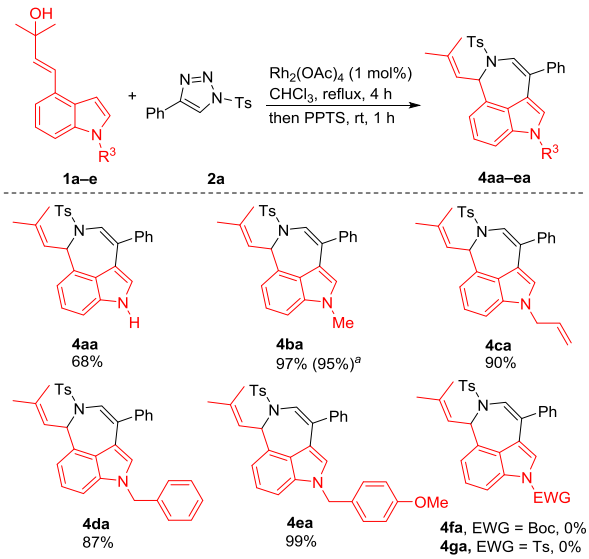
[a] Reaction conditions: **1b** (0.4 mmol), **2a** (0.2 mmol), [Rh] (5 mol%), additive (0.2 mmol), solvent (2 mL), N_2 atmosphere, reflux, 4 h. [b] Isolated yield. [c] After 4 h, the reaction mixture was cooled to room temperature, then the additive was added and stirred for 0.5 h. [d] [Rh] (1 mol%). [e] Compound **1b** (0.3 mmol). PPTS: Pyridinium *p*-toluenesulfonate.

3aa was obtained in 46% yield. When the analogue **1b** was used in this transformation, the target product **4ba** was obtained in 9% yield (Table 1, entry 1) in addition to the uncyclized product **3ba** (74% yield).[11] Encouraged by this result, the reaction conditions were further screened to improve the yield of **4ba**. Different rhodium(II) catalysts were tried in this reaction (Table 1, entries 2—4), and **4ba** was obtained in low yield. Additives such as *p*-toluenesulfonic acid and pyridinium *p*-toluenesulfonate (PPTS) were employed to promote the cyclization. Disappointingly, the reaction mixture was complicated, and it is believed that the decomposi-

tion of the related compounds was observed due to the increase in temperature and acidic conditions (Table 1, entries 5—6). We then added the acid after the mixture was cooled to room temperature. To our delight, the yield of **4ba** increased to 85% yield when using PPTS (Table 1, entry 8). A variety of rhodium(II) catalysts were examined at this stage, and $Rh_2(OAc)_4$ was still the best choice (Table 1, entries 9—13). Reducing the amount of catalyst to 1 mol% could slightly increase the yield of **4ba** to 89% (Table 1, entry 14). Various solvents were tried in this reaction, and chloroform gave the best results (Table 1, entries 15—18). At last, **4ba** could be obtained in 97% yield when reducing the amount of **1b** to 1.5 equivalents (Table 1, entry 19). We hypothesized this situation is probably due to the reaction between the intermediate **3ba** or the product **4ba** and the carbocation, which was easily generated by tertiary alcohol under acidic conditions.

With the optimal reaction conditions in hand (Table 1, entry 19), the substrate scope was investigated using a variety of indoles (Scheme 2). Surprisingly, the NH unprotected indole **1a** gave the product **4aa** in 68% yield. Other indoles with electron donating groups, such as methyl, allyl, benzyl, and *p*-methoxybenzyl, led to the corresponding products in excellent yields (**4ba**—**4ea**, 87%—99%). To test the practicality of this newly developed method, the reaction of triazole **1b** and indole **2a** was carried out in 1 mmol scale under the standard reaction conditions. The cyclization product **4ba** was isolated in 95% yield. It is worth noting that indoles with electron withdrawing groups, such as *tert*-butoxycarbonyl and tosyl, could not furnish the related products (**4fa**, **4ga**).

