JOC The Journal of Organic Chemistry

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Formal [3 + 2] Cycloadditions via Indole Activation: A Route to Pyrroloindolines and Furoindolines

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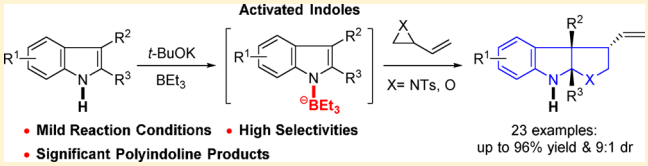
Supporting Information

ABSTRACT: Here, we describe a novel [3 + 2] cycloaddition of 3-substituted indoles with vinyl aziridines and vinyl epoxides that provides a straightforward approach to pyrroloindolines and furoindolines bearing vinyl groups (up to 96% yield and 9:1 dr). In contrary to previous reports involving Lewis acid activation, this work reports successful reactions based on the activation of indole using *t*-BuOK and BEt_3 (triethylborane), thereby preserving the free N−H group on indoles. In addition, a gram-scale reaction and a ring-closing metatheis reaction are performed to provide good demonstrations of the synthetic utility of this approach.



Fused indolines are a class of fundamental motifs that are widespread throughout an array of natural products and pharmaceutical agents.[1] As indicated in Scheme 1, (−)-physostigmine, which is isolated from Calabar bean seeds, can be used as a cholinesterase inhibitor to treat Alzheimer's disease.[2a] (−)-Debromoflustramine E, which was isolated from *Flustra foliacea*, was found to inhibit butyrylcholinesterase.[2b] Given their widespread occurrence and diverse biological acitivities, fused indoline units have been established as an important platform for the development of new synthetic methodologies.[3] For example, pyrroloindolines have traditionally been constructed from tryptophan derivatives via a Friedel−Crafts alkylation/intramolecular annulation sequence by mimicking their biosynthesis routes.[4] Garg elegantly developed another practical approach to access both pyrroloindolines and furoindolines that involves interrupted Fischer indole synthesis using hydrazines and cyclic hemiacetals as feedstocks.[5] Recently, much efforts have been devoted to pyrroloindoline synthesis through Lewis acid catalyzed formal [3 + 2] annulations of C3-substituted indoles with aziridines.[6] Although impressive advances have been achieved, the development of new strategies to synthesize fused indolines remains highly desirable from the perspective of product diversity. In this work, we describe a novel [3 + 2] cycloaddition reaction to prepare both pyrroloindolines and furoindolines from readily available C3-substituted indoles, vinyl aziridines, and vinyl epoxides with generally high yields and good selectivities.

In previously published pyrroloindoline synthesis, Lewis acids were typically required to activate aziridines for [3 + 2] cycloadditions due to the aziridines' low reactivity (Scheme 2a).[6] However, inspired by the impressive work of Yang et al. regarding pyrroloindoline synthesis via a Friedel−Crafts alkylation/intramolecular annulation sequence,[7] we expected that the same indole activation strategy could be applied for [3 + 2] cycloadditions of 3-substituted indoles with vinyl aziridines and vinyl epoxides (Scheme 2b).[8] The produced pyrroloindolines and furoindolines feature a N-free character and vinyl functional groups that allow for further synthetic operations to satisfy different requests.

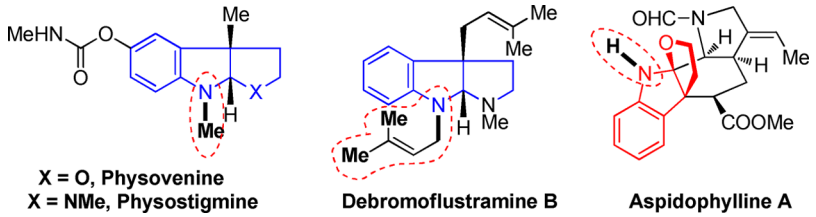
To validate the aforementioned hypothesis, we initially performed the reaction of 3-methylindole **1a** and *N*-tosyl vinylaziridine **2a** in the presence of *t*-BuOK and BEt_3 in 1,4-dioxane. To our delight, the desired pyrroloindoline product **3aa** was isolated in good yield with moderate diastereoselectivity (Table 1, entry 1; 79% yield and 5:1 dr). The structure and relative configuration of **3aa** were confirmed via X-ray crystal diffraction analysis (Figure S2).[9] An investigation of solvent effects (Table 1, entries 1−7) revealed that THF was the best choice for this transformation, affording **3aa** in excellent yield with good diastereoselectivity within a relatively short period (Table 1, entry 5; 96% yield and 6:1 dr). We found that the reaction can produce similar results at a low temperature (0 °C) and at room temperature, although a longer time is required for the low-temperature reaction (Table 1, entry 8; 95% yield and 5:1 dr). When the Ns-protected vinyl aziridine **2a′** was used instead of the Ts-protected vinyl aziridine **2a**, the reaction could proceed smoothly but produced the corresponding product **3aa′** with worse results (Table 1, entry 9; 60% yield and 3:1 dr). It was found that using smaller amount of indole substrates would result in poorer

Special Issue: Heterocycles

Received: April 29, 2016
Published: July 18, 2016

DOI: 10.1021/acs.joc.6b00991
J. Org. Chem. 2016, 81, 10491−10498

Scheme 1. Examples of Bioactive Indoline Alkaloids in Natural Products



Scheme 2. Synthesis of Fused Indolines through [3 + 2] Cycloadditions

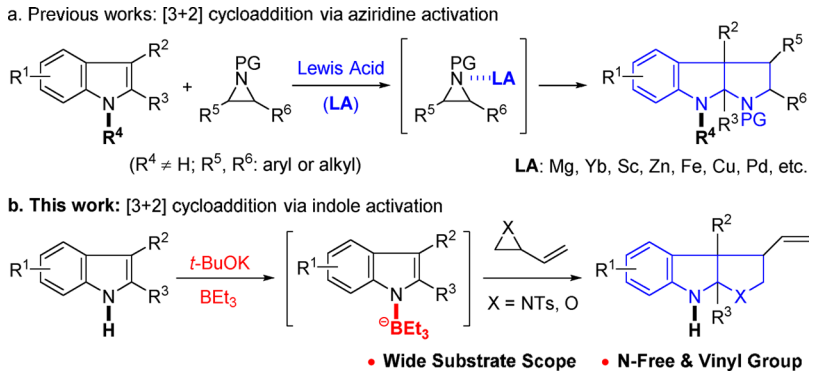
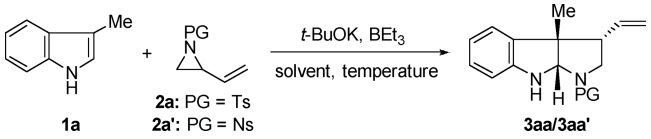


Table 1. Optimization of Reaction Conditions[a]



entry	T (°C)	solvent	time (h)	yield (%)[b]	dr[c]
1	25	1,4-dioxane	12	79	5:1
2	25	DMF	12	23	4:1
3	25	DCM	12	82	3:1
4	25	TBME	12	88	4:1
5	**25**	**THF**	**5**	**96**	**6:1**
6	25	ether	12	90	6:1
7	25	toluene	12	93	3:1
8	0	THF	12	95	5:1
9[d]	25	THF	24	60	3:1
10[e]	25	THF	5	98[c]	3:1

[a]Unless otherwise noted, the reaction conditions were as follows: **1a** (0.5 mmol, 2.5 equiv), **2a** (0.2 mmol, 1.0 equiv), BEt_3 (0.55 mmol, 2.75 equiv), *t*-BuOK (0.55 mmol, 2.75 equiv), and solvent (2.0 mL). [b]Isolated yield based on **2**. [c]Determined by ^1H NMR analysis of the reaction mixture. [d]**2a′** was used. [e]**1a** (0.2 mmol, 1.0 equiv), **2a** (0.5 mmol, 2.5 equiv), BEt_3 (0.22 mmol, 1.1 equiv), *t*-BuOK (0.22 mmol, 1.1 equiv), and solvent (2.0 mL). DMF, *N*,*N*′-dimethylformate; DCM, dichloromethane; TBME, 2-methoxy-2-methylpropane; THF, tetrahydrofuran; Ts, 4-methylbenzenesulfonyl; Ns, 4-nitrobenzenesulfonyl.

diastereomeric ratio of the corresponding products. In order to obtain high reaction efficiency and diastereoselectivity, excess indoles and BEt_3 is necessary.