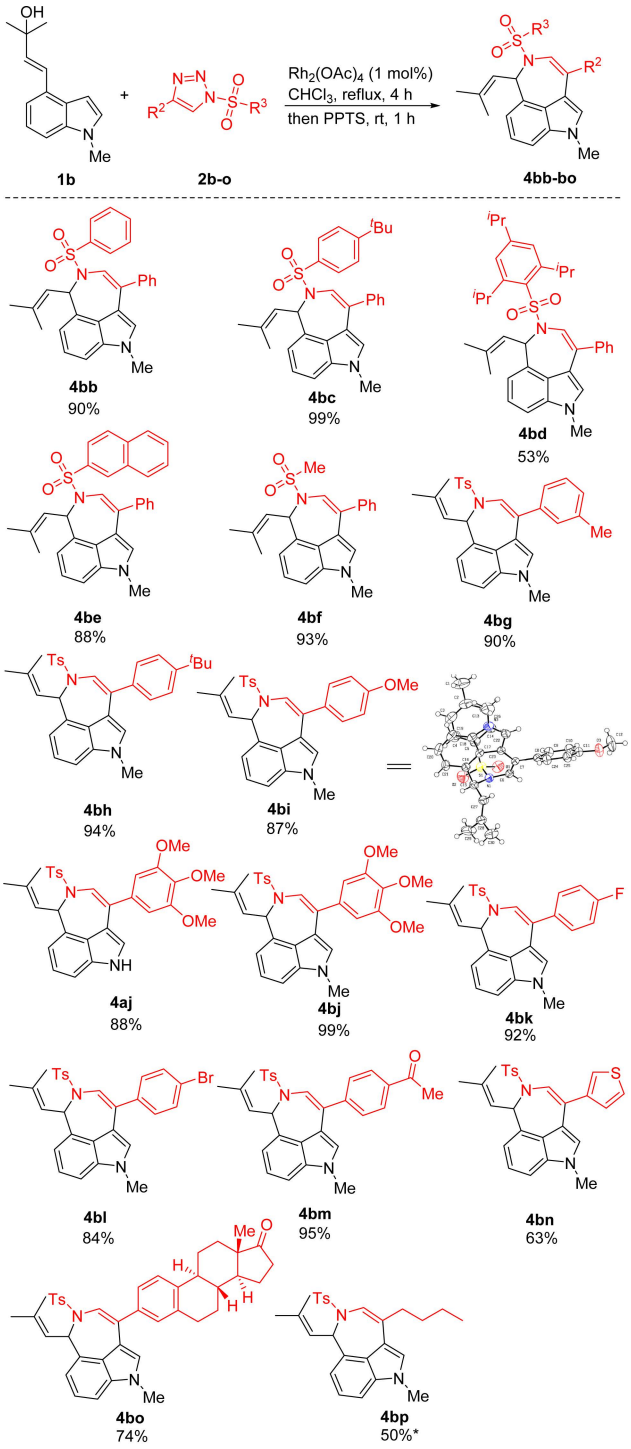
Scheme 2 The substrate scope of indoles



[a]Run in 1 mmol scale.

Then, the studies on a series of 1-sulfonyl-1,2,3-triazoles were carried out, and the results were summarized in Scheme 3. At first, the cyclization reactions of triazoles **2b**—**2f** with different sulfonyl groups were carried out under the optimized condition. It was found that the yield of **4bd** (53%) was much lower than those of other compounds (**4bb**, **4bc**, **4be**, **4bf**, 88%—99%), which may be because of the steric hindrance of *ortho*-isopropyl groups. Next, various substituents on C-4 position of triazoles were examined. Electronic effect of the benzene ring had marginal impact on the results, good to excellent yields could be achieved when substrates with electron donating groups (**2g**—**2j**) or electron withdrawing groups (**2k**—**2m**) were used. The structure of **4bi** was unambiguously confirmed by X-ray crystallographic analysis.[12] In

Scheme 3 The substrate scope of 1-sulfonyl-1,2,3-triazoles

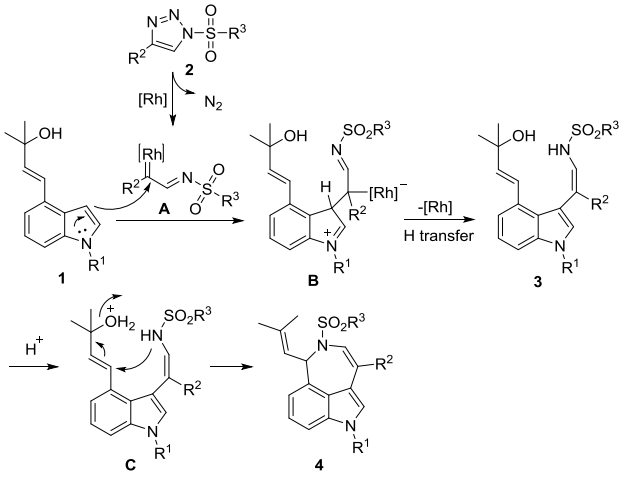


*$Rh_2(adc)_4$ (5 mol%) was employed in this reaction.

addition, thiophene derivative (**4bn**) and estron derivative (**4bo**) were obtained smoothly using this method. With slightly modified conditions, alkyl substituted triazole (**2p**) could also be applied to this reaction.

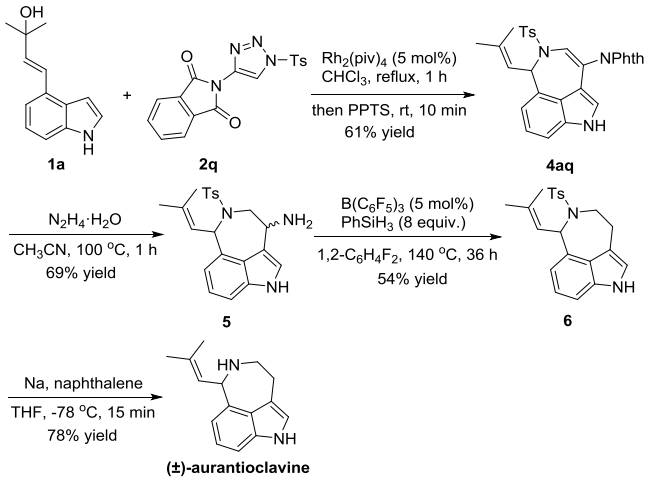
A plausible mechanism was proposed based on the reaction results and previous reports[7-8] (Scheme 4). The C-3 position of indole **1** attacked the α-imino rhodium(II) carbene, which was generated from 1-sulfonyl-1,2,3-triazole in the presence of rhodium(II) catalyst, delivering uncyclized compounds **3**. Then an acid promoted intramolecular S_N2' reaction led to the formation of final product **4**.

Scheme 4 The proposed mechanism



To further demonstrate the utility of this reaction, the total synthesis of (±)-aurantioclavine was completed using this [4+3] cyclization as the key step (Scheme 5). The tricyclic compound **4aq** could be produced smoothly employing **1a** and **2q** as starting materials under a slightly modified procedure. The reduction of the double bond and hydrazinolysis of phthalimide were achieved in one step using $N_2H_4{\cdot}H_2O$. At last, (±)-aurantioclavine was obtained after removal of the amino[13] and tosyl group.

Scheme 5 Total synthesis of (±)-aurantioclavine



Conclusions

In conclusion, we have developed a facile rhodium(II)-catalyzed [4+3] cyclization of 1-sulfonyl-1,2,3-triazoles and indoles to synthesize azepino[5,4,3-*cd*]indoles under mild conditions with good to excellent yields. In addition, by adopting this [4+3] cyclization as a key step, a concise total synthesis of (±)-aurantioclavine was completed in four steps from the known compound **1a**.

Experimental

General procedure for synthesis of 4

The mixture of **1** (0.3 mmol), **2** (0.2 mmol), and $Rh_2(OAc)_4$ (1 mol%) was heated to reflux for 4 h under N_2. Then pyridinium *p*-toluenesulfonate (0.2 mmol) was added to the mixture after cooling to room temperature, and then the mixture was stirred for 1 h at room temperature. The mixture was filtered through a pad of Celite and the eluent was concentrated *in vacuo*. The residue was purified by silica gel column chromatography.

1-(2-Methylprop-1-en-1-yl)-4-phenyl-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4aa**): Brown solid, m.p. 124—125 °C; 61.8 mg, 68% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.18—8.08 (br, 1H), 7.52—7.46 (m, 2H), 7.43—7.35 (m, 3H), 7.30—7.26 (m, 2H), 7.18—7.09 (m, 2H), 6.97—6.92 (m, 1H), 6.72 (d, *J* = 8.0 Hz, 2H), 6.67 (d, *J* = 2.6 Hz, 1H), 6.18 (t, *J* = 4.4 Hz, 2H), 5.29—5.23 (m, 1H), 2.12 (s, 3H), 1.91 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.2, 139.9, 136.8, 136.5, 135.6, 135.5, 135.3, 129.2, 128.5, 128.2, 128.0, 126.9, 124.2, 123.4, 123.2, 122.9, 119.9, 117.8, 115.7, 110.1, 60.6, 25.9, 21.3, 18.9; ESI-HRMS *m*/*z* calcd for $C_{28}H_{27}N_2O_2S^+$ $[M + H]^+$ 455.1788, found 455.1796.

6-Methyl-1-(2-methylprop-1-en-1-yl)-4-phenyl-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4ba**): Off-white solid, m.p. 65—66 °C; 90.9 mg, 97% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53—7.48 (m, 2H), 7.45—7.37 (m, 3H), 7.27—7.22 (m, 2H), 7.20—7.13 (m, 1H), 7.12—7.06 (m, 1H), 6.96 (d, *J* = 6.9 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 2H), 6.53 (s, 1H), 6.17 (d, *J* = 8.8 Hz, 1H), 6.14 (s, 1H), 5.25 (d, *J* = 8.8 Hz, 1H), 3.60 (s, 3H), 2.13 (s, 3H), 1.92 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 141.9, 140.0, 137.7, 136.7, 135.7, 135.4, 129.2, 128.7, 128.5, 128.1, 128.0, 126.9, 124.1, 123.2, 122.5, 119.3, 117.6, 114.3, 108.3, 60.7, 32.9, 25.9, 21.4, 18.9 (one carbon missed); ESI-HRMS *m*/*z* calcd for $C_{29}H_{29}N_2O_2S^+$ $[M + H]^+$ 469.1944, found 469.1951.

6-Allyl-1-(2-methylprop-1-en-1-yl)-4-phenyl-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4ca**): Brown solid, m.p. 50—51 °C; 89.0 mg, 90% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ: 7.53—7.48 (m, 2H), 7.46—7.36 (m, 3H), 7.34—7.28 (m, 2H), 7.26—7.22 (m, 1H), 7.17—7.11 (m, 1H), 6.97 (d, *J* = 7.1 Hz, 1H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.75 (s, 1H), 6.23—6.17 (m, 1H), 6.11—6.06 (m, 1H), 5.97—5.84 (m, 1H), 5.34—5.26 (m, 1H), 5.16—5.09 (m, 1H), 5.01—4.92 (m, 1H), 4.78—4.64 (m, 2H), 2.16 (s, 3H), 1.91 (s, 3H), 1.59 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (101 MHz, Acetone-d_6) δ: 143.4, 141.0, 138.3, 137.9, 136.3, 136.0, 135.6, 134.8, 129.9, 129.5, 129.3, 129.1, 128.8, 127.7, 125.1, 124.5, 123.1, 119.8, 118.2, 117.4, 115.0, 110.1, 61.3, 49.4, 25.9, 21.4, 18.9; ESI-HRMS *m*/*z* calcd for $C_{31}H_{31}N_2O_2S^+$ $[M + H]^+$ 495.2101, found 495.2105.

6-Benzyl-1-(2-methylprop-1-en-1-yl)-4-phenyl-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4da**): Off-white solid, m.p. 214—215 °C; 94.8 mg, 87% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54—7.47 (m, 2H), 7.43—7.35 (m, 3H), 7.34—7.25 (m, 5H), 7.12—6.98 (m, 4H), 6.97—6.91 (m, 1H), 6.76 (d, *J* = 8.0 Hz, 2H), 6.69 (s, 1H), 6.23—6.16 (m, 2H), 5.31—5.25 (m, 1H), 5.16 (d, *J* = 16.1 Hz, 1H), 5.10 (d, *J* = 16.1 Hz, 1H), 2.14 (s, 3H), 1.92 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.2, 140.0, 137.4, 137.0, 136.9, 135.9, 135.6, 134.7, 129.2, 128.9, 128.5, 128.3, 128.2, 128.0, 127.9, 127.0, 126.7, 124.3, 123.2, 122.6, 119.8, 117.7, 114.9, 108.9, 60.5, 50.3, 25.9, 21.5, 18.9; ESI-HRMS *m*/*z* calcd for $C_{35}H_{33}N_2O_2S^+$ $[M + H]^+$ 545.2257, found 545.2260.