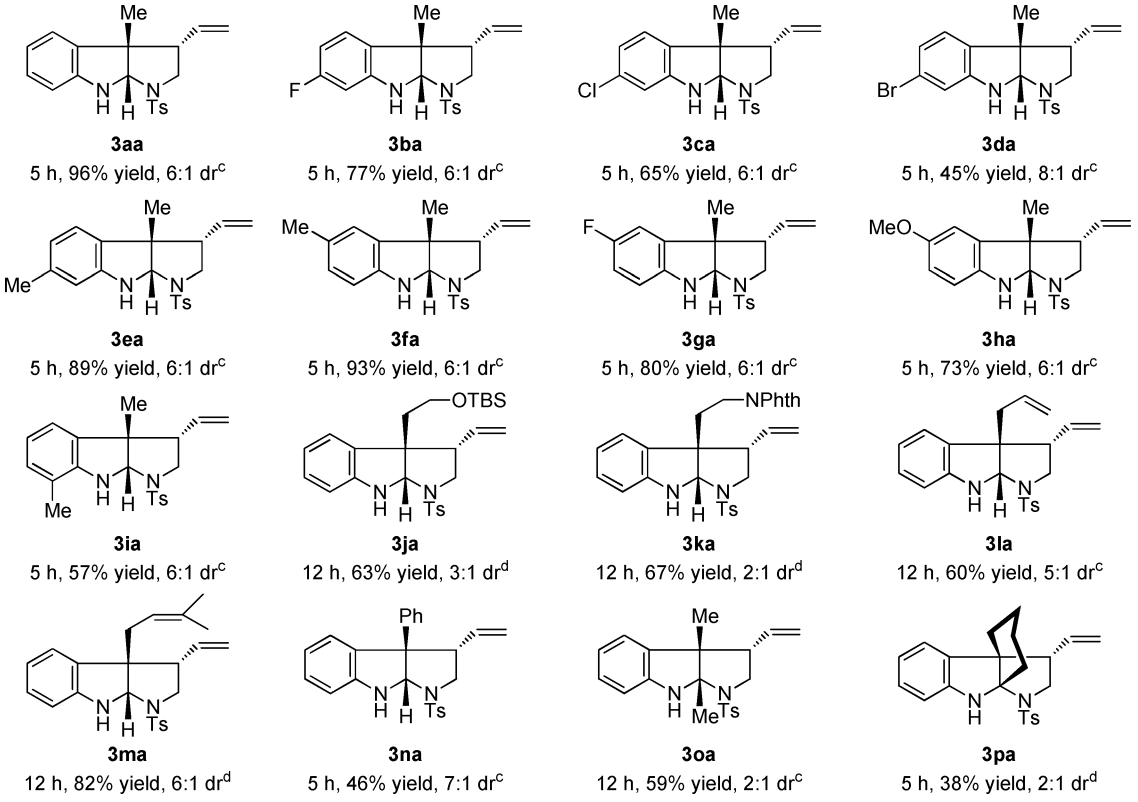
After establishing the optimized reaction conditions, we started to evaluate the scope of this cycloaddition reaction. As indicated in Scheme 3, a wide range of 3-substituted indoles were proven to be valid for the reaction. The variation of electronic characteristics and of substituent positions on the benzene ring of indoles had observable effects on the results. Except for two isolated examples (**3da** and **3ia**), good to high yields were obtained with 6:1 dr (**3aa**−**3ca** and **3ea**−**3ha**). Moreover, indoles with functionalized alkyl substituents at the 3-position were investigated. Significantly, protected hydroxyl, amine, and alkene functional groups were successfully introduced into the final pyrroloindoline products (Scheme 3, **3ja**−**3ma**: 60−82% yields and 2:1−6:1 dr). In addition, when 3-phenyl-substituted indole **1n** was applied, the corresponding pyrroloindoline **3na** could be produced in 46% yield with 7:1 dr. This cycloaddition reaction can also be successfully extended to 2,3-disubstituted indoles. For example, when 2,3-dimethylindole (**1o**) and 1,2,3,4-tetrahydrocarbazole (**1p**) were subjected to the standard reaction conditions, multisubstituted pyrroloindolines were produced with acceptable results.

Subsequently, different vinyl aziridines were examined for this [3 + 2] cycloaddition in the presence of *t*-BuOK and BEt_3 in THF (Scheme 4). Variation of the vinyl group was found to be tolerated under this reaction condition. For example, when internal propenyl-substituted aziridine **2b** and *t*-butyl acrylate-substituted aziridine **2c** were used, the corresponding pyrroloindolines **2ab** and **2ac** were obtained in moderate yields with moderate diastereoselectivities (Scheme 4). However, vinyl aziridine with a methyl at the allylic position was not converted into the desired pyrroloindoline product (Scheme 4, **3ad**) in spite of the addition of LiCl, which indicated that the steric hindrance of the substrate has an influence on the reaction efficiency. In addition, the reaction of cyclic vinyl aziridine **2e** with 3-methylindole **1a** proceeded extremely well, producing the poly-ringed indoline **3ae** in high yield with 1:1 dr.

To our knowledge, no [3 + 2] cycloaddition reaction of indoles and epoxides has been exploited for furoindoline synthesis. Here, we implemented this approach via indole activation. Notably, 1 equiv of LiCl was required as a Lewis acid to activate vinyl epoxides (see Table S1 in Supporting Information) because of the lower reactivity of vinyl epoxides relative to that of vinyl aziridines. However, the reaction did not occur in the absence of BEt_3. As a result, indoles bearing varied substituents were suitable for this reaction with vinyl epoxide

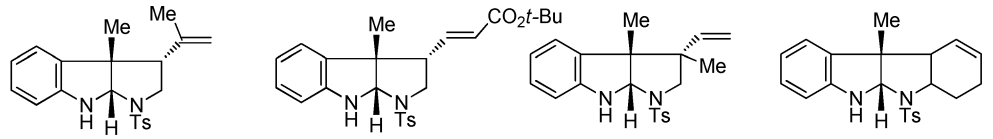
DOI: 10.1021/acs.joc.6b00991
J. Org. Chem. 2016, 81, 10491−10498

Scheme 3. Indole Scope for the Formal [3 + 2] Cycloaddition[a,b]



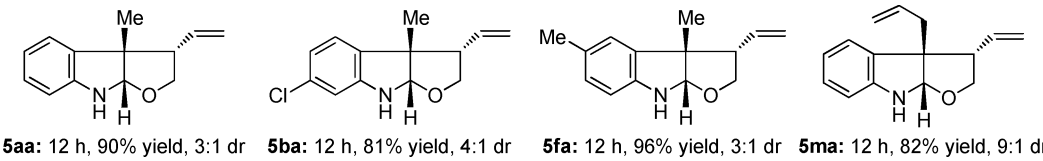
[a]Reaction conditions: **1a** (1.25 mmol, 2.5 equiv), **2a** (0.5 mmol, 1.0 equiv), BEt_3 (1.375 mmol, 2.75 equiv), *t*-BuOK (1.375 mmol, 2.75 equiv), and THF (3.75 mL). [b]Isolated yields based on **2**. [c]Determined by GC−MS analysis of the reaction mixture. [d]Determined by ^{1}H NMR analysis of the reaction mixture.

Scheme 4. Experiments with Various Vinyl Aziridines[a]



[a]See Scheme 3 for reaction conditions, and dr values were determined by ^{1}H NMR analysis of the reaction mixture.

Scheme 5. Primary Experiments with Vinyl Epoxide[a−c]



[a]Reaction conditions: **1** (0.5 mmol, 1.0 equiv), **4a** (2.0 mmol, 4.0 equiv), BEt_3 (0.55 mmol, 1.25 equiv), *t*-BuOK (0.55 mmol, 1.25 equiv), LiCl (0.5 mmol, 1.0 equiv), and THF (3.75 mL). [b]Isolated yields based on **1**. [c]All the dr values were determined by GC−MS analysis of the reaction mixture.

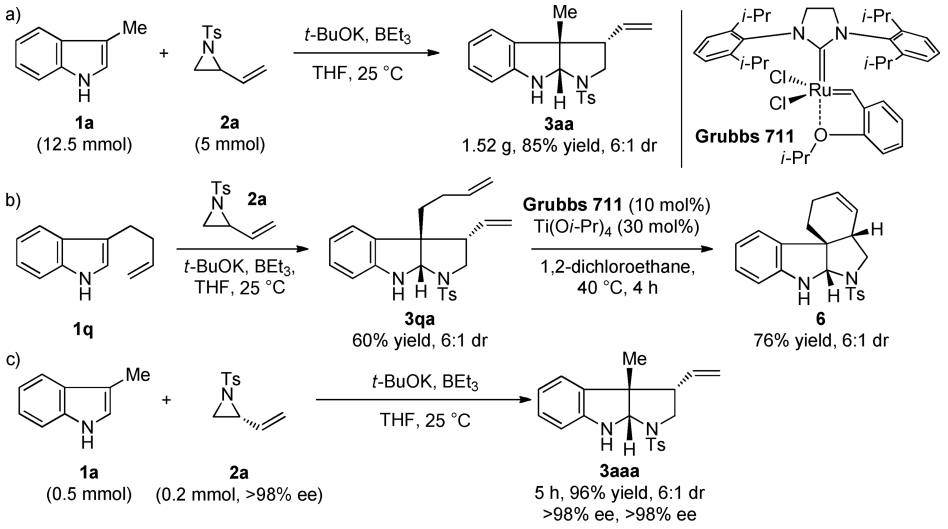
4a, and the corresponding furoindoline products were produced in high yields (Scheme 5).