6-(4-Methoxybenzyl)-1-(2-methylprop-1-en-1-yl)-4-phenyl-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4ea**): White solid, m.p. 189—190 °C; 113.8 mg, 99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52—7.47 (m, 2H), 7.43—7.35 (m, 3H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.12—7.03 (m, 2H), 6.99—6.91 (m, 3H), 6.84—6.78 (m, 2H), 6.75 (d, *J* = 8.0 Hz, 2H), 6.68—6.66 (m, 1H), 6.22—6.16 (m, 2H), 5.31—5.25 (m, 1H), 5.08 (d, *J* = 15.7 Hz, 1H), 5.02 (d, *J* = 15.7 Hz, 1H), 3.76 (s, 3H), 2.13 (s, 3H), 1.91 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.3, 142.1, 140.0, 137.3, 136.9, 135.8, 135.5, 134.7, 129.2, 128.9, 128.5, 128.3, 128.1, 128.02, 127.95, 127.0, 124.3, 123.2, 122.5, 119.6, 117.6, 114.6, 114.3, 108.9, 60.5, 55.4, 49.8, 25.9, 21.4, 18.8; ESI-HRMS *m*/*z* calcd for $C_{36}H_{35}N_2O_3S^+$ $[M + H]^+$ 575.2363, found 575.2370.

6-Methyl-1-(2-methylprop-1-en-1-yl)-4-phenyl-2-(phenylsulfonyl)-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bb**): White solid, m.p. 214—215 °C; 81.8 mg, 90% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ:

7.52—7.47 (m, 2H), 7.44—7.33 (m, 5H), 7.18—7.12 (m, 1H), 7.11—7.04 (m, 2H), 6.98—6.94 (m, 1H), 6.92—6.85 (m, 2H), 6.50 (s, 1H), 6.18 (d, *J* = 8.7 Hz, 1H), 6.15 (s, 1H), 5.29—5.22 (m, 1H), 3.57 (s, 3H), 1.93 (s, 3H), 1.60 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 139.9, 139.5, 137.7, 135.8, 135.8, 135.5, 131.2, 129.2, 128.8, 128.5, 128.0, 127.5, 126.9, 124.0, 123.2, 122.4, 119.0, 117.5, 114.2, 108.4, 60.7, 32.9, 25.9, 18.8; ESI-HRMS *m*/*z* calcd for $C_{28}H_{27}N_2O_2S^+$ $[M + H]^+$ 455.1788, found 455.1791.

2-((4-(*tert*-Butyl)phenyl)sulfonyl)-6-methyl-1-(2-methylprop-1-en-1-yl)-4-phenyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bc**): Yellow solid, m.p. 84—85 °C; 101.1 mg, 99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.56—7.49 (m, 2H), 7.45—7.35 (m, 3H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.17—7.10 (m, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.94 (d, *J* = 7.1 Hz, 1H), 6.91—6.85 (m, 2H), 6.52 (s, 1H), 6.19—6.12 (m, 2H), 5.28—5.20 (m, 1H), 3.55 (s, 3H), 1.92 (s, 3H), 1.59 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 155.1, 140.0, 137.6, 136.3, 136.3, 135.6, 135.53, 135.46, 129.2, 128.5, 128.0, 126.7, 124.4, 123.9, 123.2, 122.4, 119.4, 117.5, 114.2, 108.3, 60.5, 34.7, 32.9, 31.0, 25.8, 18.8; ESI-HRMS *m*/*z* calcd for $C_{32}H_{34}N_2NaO_2S^+$ $[M + Na]^+$ 533.2233, found 533.2236.

6-Methyl-1-(2-methylprop-1-en-1-yl)-4-phenyl-2-((2,4,6-triisopropylphenyl)sulfonyl)-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bd**): White solid, m.p. 187—188 °C; 61.6 mg, 53% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.37—7.31 (m, 5H), 7.21—7.14 (m, 2H), 7.02 (s, 2H), 6.92 (dd, *J* = 5.8, 2.2 Hz, 1H), 6.73 (s, 1H), 6.33 (d, *J* = 9.5 Hz, 1H), 6.23 (s, 1H), 5.49—5.42 (m, 1H), 4.07—3.96 (m, 2H), 3.70 (s, 3H), 2.88—2.77 (m, 1H), 1.93 (s, 3H), 1.61 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 6H), 1.09 (d, *J* = 6.7 Hz, 6H), 0.86 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 153.0, 151.5, 140.6, 137.9, 136.2, 134.2, 132.5, 130.0, 129.3, 128.4, 128.3, 127.6, 124.3, 123.7, 123.6, 122.4, 119.4, 116.8, 114.8, 108.4, 58.4, 34.2, 33.1, 29.6, 26.1, 24.71, 24.66, 23.7, 23.6, 18.9; ESI-HRMS *m*/*z* calcd for $C_{37}H_{44}N_2NaO_2S^+$ $[M + Na]^+$ 603.3016, found 603.3022.

6-Methyl-1-(2-methylprop-1-en-1-yl)-2-(naphthalen-2-ylsulfonyl)-4-phenyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4be**): Yellow solid, m.p. 110—111 °C; 88.8 mg, 88% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.71—7.67 (m, 1H), 7.60—7.55 (m, 1H), 7.52—7.47 (m, 2H), 7.46—7.34 (m, 7H), 7.20 (s, 1H), 7.17—7.10 (m, 1H), 7.00 (d, *J* = 7.1 Hz, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 6.22 (d, *J* = 8.7 Hz, 1H), 6.18 (d, *J* = 12.4 Hz, 2H), 5.22 (d, *J* = 8.6 Hz, 1H), 3.15 (s, 3H), 1.96 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 139.8, 137.5, 137.4, 136.4, 136.1, 135.0, 134.2, 131.5, 129.3, 129.1, 128.7, 128.5, 128.13, 128.06, 127.9, 127.2, 126.8, 126.3, 123.9, 123.2, 122.8, 122.4, 118.9, 117.8, 114.0, 108.5, 61.1, 32.4, 25.9, 18.9; ESI-HRMS *m*/*z* calcd for $C_{32}H_{29}N_2O_2S^+$ $[M + H]^+$ 505.1944, found 505.1943.

6-Methyl-1-(2-methylprop-1-en-1-yl)-2-(methylsulfonyl)-4-phenyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bf**): White solid, m.p. 182—183 °C; 73.0 mg, 93% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.59—7.52 (m, 2H), 7.45—7.35 (m, 3H), 7.29—7.20 (m, 2H), 7.02 (d, *J* = 6.4 Hz, 1H), 6.85 (s, 1H), 6.15—6.09 (m, 2H), 5.31 (d, *J* = 8.6 Hz, 1H), 3.75 (s, 3H), 2.38 (s, 3H), 1.93 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 139.8, 137.9, 136.1, 135.9, 134.5, 129.3, 128.5, 128.1, 123.8, 123.0, 122.8, 119.5, 117.5, 114.1, 109.0, 59.9, 39.1, 33.2, 25.9, 18.8 (one carbon missed); ESI-HRMS *m*/*z* calcd for $C_{23}H_{24}N_2NaO_2S^+$ $[M + Na]^+$ 415.1451, found 415.1452.

6-Methyl-1-(2-methylprop-1-en-1-yl)-4-(*m*-tolyl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bg**): Light yellow solid, m.p. 179—180 °C; 86.9 mg, 90% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.36—7.28 (m, 3H), 7.28—7.22 (m, 2H), 7.22—7.12 (m, 2H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.95 (d, *J* = 7.0 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 2H), 6.54 (s, 1H), 6.19—6.11 (m, 2H), 5.28—5.21 (m, 1H), 3.60 (s, 3H), 2.41 (s, 3H), 2.13 (s, 3H), 1.92 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 141.9, 140.0, 138.2, 137.7, 136.7, 135.6, 129.8, 128.8, 128.7, 128.4, 128.0, 126.9, 126.3, 124.1, 123.2, 122.4, 119.1, 117.6, 114.3, 108.3, 60.7, 32.9, 25.9, 21.6, 21.4, 18.9 (two carbon missed); ESI-HRMS *m*/*z* calcd for $C_{30}H_{31}N_2O_2S^+$ $[M + H]^+$ 483.2101, found 483.2106.

4-(4-(*tert*-Butyl)phenyl)-6-methyl-1-(2-methylprop-1-en-1-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bh**): Light yellow solid, m.p. 174—175 °C; 98.6 mg, 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.48—7.39 (m, 4H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.18—7.12 (m, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.95 (d, *J* = 7.0 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 2H), 6.58 (s, 1H), 6.16 (d, *J* = 8.8 Hz, 1H), 6.13 (s, 1H), 5.28—5.21 (m, 1H), 3.59 (s, 3H), 2.11 (s, 3H), 1.92 (s, 3H), 1.58 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 151.1, 141.8, 137.7, 137.0, 136.6, 135.7, 135.5, 128.8, 128.0, 126.9, 125.4, 124.1, 123.3, 122.4, 119.0, 117.5, 114.2, 108.3, 60.7, 34.8, 32.9, 31.5, 25.9, 21.3, 18.9 (two carbon missed); ESI-HRMS *m*/*z* calcd for $C_{33}H_{37}N_2O_2S^+$ $[M + H]^+$ 525.2570, found 525.2573.

4-(4-Methoxyphenyl)-6-methyl-1-(2-methylprop-1-en-1-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bi**): Off-white solid, m.p. 211—212 °C; 86.8 mg, 87% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.46—7.41 (m, 2H), 7.23—7.19 (m, 2H), 7.18—7.12 (m, 1H), 7.11—7.05 (m, 1H), 6.98—6.91 (m, 3H), 6.66 (d, *J* = 8.1 Hz, 2H), 6.53 (s, 1H), 6.16 (d, *J* = 8.8 Hz, 1H), 6.09 (s, 1H), 5.24 (d, *J* = 8.8 Hz, 1H), 3.86 (s, 3H), 3.59 (s, 3H), 2.12 (s, 3H), 1.92 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 159.6, 141.8, 137.7, 136.6, 135.7, 135.6, 135.4, 132.3, 130.3, 128.7, 128.0, 126.8, 124.1, 123.2, 122.4, 118.5, 117.6, 114.5, 113.9, 108.2, 60.7, 55.5, 32.9, 25.9, 21.3, 18.9; ESI-HRMS *m*/*z* calcd for $C_{30}H_{31}N_2O_3S^+$ $[M + H]^+$ 499.2050, found 499.2053.