To illustrate the synthetic utility of the described methodology, a gram-scale reaction of 3-methylindole **1a** and *N*-Ts vinyl aziridine **2a** was performed under the standard conditions. After 5 h, 1.52 g of pyrroloindolines **3aa** was isolated in an 85% yield with 6:1 dr (Scheme 6a). Moreover, an intramolecular ring-closing metathesis reaction of cycloadduct **3qa** produced a complex molecule **6** that bears a polycyclic spiro-indoline structure in good yield with reserved diastereopurity (Scheme 6b).[10] In addition, when enantiopure vinyl aziridines were employed, the enanoselectivities of the products were preserved (Scheme 6c).

In summary, we developed a novel [3 + 2] cycloaddition of 3-substituted indoles with vinyl aziridines and vinyl epoxides via the in situ activation of indoles. In this manner, an alternative route to pyrroloindoline and furoindoline scaffolds bearing vinyl and free N−H groups was exploited with moderate to good reaction efficiencies and selectivities.

DOI: 10.1021/acs.joc.6b00991
J. Org. Chem. 2016, 81, 10491−10498

Scheme 6. Demonstration of Synthetic Utility



EXPERIMENTAL SECTION

General Information. Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All solvents were treated using known methods, and substrates **1** and **2** were easily prepared using known methods (see Supporting Information for details). The ^{1}H NMR spectra were recorded on 400/600 MHz spectrophotometers. The chemical shifts (δ) are reported in parts per million using the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). The data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet), coupling constants (Hz), and integration. The ^{13}C NMR spectra were recorded at 400 (100 MHz) with complete proton decoupling spectrophotometers ($CDCl_3$: 77.0 ppm). High-resolution mass spectra (HRMS) were equipped with an ESI source and a TOF detector. The IR spectra were recorded on an IR spectrophotometer. The melting points were measured with a digital melting point detector.

General Procedure for Pyrroloindoline Synthesis. Indole **1** (1.25 mmol, 2.5 equiv) and *t*-BuOK (1.375 mmol, 2.75 equiv) were dissolved in 3.75 mL of THF, and the mixture was stirred at room temperature for 15 min under argon atmosphere. BEt_3 (1.375 mL, 2.75 equiv) was then added, and the mixture was stirred for an additional 15 min. Subsequently, vinyl aziridine **2** (0.5 mmol, 1 equiv) was added, and the reaction mixture was stirred at room temperature for 5−12 h. After the reaction had finished (monitored by TLC), the product was purified by flash column chromatography. The diastereomeric ratio was determined by ^{1}H NMR or GC−MS analysis of the reaction mixture.

General Procedure for Furoindoline Synthesis. Indole **1** (0.5 mmol, 1.0 equiv) and *t*-BuOK (0.55 mmol, 1.1 equiv) were dissolved in 3.75 mL of THF, and the mixture was stirred at room temperature for 15 min under argon atmosphere. BEt_3 (0.55 mL, 1.1 equiv) was then added, and the mixture was stirred for an additional 15 min. After vinyl epoxide **4** (2.0 mmol, 4 equiv) and LiCl (0.5 mmol, 1 equiv) were introduced, the reaction mixture was stirred at room temperature for 12 h. After the reaction had finished (monitored by TLC), the product was purified by flash column chromatography. The diastereomeric ratio was determined by GC−MS analysis of the reaction mixture.

Procedure for Demonstrating Synthetic Utility. To a solution of **3qa** (39.5 mg, 0.1 mmol) in 1,2-dichloroethane (5.0 mL) was added titanium(IV) isopropoxide (9 μL, 0.03 mmol). This reaction mixture was stirred at room temperature for 15 min. Subsequently, a first-generation Grubbs catalyst (7 mg, 10 mol %) was introduced, and the system was stirred at 40 °C for 4 h. The solvent was removed in vacuo, and the crude material was purified by column chromatography (silica, 5% EtOAc in hexanes) to provide the title compound **6** in 76% yield. The diastereomeric ratio of **6** was determined to be 6:1 via ^{1}H NMR analysis of the reaction mixture.

*3a-Methyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]-indole (**3aa**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 170 mg, yield 96%, dr = 6:1; white solid, mp 115−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (t, J = 8.1 Hz, 2H, major + minor), 7.31 (t, J = 6.5 Hz, 2H, major + minor), 7.11−7.02 (m, 1H, major + minor), 6.96 (dd, J = 12.2, 7.5 Hz, 1H, major + minor), 6.76−6.64 (m, 1H, major + minor), 6.61 (t, J = 7.8 Hz, 1H, major + minor), 5.74 (m, 1H, major), 5.40−5.28 (m, 1H, minor), 5.18 (dd, J = 10.2, 1.5 Hz, 1H, major), 5.05 (m, 2H, major, 1H, minor), 4.89 (s, 1H, minor), 4.83 (s, 1H, minor), 3.48 (m, 1H, major + minor), 3.16−3.07 (m, 1H, minor), 3.04−2.93 (m, 1H, major), 2.88 (d, J = 9.2 Hz, 1H, minor), 2.51−2.33 (m, 3H, major), 1.31−1.23 (s, 3H, major), 1.03 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.2, 147.7, 143.7, 143.6, 136.4, 135.4, 134.3, 134.0, 133.6, 129.9, 129.8, 129.2, 128.5, 128.4 127.3, 127.1, 125.3, 122.0, 119.1, 118.6, 118.6, 118.1, 109.7, 109.5, 85.3, 84.8, 56.8, 55.9, 53.4, 52.2, 51.7, 51.5, 29.7, 24.4, 21.5, 19.4; IR (in KBr) 2925, 2866, 1609, 1596, 1490, 1470, 1456, 1374 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{22}N_2O_2S$ $[M + H]^+$ 355.1475, found 355.1480.

*6-Fluoro-3a-methyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydro-pyrrolo[2,3-b]indole (**3ba**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 143 mg, yield 77%, dr = 6:1; white solid, mp 109−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72 (t, J = 7.9 Hz, 2H, major + minor), 7.31 (d, J = 8.1 Hz, 2H, major + minor), 6.86 (dd, J = 8.2, 5.6 Hz, 1H, major + minor), 6.41−6.25 (m, 2H, major + minor), 5.75−5.63 (m, 1H, major), 5.40−5.27 (m, 1H, minor), 5.24−4.94 (m, 3H, major + minor, 1H, minor), 4.90 (s, 1H, major), 3.51 (dd, J = 10.5, 7.1 Hz, 1H, major + minor), 3.14−3.04 (m, 1H, minor), 2.99 (t, J = 10.9 Hz, 1H, major), 2.90−2.77 (m, 1H, minor), 2.48−2.41 (m, 3H, major + minor, 1H, major), 1.60 (s, 3H, minor), 1.27−1.19 (s, 3H, major), 1.00 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 164.6, 162.2, 150. 4, 150.3, 143.6, 143.5, 136.0, 134.9, 133.7, 133.5, 129.7, 129.7, 127.1, 126.8, 125.8, 125.7, 124.5, 124.4, 122.5, 122.4, 118.7, 118.2, 105.0, 104.8, 104.8, 104.6, 97.4, 97.1, 96.8, 85.6, 85.2, 56.2, 55.2, 53.3, 52.2, 51.7, 29.8, 24.7, 21.7, 19.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ(ppm) −126.11; IR (in KBr) 2885, 2848, 1642, 1615, 1604, 1588, 1563, 1512, 1503, 1493, 1485, 1461, 1445, 1380 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}FN_2O_2S$ $[M + Na]^+$ 395.1200, found 395.1205.