1-(2-Methylprop-1-en-1-yl)-2-tosyl-4-(3,4,5-trimethoxyphenyl)-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4aj**): Red solid, m.p. 90—91 °C; 95.9 mg, 88% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.85—8.69 (br, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.92 (d, *J* = 7.1 Hz, 1H), 6.79—6.72 (m, 3H), 6.71 (s, 2H), 6.23—6.12 (m, 2H), 5.32—5.22 (m, 1H), 3.90 (s, 3H), 3.84 (s, 6H), 2.14 (s, 3H), 1.89 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 153.1, 142.5, 137.8, 136.8, 136.4, 135.7, 135.4, 135.22, 135.16, 128.3, 126.8, 124.7, 123.2, 123.0, 122.7, 119.0, 117.6, 115.0, 110.4, 106.3, 61.0, 60.7, 56.3, 25.8, 21.2, 18.8; ESI-HRMS *m*/*z* calcd for $C_{31}H_{33}N_2O_5S^+$ $[M + H]^+$ 545.2105, found 545.2108.

6-Methyl-1-(2-methylprop-1-en-1-yl)-2-tosyl-4-(3,4,5-trimethoxyphenyl)-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bj**): Light yellow solid, m.p. 60—61 °C; 110.6 mg, 99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.28—7.23 (m, 3H), 7.19—7.15 (m, 1H), 7.13—7.09 (m, 1H), 6.98—6.94 (m, 1H), 6.74—6.70 (m, 4H), 6.63 (s, 1H), 6.19—6.14 (m, 2H), 5.26 (d, *J* = 8.8 Hz, 1H), 3.91 (s, 3H), 3.88 (s, 6H), 3.63 (s, 3H), 2.15 (s, 3H), 1.92 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 153.2, 142.1, 138.0, 137.7, 136.6, 135.6, 135.5, 135.3, 128.7, 128.1, 126.8, 123.9, 123.0, 122.5, 118.9, 117.6, 114.0, 108.3, 106.3, 61.0, 60.7, 56.4, 33.0, 25.9, 21.4, 18.8 (one carbon missed); ESI-HRMS *m*/*z* calcd for $C_{32}H_{35}N_2O_5S^+$ $[M + H]^+$ 559.2261, found 559.2265.

4-(4-Fluorophenyl)-6-methyl-1-(2-methylprop-1-en-1-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bk**): White solid, m.p. 203—204 °C; 89.5 mg, 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.49—7.43 (m, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.20—7.14 (m, 1H), 7.13—7.06 (m, 3H), 6.96 (d, *J* = 7.0 Hz, 1H), 6.70 (d, *J* = 8.1 Hz, 2H), 6.49 (s, 1H), 6.16 (d, *J* = 8.8 Hz, 1H), 6.10 (s, 1H), 5.22 (d, *J* = 8.8 Hz, 1H), 3.61 (s, 3H), 2.14 (s, 3H), 1.92 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 162.7 (d, *J* = 247.5 Hz), 142.0, 137.8, 136.7, 136.0, 135.8, 135.7, 134.4, 130.8 (d, *J* = 7.9 Hz), 128.5, 128.1, 126.9, 124.0, 123.1, 122.6, 119.4, 117.7, 115.4 (d, *J* = 21.4 Hz), 114.4, 108.4, 60.6, 32.9, 25.9, 21.4, 18.9; ESI-HRMS *m*/*z* calcd for $C_{29}H_{28}FN_2O_2S^+$ $[M + H]^+$ 487.1850, found 487.1855.

4-(4-Bromophenyl)-6-methyl-1-(2-methylprop-1-en-1-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bl**): Light yellow solid, m.p. 209—210 °C; 92.0 mg, 84% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.53 (d, *J* = 8.4 Hz, 2H), 7.41—7.34 (m, 2H), 7.27—7.21 (m, 2H), 7.20—7.14 (m, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 6.95 (d, *J* =

7.0 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 2H), 6.50 (s, 1H), 6.16 (d, *J* = 8.8 Hz, 1H), 6.12 (s, 1H), 5.21 (d, *J* = 8.8 Hz, 1H), 3.62 (s, 3H), 2.14 (s, 3H), 1.91 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 142.1, 139.0, 137.8, 136.6, 135.8, 135.6, 134.1, 131.7, 130.8, 128.4, 128.2, 126.8, 123.9, 123.0, 122.6, 122.0, 119.5, 117.7, 114.0, 108.4, 60.6, 33.0, 25.9, 21.4, 18.9; ESI-HRMS *m*/*z* calcd for $C_{29}H_{27}BrN_2NaO_2S^+$ $[M + Na]^+$ 569.0869, found 569.0869.

1-(4-(6-Methyl-1-(2-methylprop-1-en-1-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indol-4-yl)phenyl)ethan-1-one (**4bm**): Light yellow solid, m.p. 163—164 °C; 97.0 mg, 95% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.03—7.97 (m, 2H), 7.63—7.57 (m, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.21—7.15 (m, 1H), 7.11 (d, *J* = 8.3 Hz, 1H), 6.96 (d, *J* = 6.9 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 2H), 6.52 (s, 1H), 6.21 (s, 1H), 6.17 (d, *J* = 8.8 Hz, 1H), 5.26—5.19 (m, 1H), 3.62 (s, 3H), 2.65 (s, 3H), 2.15 (s, 3H), 1.91 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 197.8, 145.1, 142.2, 137.8, 136.8, 136.7, 135.9, 135.6, 133.7, 129.4, 128.7, 128.34, 128.27, 126.9, 124.0, 123.0, 122.7, 120.3, 117.7, 113.7, 108.4, 60.6, 33.0, 26.8, 25.9, 21.4, 18.9; ESI-HRMS *m*/*z* calcd for $C_{31}H_{31}N_2O_3S^+$ $[M + H]^+$ 511.2050, found 511.2059.