*6-Chloro-3a-methyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydro-pyrrolo[2,3-b]indole (**3ca**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 126 mg, yield 65%, dr = 6:1; white solid, mp 125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.85−7.72 (m, 2H, major + minor), 7.37−7.25 (m, 2H, major + minor), 6.85 (t, J = 9.5 Hz, 1H, major + minor), 6.65 (m,

DOI: 10.1021/acs.joc.6b00991
J. Org. Chem. 2016, 81, 10491−10498

1H, major + minor), 6.57 (dd, J = 7.0, 1.8 Hz, 1H, major + minor), 5.68 (m, 1H, major), 5.43 (d, J = 1.5 Hz, 1H, minor), 5.26−5.03 (m, 2H, major + minor), 5.16 (s, 1H, major), 5.00 (s, 1H, minor), 3.53 (dd, J = 10.5, 7.1 Hz, 1H, major), 3.45 (dd, J = 9.7, 6.3 Hz, 1H, minor), 2.97 (t, J = 10.9 Hz, 2H, major), 2.51−2.36 (m, 2H, minor), 2.43 (s, 3H), 2.28 (d, J = 0.9 Hz, 1H, major + minor), 1.26 (s, 3H, minor), 1.24 (s, 3H, major), 1.00 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.2, 147.7, 143.7, 143.6, 136.4, 135.4, 134.3, 134.0, 133.6, 129.9, 129.8, 129.2, 128.5, 128.4, 127.3, 127.1, 125.3, 122.0, 119.1, 118.6, 118.6, 118.1, 109.7, 109.5, 85.3, 84.8, 56.8, 55.9, 53.4, 52.2, 51.7, 51.5, 29.7, 24.4, 21.5, 19.4; IR (in KBr) 2929, 2870, 1640, 1607, 1483, 1442, 1338, 1376 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}ClN_2O_2S$ [M + Na]$^+$ 411.0904, found 411.0914.

*6-Bromo-3a-methyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3da**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 98 mg, yield 45%, dr = 8:1; light-yellow solid, mp 142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.71 (t, J = 7.7 Hz, 2H, major + minor), 7.31 (t, J = 6.6 Hz, 2H, major + minor), 7.14 (m, 1H, major + minor), 7.03 (dd, J = 8.9, 2.0 Hz, 1H, major + minor), 6.48 (dd, J = 8.3, 5.9 Hz, 1H, major + minor), 5.70 (m, 1H, major), 5.23 (d, J = 10.7 Hz, 1H, major + minor), 5.16−4.98 (m, 2H, major + minor, 1H, minor), 4.87 (s, 1H, major + minor), 3.48 (m, 1H, major + minor), 3.14−3.06 (m, 1H, minor), 2.99 (t, J = 10.9 Hz, 1H, major), 2.85 (dd, J = 15.3, 6.3 Hz, 1H, minor), 2.50−2.37 (m, 3H, major + minor, 1H, major), 1.23 (s, 3H, major), 1.01 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 148.0, 147.9, 143.6, 143.5, 135.9, 135.8, 133.6, 133.0, 131.3, 130.9, 129.7, 128.0, 127.07, 126.8, 125.0, 119.2, 118.4, 111.8, 111.0, 110.7, 110.2, 109.0, 85.2, 84.8, 56.9, 56.0, 53.1, 52.2, 51.7, 51.4, 27.6, 24.4, 21.7, 19.6; IR (in KBr) 2879, 1636, 1604, 1562, 1516, 1482, 1387 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}BrN_2O_2S$ [M + Na]$^+$ 455.0399, found 455.0399.

*3a,6-Dimethyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-b]indole (**3ea**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 164 mg, yield 89%, dr = 6:1; light-yellow solid, mp 123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72 (dd, J = 11.3, 4.8 Hz, 2H, major + minor), 7.30 (t, J = 6.4 Hz, 2H, major + minor), 6.84 (dd, J = 9.9, 7.5 Hz, 1H, major + minor), 6.53 (d, J = 7.3 Hz, 1H, minor), 6.49 (d, J = 7.6 Hz, 1H, major), 6.44 (d, J = 6.8 Hz, 1H, major + minor), 5.73 (m, 1H, major), 5.28 (m, 1H, minor), 5.17 (dd, J = 10.2, 1.5 Hz, 1H, major), 5.13−5.01 (m, 2H, major + minor), 5.00−4.94 (m, 1H, minor), 3.50 (dd, J = 10.5, 7.1 Hz, 1H, major), 3.45 (dd, J = 9.8, 6.3 Hz, 1H, minor), 3.15−3.07 (m, 1H, minor), 2.99 (t, J = 10.9 Hz, 1H, major), 2.86 (dd, J = 15.3, 6.4 Hz, 1H, minor), 2.42 (s, 3H, major + minor, m, 1H, major), 2.25 (s, 3H, major + minor), 1.25 (s, 3H, major + minor), 1.01 (s, 3H, major + minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.4, 147.8, 143.5, 143.4, 138.3, 138.3, 136.6, 135.6, 134.5, 134.1, 130.9, 129.7, 129.7, 127.3, 127.0, 126.3, 124.9, 121.6, 119.7, 119.4, 118.3, 117.7, 110.4, 110.2, 85.4, 85.0, 56.6, 55.6, 53.4, 52.2, 51.7, 51.5, 29.6, 24.5, 21.4, 21.3, 19.5; IR (in KBr) 2880, 1633, 1606, 1572, 1517, 1486 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_2S$ [M + Na]$^+$ 391.1451, found 391.1458.

*3a,5-Dimethyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-b]indole (**3fa**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 171 mg, yield 93%, dr = 6:1; light-yellow solid, mp 112−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (dd, J = 13.1, 5.1 Hz, 2H, major + minor), 7.29 (t, J = 6.5 Hz, 2H, major + minor), 6.92−6.80 (m, 1H, major + minor), 6.76 (d, J = 9.1 Hz, 1H, major + minor), 6.50 (t, J = 7.4 Hz, 1H, major + minor), 5.75 (m, 1H, major), 5.42−5.25 (m, 1H, minor), 5.22−4.93 (m, 2H, major + minor), 5.08 (s, 1H, major + minor)4.14 (s, 1H, major + minor), 3.50 (dd, J = 10.4, 7.1 Hz, 1H, major + minor), 3.43 (dd, J = 9.8, 6.3 Hz, 1H, major + minor), 3.16−3.09 (m, 1H major), 2.98 (t, J = 10.9 Hz, 1H, major), 2.87 (dd, J = 15.0, 6.1 Hz, 1H, minor), 2.55−2.29 (m, 1H, minor), 2.32 (s,3H, major + minor), 2.24 (s, 3H, minor), 2.20 (s, 3H, major), 1.28−1.21 (s, 3H, major), 1.02 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 146.7, 145.2, 143.4, 143.3, 136.2, 135.2, 134.4, 133.9, 133.7, 129.7, 129.6, 129.3, 128.7, 128.7, 128.3, 127.8, 127.2, 126.9, 125.8, 122.6, 118.5, 117.7, 109.6, 109.4, 85.5, 85.1, 57.0, 56.0, 53.5, 52.4, 51.9, 51.5, 24.6, 21.7, 21.7, 21.1, 21.1, 19.8; IR (in KBr) 2920, 2877, 1645, 1615, 1598, 1492, 1450, 1383 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_2S$ [M + Na]$^+$ 391.1451, found 391.1450.

*5-Fluoro-3a-methyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ga**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 149 mg, yield 80%, dr = 6:1; white solid, mp 135−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.75 (t, J = 9.9 Hz, 2H, major + minor), 7.33 (t, J = 7.7 Hz, 2H, major + minor), 6.77 (dd, J = 8.6, 6.4 Hz, 1H, major + minor), 6.75−6.70 (m, 1H, major + minor), 6.68 (d, J = 8.1 Hz, 1H, minor), 6.56−6.49 (m, 1H, major), 5.79−5.68 (m, 1H, major), 5.38−5.29 (m, 1H, minor), 5.24 (d, J = 10.3 Hz, 1H, major), 5.15 (d, J = 1.3 Hz, 1H, minor), 5.12 (s, 1H, major + minor), 5.10 (d, J = 8.1 Hz, 1H, major), 5.04 (t, J = 12.7 Hz, 1H, minor), 4.79 (s, 1H, major + minor), 3.54 (dd, J = 10.5, 7.2 Hz, 1H, major), 3.46 (dd, J = 9.8, 6.5 Hz, 1H, minor), 3.14 (d, J = 6.7 Hz, 1H, minor), 3.01 (t, J = 11.0 Hz, 1H, major), 2.87 (d, J = 8.9 Hz, 1H, minor), 2.44 (s, 4H, major + minor), 1.26 (s, 3H, major), 1.02 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 157.6, 155.2, 155.2, 144.9, 143.6, 143.5, 135.9, 134.9, 133.6, 133.2, 130.6, 130.5, 129.7, 129.6, 127.1, 126.7, 119.0, 118.3, 114.6, 114.5 114.4, 114.3, 112.5, 112.3, 110.0, 109.9, 109.7, 109.7, 109.5, 109.3, 85.8, 85.4, 57.0, 57.0, 53.0, 52.2, 51.7, 51.4, 29.8, 24.2, 21.7, 19.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ(ppm) −126.1; IR (in KBr) 2923, 2850, 1597, 1491, 1450, 1380 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}FN_2O_2S$ [M + Na]$^+$ 395.1200, found 395.1200.