6-Methyl-1-(2-methylprop-1-en-1-yl)-4-(thiophen-3-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bn**): White solid, m.p. 144—145 °C; 59.8 mg, 63% yield; ^{1}H NMR (400 MHz, Acetone-d_6) *δ*: 7.59—7.52 (m, 2H), 7.31—7.22 (m, 4H), 7.19—7.12 (m, 1H), 6.97—6.91 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.21 (s, 1H), 6.16 (d, *J* = 8.9 Hz, 1H), 5.30—5.19 (m, 1H), 3.74 (s, 3H), 2.18 (s, 3H), 1.90 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (101 MHz, Acetone-d_6) *δ*: 143.4, 141.5, 138.9, 137.9, 136.2, 135.4, 130.6, 130.0, 129.3, 129.2, 127.7, 126.8, 125.0, 124.5, 124.2, 123.0, 119.3, 118.1, 114.2, 109.6, 61.6, 33.1, 25.9, 21.4, 18.9; ESI-HRMS *m*/*z* calcd for $C_{27}H_{27}N_2O_2S_2^+$ $[M + H]^+$ 475.1508, found 475.1515.

(8*R*,9*S*,13*S*,14*S*)-13-Methyl-3-(6-methyl-1-(2-methylprop-1-en-1-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indol-4-yl)-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (**4bo**): Yellow solid, m.p. 160—161 °C; 95.4 mg, 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.37—7.27 (m, 3H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.19—7.12 (m, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.95 (d, *J* = 7.0 Hz, 1H), 6.67 (d, *J* = 7.9 Hz, 2H), 6.62—6.55 (m, 1H), 6.15 (s, 2H), 5.23 (d, *J* = 8.7 Hz, 1H), 3.61 (s, 3H), 3.07—2.91 (m, 2H), 2.61—2.42 (m, 2H), 2.42—2.30 (m, 1H), 2.24—1.96 (m, 8H), 1.91 (s, 3H), 1.77—1.41 (m, 8H), 0.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 220.8, 141.8, 139.8, 137.7, 137.5, 136.9, 136.7, 135.7, 135.6, 135.4, 129.6, 128.7, 128.0, 126.9, 126.7, 125.4, 124.1, 123.2, 122.4, 119.1, 117.6, 114.2, 108.2, 60.7, 50.7, 48.1, 44.5, 38.4, 36.0, 32.9, 31.8, 29.6, 26.7, 25.9, 21.8, 21.4, 18.9, 14.0; ESI-HRMS *m*/*z* calcd for $C_{41}H_{45}N_2O_3S^+$ $[M + H]^+$ 645.3145, found 645.3148.

4-Butyl-6-methyl-1-(2-methylprop-1-en-1-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indole (**4bp**): Yellow oil; 44.8 mg, 50% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.15 (d, *J* = 8.0 Hz, 2H), 7.13—7.07 (m, 1H), 7.04 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 6.9 Hz, 1H), 6.82 (s, 1H), 6.65 (d, *J* = 7.9 Hz, 2H), 6.06 (d, *J* = 8.5 Hz, 1H), 5.99 (s, 1H), 5.12 (d, *J* = 8.6 Hz, 1H), 3.66 (s, 3H), 2.60—2.48 (m, 1H), 2.40—2.27 (m, 1H), 2.12 (s, 3H), 1.92 (s, 3H), 1.60 (s, 3H), 1.58—1.47 (m, 2H), 1.45—1.29 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 141.7, 137.6, 136.6, 135.7, 135.5, 133.4, 127.9, 126.8, 125.8, 124.0, 123.4, 122.2, 117.8, 117.2, 113.6, 108.1, 60.0, 32.9, 32.7, 31.6, 25.8, 22.5, 21.4, 18.7, 14.0; ESI-HRMS *m*/*z* calcd for $C_{27}H_{33}N_2O_2S^+$ $[M + H]^+$ 449.2257, found 449.2257.

Total synthesis of (±)-aurantioclavine

The mixture of **1a** (604 mg, 3.0 mmol), **2q** (737 mg, 2.0 mmol), and $Rh_2(piv)_4$ (61 mg, 0.1 mmol) was heated to reflux for 1 h under N_2. Then pyridinium *p*-toluenesulfonate (251 mg, 1.0 mmol) was added to the mixture after cooling to room temperature, and then the mixture was stirred for 10 min at room temperature. The mixture was filtered through a pad of Celite and the eluent was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*V*(PE) : *V*(EtOAc) = 5 : 1 to 3 : 1) to give the product **4aq**.

2-(1-(2-Methylprop-1-en-1-yl)-2-tosyl-2,6-dihydro-1*H*-azepino[5,4,3-*cd*]indol-4-yl)isoindoline-1,3-dione (**4aq**): Yellow solid, m.p. 145—146 °C; 639 mg, 61% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.30—8.18 (br, 1H), 8.02—7.87 (m, 2H), 7.87—7.75 (m, 2H), 7.48 (d, *J* = 7.9 Hz, 2H), 7.12—6.95 (m, 2H), 6.88 (d, *J* = 6.9 Hz, 1H), 6.77 (d, *J* = 7.9 Hz, 2H), 6.69—6.60 (m, 1H), 6.41 (s, 1H), 6.18 (d, *J* = 9.0 Hz, 1H), 5.49 (d, *J* = 9.0 Hz, 1H), 2.08 (s, 3H), 1.91 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 167.7, 167.4, 142.6, 136.8, 136.0, 135.9, 134.6, 132.0, 128.5, 127.1, 124.1, 123.9, 123.7, 123.1, 122.7, 122.1, 121.4, 117.8, 112.4, 110.5, 60.3, 25.6, 21.3, 18.8; ESI-HRMS *m*/*z* calcd for $C_{30}H_{26}N_3O_4S^+$ $[M + H]^+$ 524.1639, found 524.1639.