*5-Methoxy-3a-methyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ha**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 140 mg, yield 73%, dr = 6:1; white solid, mp 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.85−7.62 (m, 2H, major + minor), 7.38−7.21 (m, 2H, major + minor), 6.69−6.57 (m, 2H, major + minor), 6.54 (t, J = 7.4 Hz, 1H, major + minor), 5.85−5.69 (m, 1H, major), 5.37 (m, 1H, minor), 5.19 (d, J = 10.3 Hz, 2H, major), 5.11 (s, 1H, major + minor), 5.09−5.01 (m, 2H, minor), 4.69 (s, 1H, major + minor), 3.74−3.62 (m, 3H, major + minor), 3.53 (dd, J = 10.5, 7.1 Hz, 1H, major), 3.45 (dd, J = 9.8, 6.3 Hz, 1H, minor), 3.15 (s, 1H, minor), 3.00 (t, J = 10.9 Hz, 1H, major), 2.88 (dd, J = 15.2, 6.4 Hz, 1H, minor), 2.50−2.34 (m, 1H, major), 2.42 (s, 3H, major + minor), 1.24 (s, 3H, major), 1.02 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 153.3, 152.8, 143.3, 143.2, 142.7, 141.1, 135.9, 135.8, 134.0, 133.4, 130.6, 129.5, 129.5, 127.0, 126.8, 118.6, 117.9, 112.7, 112.6, 112.3, 110.2, 109.8, 109.0, 85.6, 85.3, 57.0, 55.8, 53.0, 52.3, 51.7, 51.2, 29.7, 24.1, 21.6, 19.4; IR (in KBr) 2931, 2885, 1634, 1598, 1493, 1468, 1381 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_3S$ [M + Na]$^+$ 407.1400, found 407.1400.

*3a,7-Dimethyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-b]indole (**3ia**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 105 mg, yield 57%, dr = 6:1; white solid, mp 130−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.80−7.66 (m, 2H, major + minor), 7.31 (t, J = 7.2 Hz, 2H, major + minor), 6.95−6.85 (m, 1H, major + minor), 6.82 (t, J = 9.6 Hz, 1H, major + minor), 6.64 (m, 1H, major + minor), 5.72 (m, 1H, major), 5.36 (s, 1H, minor), 5.22−5.10 (m, 2H, major), 5.08 (s, 1H, minor), 5.01 (t, J = 12.0 Hz, 1H, minor), 4.60 (s, 1H, major + minor), 3.53 (dd, J = 10.4, 7.1 Hz, 1H, major), 3.46 (dd, J = 9.7, 6.3 Hz, 1H, minor), 3.13 (dd, J = 9.6, 6.9 Hz, 1H, minor), 3.02−2.92 (m, 1H, major), 2.90 (s, 1H, minor), 2.52−2.37 (s, 3H, major + minor, m, 1H, major), 2.13 (s, 1H, minor), 2.10 (s, 3H, major), 1.27 (s, 3H, major), 1.01 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 147.4, 145.8, 143.2, 136.1, 134.9, 133.9, 133.8, 133.7, 132.6, 129.5, 129. 1, 129.0, 128.2, 127.0, 126.8, 122. 6, 119.4, 119.2, 119.0, 118.9, 118.6, 118. 6, 118.4, 117.8, 85.2, 84.4, 57.1, 56.1, 53.5, 52.2, 51.6, 51.4, 30.9, 24.6, 21.6, 21.6, 19.4, 16.8; IR (in KBr) 2925, 2871, 1640, 1598, 1485, 1470 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_2S$ [M + Na]$^+$ 391.1451, found 391.1450.

*3a-(2-((tert-Butyldimethylsilyl)oxy)ethyl)-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ja**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1;

DOI: 10.1021/acs.joc.6b00991
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reaction time = 12 h, 157 mg, yield 63%, dr = 3:1; white solid, mp 97−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.83 (d, J = 8.2 Hz, 2H, major + minor), 7.38 (d, J = 8.1 Hz, 2H, major + minor), 7.17−7.07 (m, 1H, major + minor), 7.00 (d, J = 7.2 Hz, 1H, major + minor), 6.79 (dd, J = 13.8, 6.5 Hz, 1H, minor), 6.75 (dd, J = 9.1, 2.4 Hz, 1H, major), 6.68 (d, J = 7.8 Hz, 1H, minor), 6.64 (d, J = 7.8 Hz, 1H, major), 5.78 (m, 1H, major), 5.57 (s, 1H, major), 5.40−5.36 (m, 1H, minor), 5.30−5.07 (m, 2H, major + minor), 4.95 (s, 1H, minor), 4.80 (s, 1H, major + minor), 3.60 (dd, J = 10.6, 7.0 Hz, 1H, major), 3.54−3.36 (m, 2H, major + minor), 3.21 (m, 1H, minor), 3.06 (t, J = 11.0 Hz, 1H, major + minor), 2.66−2.56 (m, 1H, major + minor), 2.52 (s, 3H, major + minor), 2.06 (m, 1H, major), 1.87 (m, 1H, minor), 1.81 (s, 1H, major), 1.69 (m, 1H, minor), 0.97−0.92 (s, 9H, major), 0.92−0.90 (s, 9H, minor), 0.04 (s, 6H, major), 0.00 (s, 6H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.9, 148.3, 143.4, 143.3, 136.5, 135.5, 134.7, 134.0, 130.5, 129.6, 129.6, 128.4, 128.4, 127.1, 126.9, 126.4, 125.5, 122.5, 118.8, 118.6, 118.2, 117.8, 109.6, 109.1, 82.7, 82.4, 59.6, 59.4, 59.3, 58.6, 53.2, 52.3, 52.0, 50.9, 40.9, 35.5, 29.2, 26.2, 26.1, 21.7, 18.4, −5.0, −5.27, −5.29; IR (in KBr) 2929, 2883, 2854, 1610, 1596, 1485, 1470 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{38}N_2O_3SSi$ $[M + H]^+$ 499.2445, found 499.2445.

*2-(2-((3S,3aS,8aS)-1-Tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indol-3a-yl)ethyl)isoindoline-1,3-dione (**3ka**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 8/1; reaction time = 12 h, 172 mg, yield 67%, dr = 2:1; yellow solid, mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.13 (s, 1H, major + minor), 7.84−7.59 (m, 9H, major + minor), 7.31 (d, J = 7.9 Hz, 3H, major + minor), 7.18−7.04 (m, 4H, major + minor), 7.00 (dd, J = 7.0, 5.1 Hz, 2H, major + minor), 6.65 (t, J = 7.4 Hz, 1H, major + minor), 6.55 (d, J = 8.0 Hz, 1H, major + ,minor), 5.78−5.57 (m, 1H, major + minor), 5.50 (s, 1H, major + minor), 5.13 (dd, J = 34.0, 13.5 Hz, 2H, major + minor), 4.03−3.95 (m, 1H, major + minor), 3.67−3.41 (m, 2H, major + minor), 3.38−3.19 (m, 1H, major + minor), 3.17−3.11 (m, 1H, major + minor), 2.99 (t, J = 11.0 Hz, 1H, major + minor), 2.43 (s, J = 12.7 Hz, 3H, major + minor), 2.28−2.15 (m, 1H, major + minor), 1.88−1.52 (m, 1H, major + minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 168.4, 167.9, 149.9, 143. 7, 136.3, 136.2, 133.9, 133.7, 132.1, 132.0, 129.9, 128.8, 127.4, 127.1, 125.8, 125.4, 123.2, 123.1, 122.1, 122.1, 119.4, 119.4, 118.9, 118.8, 112.3, 111.2, 109.5, 105.1, 82.5, 59.3, 53. 3, 51.2, 38.5, 36.4, 34.0, 24.5, 21.6; IR (in KBr) 3393, 2380, 1772, 1708, 1399, 1160 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{27}N_3O_4S$ $[M + H]^+$ 514.1795, found 514.1802.

*3a-Allyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3la**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1 ; reaction time = 12 h, 114 mg, yield 60%, dr = 5:1; brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.74 (dd, J = 12.5, 7.5 Hz, 2H, major + minor), 7.32−7.24 (m, 2H, major + minor), 7.07−6.98 (m, 1H, major + minor), 6.95 (t, J = 9.1 Hz, 1H, major + minor), 6.72−6.60 (m, 1H, major + minor), 6.60−6.51 (m, 1H, major + minor), 5.77−5.60 (m, 1H, major), 5.48−5.32 (m, 1H, major, 2H, minor), 5.30−5.25 (s, 1H, major), 5.20 (s, 1H, minor), 5.20−5.14 (m, 1H, major + minor), 5.08 (d, J = 16.9 Hz, 1H, major + minor), 5.01−4.94 (m, 1H, major), 4.94 (s, 1H, major), 4.85 (t, J = 7.7 Hz, 1H, minor), 4.71 (dd, J = 15.9, 6.9 Hz, 1H, minor), 4.50−4.19 (m, 1H, major + minor), 3.51 (dd, J = 10.6, 7.0 Hz, 1H, major), 3.42 (dt, J = 13.1, 6.6 Hz, 1H, minor), 3.12 (dt, J = 14.4, 7.2 Hz, 1H, minor), 3.03−2.89 (m, 1H, major), 2.59 (m, 1H, major), 2.41 (s, 3H, major, 1H, minor), 2.22 (dd, J = 14.0, 8.1 Hz, 1H, major), 1.96 (dt, J = 18.6, 9.3 Hz, 1H, minor), 1.25 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.4, 148.1, 143.4, 143.3, 136.1, 136.0, 135.0, 133.8, 133.7, 133.1, 133.0, 132.7, 130.7, 129.5, 128.3, 127.2, 127.1, 126.8, 125.3, 122.4, 118.7, 118.6, 118.6, 118.2, 118.2, 109.4, 109.1, 82.2, 81.6, 60.2, 59.5, 52.2, 51.4, 51.0, 41.7, 37.1, 29.7, 21.6, 14.3; IR (in KBr) 2886, 1638, 1606, 1516, 1485 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{24}N_2O_2S$ $[M + H]^+$ 381.1631, found 381.1631.

*3a,4-Dimethyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ma**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 12 h, 168 mg, yield 82%, dr = 6:1; brown solid, mp 95−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72 (t, J = 8.1 Hz, 2H, major + minor), 7.29 (d, J = 8.1 Hz, 2H, major + minor), 7.03 (m, 1H), 6.97 (d, J = 6.8 Hz, 1H, major), 6.91 (d, J = 6.5 Hz, 1H, minor), 6.65 (m, 1H, major + minor), 6.58 (d, J = 7.7 Hz, 1H, major + minor), 5.73 (m, 1H, major), 5.48−5.30 (m, 1H, minor), 5.20−5.12 (m, 2H, major, 1H, minor), 5.09−5.00 (m, 1H, major + minor, 1H, minor), 4.81 (t, J = 7.3 Hz, 1H, major + minor), 3.50 (dd, J = 10.6, 7.1 Hz, 1H, major), 3.44−3.37 (m, 1H, minor), 3.11 (m, 1H, minor), 3.00 (t, J = 11.0 Hz, 1H, major), 2.94−2.86 (m, 1H, minor), 2.61 (m, 1H, major), 2.49−2.34 (s, 3H, major + minor), 2.24 (d, J = 7.6 Hz, 1H, major + minor), 1.58 (s, 3H, major + minor), 1.53 (s, 3H, major + minor), 1.25 (s, 3H, major + minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.2, 148.0, 143.3, 143.2, 136.1, 136.1, 135.1, 134.4, 134.2, 134.0, 131.5, 129.5, 128.2, 128.2, 128.1, 127.1, 126.8, 125.3, 122.4, 118.6, 118.4, 118.2, 118.2, 117.9, 117.9, 114.3, 109.4, 109.2, 82. 4, 81.6, 65.2, 60.9, 60.4, 60.1, 52.3, 51.6, 51.3, 40.0, 34.9, 26.0, 21.6, 18.07; IR (in KBr) 2922, 2852, 1638, 1604, 1559, 1541, 1508, 1483, 1466, 1375 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{28}N_2O_2S$ $[M + H]^+$ 409.1944, found 409.1936.

*3a-Phenyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3na**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 96 mg, yield 46%, dr = 7:1; light-pink solid, mp 150−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (t, J = 7.7 Hz, 2H, major + minor), 7.30 (d, J = 8.1 Hz, 1H, major + minor), 7.25 (d, J = 8.2 Hz, 1H, major + minor), 7.22−7.05 (m, 6H, major + minor), 7.05−6.92 (m, 2H, major + minor), 6.76−6.69 (m, 1H, major + minor), 6.65 (dd, J = 14.7, 7.8 Hz, 1H, major + minor), 5.78 (m, 1H, major), 5.63 (s, 1H, minor), 5.40 (s, 1H, major), 5.08 (d, J = 10.4 Hz, 1H, major), 4.96−4.78 (m, 1H, minor), 4.73−4.65 (m, 1H, minor), 3.74 (dd, J = 9.5, 5.7 Hz, 1H, major), 3.53 (dd, J = 9.8, 5.1 Hz, 1H, minor), 3.44−3.34 (m, 1H, minor), 3.25−3.11 (m, 2H, major), 2.44 (s, 3H, major), 2.38 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 150.0, 147.4, 143.6, 143.5, 141.4, 140.4, 136.2, 136.1, 133.3, 129.8, 129.7, 128.8, 128.5, 128.4, 128.2, 127.6, 127.0, 127.0, 126.6, 126.5, 126.3, 123.0, 119.6, 118.6, 118.4, 117.4, 110. 7, 110.1, 86.6, 82.8, 64.6, 64.5, 54.3, 52.6, 52.3, 51. 4, 21.8, 21.7; IR (in KBr) 1640, 1594, 1484, 1469 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}N_2O_2S$ $[M + H]^+$ 417.1631, found 417.1620.

*3a,8a-Dimethyl-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3oa**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 12 h, 109 mg, yield 59%, dr = 2:1; white solid, mp 135−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.66 (d, J = 8.2 Hz, 1H, minor), 7.58 (d, J = 8.2 Hz, 1H, major), 7.18 (dd, J = 13.5, 8.1 Hz, 2H, major + minor), 7.03−6.91 (m, 2H, major + minor), 6.68 (t, J = 7.3 Hz, 1H, minor), 6.62 (t, J = 7.4 Hz, 1H, major), 6.49 (d, J = 7.7 Hz, 1H, major + minor), 5.94 (m, 1H, major), 5.73 (dd, J = 17.0, 9.0 Hz, 1H, minor), 5.23 (m, 2H, major), 5.07 (m, 2H, minor), 3.40 (t, J = 6.3 Hz, 1H, major), 3.22 (d, J = 4.9 Hz, 2H, minor), 2.91−2.81 (m, 1H, minor), 2.75 (m, 2H, major), 2.39 (d, J = 10.6 Hz, 3H, minor), 2.36 (s, 3H, major), 1.75 (s, 3H, major), 1.72 (s, 3H, minor), 1,25 (s, 1H, major + minor), 1.15 (s, 3H, major), 1.11 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 147.5, 146.5, 142.4, 142. 8, 137.0, 136.9, 135.2, 134.2, 133.8, 130.2, 129.3, 128.0, 127.9, 127.0, 126.9, 125.0, 121.9, 118.9, 118.9, 118.6, 117.6, 109.3, 109.1, 91.5, 91.3, 58.78, 58.6, 52.0, 51.4, 50.8, 50.2, 29.8, 23.9, 23.1, 21.7, 21.6, 18.8; IR (in KBr) 2861, 1639, 1595, 1508, 1486, 1467,1378 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_2S$ $[M + H]^+$ 369.1621, found 369.1631.