The solution of **4aq** (639 mg, 1.22 mmol) and $N_2H_4{\cdot}H_2O$ (50 wt%, 1.2 mL) in CH_3CN (12 mL) was heated to reflux for 1 h, and a large quantity of white solid appeared in the mixture. Then the mixture was filtered and the eluent was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (*V*(PE) : *V*(EtOAc) = 1 : 1) to give the product **5** (*dr* = 1.5 : 1) as a mixture of isomers.

1-(2-Methylprop-1-en-1-yl)-2-tosyl-2,3,4,6-tetrahydro-1*H*-azepino[5,4,3-*cd*]indol-4-amine (**5**): Yellow solid, m.p. 79—80 °C; 333 mg, 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.55—8.70 (m, 1H), 7.83—7.24 (m, 2H), 7.23—6.96 (m, 3H), 6.93—6.82 (m, 1H), 6.79—6.60 (m, 2H), 6.27—5.99 (m, 1H), 5.32—5.08 (m, 2H), 5.06—4.27 (m, 2H), 2.16—2.07 (m, 3H), 1.95—1.86 (m, 3H), 1.72—1.66 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 148.0, 143.9, 142.3, 142.2, 139.6, 137.8, 137.4, 136.4, 136.3, 136.0, 134.8, 128.3, 128.2, 128.1, 127.3, 127.1, 126.5, 123.3, 123.0, 122.5, 122.1, 121.9, 121.7, 119.7, 118.3, 114.4, 110.3, 110.2, 108.1, 59.2, 59.1, 51.1, 43.0, 25.9, 25.7, 21.3, 21.2, 18.61, 18.57; ESI-HRMS *m*/*z* calcd for $C_{22}H_{26}N_3O_2S^+$ $[M + H]^+$ 396.1740, found 396.1722.

The $B(C_6F_5)_3$ (10 mg, 0.02 mmol) was weighted in glove box and placed in sealed tube. Then compound **5** (158 mg, 0.40 mmol), phenylsilane (0.39 mL, 3.20 mmol) and 1,2-difluorobenzene (4 mL) were added to the sealed tube under N_2. The reaction mixture produced a large quantity of white solid. The solid disappeared after the mixture was heated to 140 °C for 36 h. The mixture was cooled to room temperature and the solvent was evaporated *in vacuo*. The residue was purified by silica gel column chromatography (*V*(PE) : *V*(EtOAc) = 3 : 1) to give the product **6**.

1-(2-Methylprop-1-en-1-yl)-2-tosyl-2,3,4,6-tetrahydro-1*H*-azepino[5,4,3-*cd*]indole (**6**): Light yellow solid, m.p. 171—172 °C; 82 mg, 54% yield; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.15—7.97 (br, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 1H), 7.08—6.99 (m, 3H), 6.86 (s, 1H), 6.77 (d, *J* = 7.2 Hz, 1H), 6.25 (d, *J* = 9.0 Hz, 1H), 5.35 (d, *J* = 9.1 Hz, 1H), 4.00 (dt, *J* = 14.8, 4.2 Hz, 1H), 3.77—3.65 (m, 1H), 3.28—3.14 (m, 1H), 3.01 (dt, *J* = 16.2, 3.4 Hz, 1H), 2.29 (s, 3H), 1.83 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 142.4, 138.5, 137.2, 136.3, 135.6, 129.0, 127.2, 124.5, 123.5, 121.8, 121.4, 118.0, 113.9, 109.5, 59.9, 44.2, 28.5, 25.9, 21.5, 18.7; ESI-HRMS *m*/*z* calcd for $C_{22}H_{25}N_2O_2S^+$ $[M + H]^+$ 381.1631, found 381.1644.

To the solution of naphthalene (276 mg, 2.16 mmol) in anhydrous THF (2 mL) was added Na (50 mg, 2.16 mmol) at room temperature under N_2. The mixture was stirred at room temperature for 10 min and the mixture turned into dark green. Then a solution of **6** (82 mg, 0.22 mmol) in anhydrous THF (2 mL) was added to the mixture dropwise after cooling down to –78 °C. Ethanol was added to the mixture to quench the reaction at –78 °C after 15 min. The mixture was diluted with water and extracted with EtOAc 3 times. The combined organic layers were washed with brine, dried with Na_2SO_4, filtered and concentrated. The residue was purified by silica gel (basify with NaOH, pH = 8—9) column chromatography (EtOAc) to give (±)-aurantioclavine.

(±)-Aurantioclavine: Off-white solid, m.p. 179—180 °C; 38 mg, 78% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.22—8.06 (br, 1H), 7.22 (d, J = 8.0 Hz, 1H), 7.09 (t, J = 7.7 Hz, 1H), 7.00 (s, 1H), 6.84 (d, J = 7.4 Hz, 1H), 5.46 (d, J = 9.2 Hz, 1H), 4.90 (d, J = 9.1 Hz, 1H), 3.61—3.49 (m, 1H), 3.18—2.96 (m, 3H), 1.85 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 138.6, 137.3, 133.4, 127.8, 125.5, 121.7, 121.1, 118.0, 115.9, 109.3, 62.8, 49.0, 31.1, 26.0, 18.5; ESI-HRMS m/z calcd for $C_{15}H_{19}N_2^+$ $[M + H]^+$ 227.1543, found 227.1563.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.202000657.

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[11] The double bond configuration of **3ba** was confirmed by X-ray crystallographic analysis. CCDC-2052432 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. We speculated the configuration of double bond of analogue **3aa** was same as that of **3ba**.

[12] The structure of **4bi** was confirmed by X-ray crystallographic analysis. CCDC-2040400 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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