*10-Tosyl-12-vinyl-6,7,8,9-tetrahydro-5H-8a,4b-(epiminoethano)-carbazole (**3pa**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 5 h, 75 mg, yield 38%, dr = 2:1; white solid, mp 183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.75 (d, J = 8.1 Hz, 1H, major), 7.54 (d, J = 8.1 Hz, 1H, major + minor, 1H, minor), 7.24 (d, J = 7.0 Hz, 1H, major + minor), 7.14 (d, J = 8.0 Hz, 1H, major + minor), 7.08−6.92 (m, 2H, major + minor), 6.65 (m, 2H, major + minor), 6.08−5.91 (m, 1H, major), 5.79−5.63 (m, 1H, minor), 5.36 (s, 1H, major), 5.27 (d, J = 10.1 Hz, 1H, major), 5.19 (d, J = 17.2 Hz, 1H, major), 5.08 (d, J = 10.2 Hz, 1H, minor), 4.94 (d, J = 17.0 Hz, 2H, minor), 3.64−3.52 (m, 1H, minor), 3.49 (t, J = 8.0 Hz, 1H, major), 3.38−3.20 (m, 1H, minor), 3.10 (dd, J = 18.1, 8.1 Hz, 1H, major), 2.83 (m, 2H, major), 2.50−2.44 (m, 2H, minor),

DOI: 10.1021/acs.joc.6b00991
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2.45 (s, 3H, minor), 2.38 (s, 3H, major), 2.07 (d, J = 13.3 Hz, 1H, major + minor), 1.94 (m, 1H, major), 1.73 (m, 2H, major + minor), 1.39 (d, J = 13.4 Hz, 2H, major + minor), 1.33−1.10 (m, 2H, major + minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 147.6, 147.2, 143.1, 142.9, 137.8, 137.1, 134.4, 134.2, 132.8, 132.6, 129.5, 129.4, 128.2, 127.7, 127.1, 127.0, 124.7, 121.8, 119.2, 118.9, 118.8, 118.0, 110.2, 109.8, 91.8, 91.0, 57.7, 57.0, 51.5, 51.2, 50.6, 45.7, 34.3, 34.1, 32.6, 27.2, 22.4, 21.5, 21.4, 20.9, 20.5, 19.4; IR (in KBr) 3398, 2922, 1609, 1466, 1316, 1143, 1089 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{26}N_2O_2S$ $[M + H]^+$ 395.1789, found 395.1789.

*3a-Methyl-3-(prop-1-en-2-yl)-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ab**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 12 h, 77 mg, yield 42%, dr = 5:1; white solid, mp 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72 (t, J = 9.6 Hz, 2H, major + minor), 7.29 (t, J = 10.3 Hz, 2H, major + minor), 7.09−6.97 (m, 1H, major + minor), 6.92 (d, J = 7.4 Hz, 1H, major + minor), 6.72 (m, 1H, minor), 6.63 (t, J = 7.4 Hz, 1H, major), 6.57 (t, J = 7.6 Hz, 1H, major + minor), 5.13 (d, J = 5.6 Hz, 1H, major + minor), 4.95 (s, 1H, major), 4.84 (s, 1H, minor), 4.68 (d, J = 7.8 Hz, 1H, major + minor), 3.47 (dd, J = 10.3, 7.0 Hz, 1H, major), 3.34 (d, J = 6.8 Hz, 1H, minor), 3.28 (m, 1H, minor), 3.20 (t, J = 10.9 Hz, 1H, major), 3.02 (m, 1H, minor), 2.54 (dd, J = 11.3, 6.9 Hz, 1H, major), 2.42 (s, 3H, major + minor), 1.63 (s, 3H, major), 1.54 (s, 3H, minor), 1.42−1.33 (m, 3H, major), 1.09 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.1, 147.3, 143.6, 142.9, 140.6, 136.4, 129.8, 129.7, 129.3, 128.4, 128.3, 127.2, 127.1, 125.0, 122.5, 119.2, 118.6, 114.9, 114.7, 109.7, 109.0, 105.1, 85.3, 85.0, 56.6, 56.2, 54.8, 53.0, 51.3, 50.3, 26.0, 23.1, 21.6, 21.4, 19. 8; IR (in KBr):3393, 2921, 1609, 1486, 1339, 1163, 1093 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_2S$ $[M + H]^+$ 369.1631, found 369.1633.

*(E)-tert-Butyl 3-(3a-methyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indol-3-yl)acrylate (**3ac**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 12 h, 114 mg, yield 50%, dr= 2:1; white solid, mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (d, J = 8.2 Hz, 2H, major + minor), 7.31 (d, J = 8.0 Hz, 2H, major + minor), 7.06 (t, J = 7.6 Hz, 1H, major + minor), 6.89 (d, J = 7.4 Hz, 1H, major + minor), 6.79 (dd, J = 15.7, 8.6 Hz, 1H, major + minor), 6.70 (t, J = 7.4 Hz, 1H, major + minor), 6.61 (d, J = 7.8 Hz, 1H, major + minor), 5.74 (d, J = 15.6 Hz, 1H, major + minor), 5.13 (s, 1H, major + minor), 4.85 (s, 1H, major + minor), 3.54 (dd, J = 10.6, 7.0 Hz, 1H, major), 3.52 (dd, J = 10.6, 7.0 Hz, 1H, minor), 3.03 (t, J = 11.0 Hz, 1H, major), 3.01 (t, J = 11.0 Hz, 1H, minor), 2.56 (s, 3H, minor), 2.44 (s, 3H, major), 1.47 (s, 9H, major), 1.45 (s, 9H, minor), 1.28 (s, 3H, major), 1.01 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major) 166.45, 150.5, 145.3, 143.8, 137.6, 131.5, 130.2, 129.8, 128.5, 127.6, 126.6, 120.6, 111.2, 86.2, 82.3, 59.2, 53.0, 52.8, 29.6, 25.9, 23.1; IR (in KBr) 2885, 1619, 1531, 1456, 1369 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{30}N_2O_4S$ $[M + H]^+$ 455.1999, found 455.2008.

*10b-Methyl-5-tosyl-3,4,4a,5,5a,6,10b,10c-octahydroindolo[2,3-b]indole (**3ae**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 12 h, 167 mg, yield 88%, dr = 2:1; white solid, mp 177−178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (dd, J = 14.1, 8.0 Hz, 2H, major + minor), 7.33 (d, J = 7.9 Hz, 1H, major), 7.23 (d, J = 7.7 Hz, 1H, major + minor, 1H, minor), 7.01 (m, 2H, major + minor), 6.73−6.46 (m, 2H, major + minor), 5.96 (d, J = 9.7 Hz, 1H, major), 5.72 (d, J = 10.0 Hz, 1H, minor), 5.62 (d, J = 10.9 Hz, 1H, major + minor), 5.42 (s, 1H, major), 5.19 (s, 1H, minor), 5.09 (s, 1H, major + minor), 3.09−2.87 (m, 1H, major + minor), 2.65 (d, J = 9.1 Hz, 1H, minor), 2.52 (m, 1H, major + minor), 2.44 (s, 3H, minor), 2.40 (s, 3H, major), 2.30 (d, J = 11.1 Hz, 1H, major), 2.23 (m, 1H, minor), 2.13 (d, J = 17.3 Hz, 1H, major + minor, 1.95 (s, 1H, major), 1.79−1.64 (m, 1H, minor), 1.54−1.40 (s, 3H, major), 0.89 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.3, 147.3, 143.9, 143.0, 139.0, 134.2, 133.3, 130.2, 129.8, 129.6, 129.2, 128.8, 128.4, 128.2, 127.6, 127.0, 123.8, 122.9, 122.9, 121.8, 118.5, 118.5, 109.2, 108.5, 89.1, 86.7, 61.2, 61.1, 53.6, 53.5, 51.9, 51.6, 28.0, 26.7, 25.6, 25.3, 24.3, 21.6, 21.45, 17.8; IR (in KBr) 2921, 1332, 1163 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{24}N_2O_2S$ $[M + H]^+$ 381.1631, found 381.1624.

*3a-Methyl-3-vinyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (**5aa**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 10/1; reaction time = 12 h, 97 mg, yield 90%, dr = 3:1; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.04−6.93 (m, 2H, major + minor), 6.71 (t, J = 7.4 Hz, 1H, minor), 6.69−6.60 (m, 1H, major), 6.58−6.48 (m, 1H, major + minor), 5.84 (m, 1H, minor), 5.52 (m, 1H, major), 5.37 (s, J = 2.3 Hz, 1H, major), 5.27−5.08 (m, 2H, major + minor, 1H, minor), 4.75 (s, 1H, major + minor), 3.89 (dd, J = 8.4, 6.7 Hz, 1H, major), 3.71 (dd, J = 10.9, 4.0 Hz, 2H, minor), 3.38 (dd, J = 11.3, 8.6 Hz, 1H, major), 2.80 (m, 1H, major, major + minor), 1.42−1.37 (s, 3H, major), 1.25 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.2, 148.0, 136.7, 134. 1, 129.2, 127.9, 127. 7, 125.4, 122.7, 122.4, 118.6, 117.9, 117.6, 116.5, 108.3, 108.0, 107.7, 100.1, 99.3, 72.1, 70.8, 56.2, 54.7, 24.8, 24.6, 24.5, 20.9; IR (in KBr) 2923, 2852, 1585, 1486 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{15}NO$ $[M + H]^+$ 202.1226, found 202.1232.

*6-Chloro-3a-methyl-3-vinyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]-indole (**5ba**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 10/1; reaction time = 12 h, 95 mg, yield 81%, dr = 1:1; brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.35−6.99 (m, 2H, major + minor, 1H, minor), 6.95 (d, J = 1.4 Hz, 1H, major), 6.34 (dd, J = 10.7, 6.1 Hz, 1H, major + minor), 5.82−5.68 (m, 1H, minor), 5.52−5.35 (m, 1H, major), 5.28 (s, 1H, major), 5.22−4.97 (m, 2H, major + minor, 1H, minor), 4.40 (s, 1H, major + minor), 3.83 (dd, J = 8.2, 7.0 Hz, 1H, major), 3.71−3.57 (m, 2H, minor), 3.29 (dd, J = 11.1, 8.7 Hz, 1H, major), 2.77−2.64 (m, 1H, major), 1.37−1.27 (s, 3H, major, m, 1H, minor), 1.17 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 148.2, 147.0, 136.1, 133.3, 131.5, 130.4, 130.3, 128.2, 125.6, 118.6, 116.9, 116.0, 110.2, 109.6, 109.3, 109. 0, 100. 1, 99.4, 72.2, 70.8, 56.4, 56.4, 56.0, 54.6, 24.4, 20.8; IR (in KBr) 3080, 2928, 2854, 1641, 1604, 1481, 1376 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{14}ClNO[M]^+$ 235.0758, found 235.0751.

*3a,5-Dimethyl-3-vinyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (**5fa**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 10/1; reaction time = 12 h, 103 mg, yield 96%, dr= 3:1; light-yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.85 (t, J = 5.6 Hz, 1H, major + minor, 1H, minor), 6.78 (s, 1H, major), 6.58−6.38 (m, 1H, major + minor), 5.84 (ddt, J = 17.1, 10.4, 8.4 Hz, 1H, minor), 5.55 (m, 1H, major), 5.38 (d, J = 4.5 Hz, 1H, major), 5.31−5.05 (m, 2H, major + minor, 1H, minor), 4.03 (s, 1H, major + minor), 3.90 (dd, J = 8.4, 6.7 Hz, 1H, major), 3.73 (ddd, J = 11.7, 8.7, 4.0 Hz, 2H, minor), 3.39 (dd, J = 11.3, 8.5 Hz, 1H, major), 2.80 (m, 1H, major), 2.31−2.20 (d, J = 2.25 Hz, 3H, major + minor), 1.47−1.35 (s, 3H, major, m, 1H, minor), 1.26 (s, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 146.9, 136.7, 134.1, 129.5, 128.1, 127.0, 126.0, 123.1, 117.8, 116.4, 115.8, 109.1, 108.3, 107.8, 100.4, 99.7, 72.2, 70.9, 56.4, 56.2, 54. 7, 46.3, 24.6, 24.5, 20.9, 20.9; IR (in KBr) 3017, 1637, 1607, 1493, 1386 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{17}NO$ $[M + H]^+$ 215.1310, found 215.1309.

*3a-Allyl-3-vinyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (**5ma**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 10/1; reaction time = 24 h, 93 mg, yield 82%, dr= 9:1 ; brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.10−6.95 (m, 2H, major + minor), 6.74 (dd, J = 13.3, 5.9 Hz, 1H, minor), 6.71−6.64 (m, 1H, major), 6.61−6.50 (m, 1H, major + minor), 5.93 (dm, 1H, minor), 5.63−5.41 (m, 2H, major + minor, 1H, major), 5.32 (d, J = 5.9 Hz, 1H, minor), 5.24−5.12 (m, 1H, major + minor, 1H, major), 4.98 (m, 2H, major + minor), 4.62 (s, 1H, major + minor), 3.90 (dd, J = 8.5, 6.7 Hz, 1H, major), 3.78−3.66 (m, 2H, minor), 3.41 (dd, J = 11.3, 8.5 Hz, 1H, major), 3.00−2.82 (m, 1H, major + minor), 2.73−2.60 (m, 1H, major), 2.59−2.50 (m, 1H, minor), 2.49−2.35 (m, 1H, major), 2.31 (m, 1H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 149.5, 148.2, 143.5, 143.4, 136.3, 135.3, 133.9, 133.2, 132.9, 130.9, 129.6, 128.4, 127.4, 127.2, 127.0, 125.5, 122.5, 118.7, 118.4, 118.3, 109.5, 109.2, 82.3, 81.7, 60.4, 59.6, 52.4, 51.6, 51.6, 51.2, 41.8, 37.3, 29.8, 21.7; IR (in KBr) 3077, 1638, 1607, 1516, 1484 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{17}NO$ $[M + H]^+$ 227.1310, found 227.1304.

DOI: 10.1021/acs.joc.6b00991
J. Org. Chem. 2016, 81, 10491−10498

*3a-(But-3-en-1-yl)-1-tosyl-3-vinyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3qa**):* Flash column chromatography eluent, petroleum ether/ethyl acetate = 12/1; reaction time = 12 h, 118 mg, yield 60%, dr = 7:1; brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (d, J = 8.2 Hz, 2H, major + minor), 7.30 (d, J = 8.1 Hz, 2H, major + minor), 7.04 (t, J = 7.7 Hz, 1H, major + minor), 6.93 (d, J = 7.4 Hz, 1H, major + minor), 6.72 (m, 1H, minor), 6.66 (t, J = 7.4 Hz, 1H, major), 6.61 (d, J = 7.8 Hz, 1H, minor), 6.56 (d, J = 7.8 Hz, 1H, major), 5.81−5.48 (m, 2H, major, 1H, minor), 5.26 (d, J = 4.5 Hz, 1H, major), 5.20−5.02 (m, 2H, major + minor, 1H, minor), 4.87 (dd, J = 13.0, 5.7 Hz, 2H, major + minor, 1H, minor), 4.76 (s, 1H, major + minor), 3.50 (dd, J = 10.5, 7.0 Hz, 1H, major), 3.38 (d, J = 5.9 Hz, 1H, minor), 3.15 (d, J = 4.6 Hz, 1H, minor), 2.97 (t, J = 10.9 Hz, 1H, major + minor), 2.57−2.48 (m, 1H, major), 2.43 (s, 3H, major + minor), 1.85 (m, 2H, major + minor), 1.66−1.57 (m, 1H, major + minor), 1.55−1.44 (m, 1H, major + minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major + minor) 150.06, 148.59, 143.69, 143.6, 138.0, 138.0, 136.5, 134.7, 134.2, 131.0, 129.8, 129.8, 128.6, 128.5, 127.2, 127.1, 126.9, 125.7, 122.8, 119.0, 118.8, 118.5, 117.8, 114.6, 114.5, 109.8, 109.2, 82.8, 82.6, 60.5, 59.8, 52.8, 52.8, 51.4, 51.3, 37.6, 32.2, 28.6, 28.5, 21.56, 14.2; IR (in KBr) 2923, 1608, 1466, 1341, 1160 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{26}N_2O_2S$ $[M + H]^+$ 395.1788, found 395.1789.

*6-Tosyl-2,4a,5,6,6a,7-hexahydro-1H-isoindolo[1,7ab]indole (**6**):* Flash column chromatography eluent, hexanes/ethyl acetate = 20/1; reaction time = 4 h, 28 mg, yield 76%, dr = 6:1; white solid, mp 174−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm, major) 7.64 (d, J = 8.2 Hz, 2H), 7.29−7.21 (m, 3H), 7.06 (t, J = 7.6 Hz, 1H), 6.66 (t, J = 8.1 Hz, 2H), 5.90−5.63 (m, 2H), 4.99 (s, 1H), 4.84 (s, 1H), 3.51 (dd, J = 9.4, 7.0 Hz, 1H), 2.84 (dd, J = 12.5, 9.5 Hz, 1H), 2.39 (s, 4H), 2.27 (s, 2H), 1.85 (d, J = 4.1 Hz, 1H), 1.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm, major) 149.9, 143.4, 136.2, 130. 6, 129.8, 129.6, 128.6, 126.8, 126.3, 123.3, 119.5, 111.0, 84.1, 55.2, 51.2, 43.8, 29.7, 23.7, 21.5; IR (in KBr) 3360, 2920, 1710, 1655, 1470, 1341, 1152, 1091 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{22}N_2O_2S$ $[M + H]^+$ 367.1475, found 367.1468.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00991.

X-ray data for **3aa** (CIF)

General information, details for condition optimization, and spectroscopic data of **3**, **5**, and **6**(PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the National Natural Science Foundation of China (Nos. 21232003, 21472057, and 21572074) and other financial support (Nos. 201422, CCNU15A02007, and 2015CFA033) for support of this research.

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DOI: 10.1021/acs.joc.6b00991
J. Org. Chem. 2016, 81, 10491−10498