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Access to Indole-Annulated Medium-Sized Lactams through Protonation/Deuteration-Induced Ring-Opening of Spiroindolines

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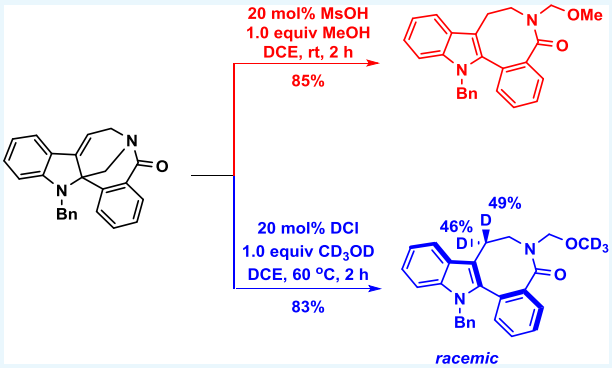
ABSTRACT: A protocol has been developed to access indole-annulated eight- and nine-membered lactams through protonation-induced ring-opening of spiroindolines, which are dearomative Heck products of tetrahydro-β-carbolines or hexahydroazepino[3,4-*b*]-indoles. Brønsted acids and nucleophiles were explored and compared in the transformation. A combination of deuterated hydrochloride and deuterated methanol enables deuterative ring-opening of spiroindolines to afford medium-sized lactam diastereoisomers with a deuterium content ratio around 1:1.

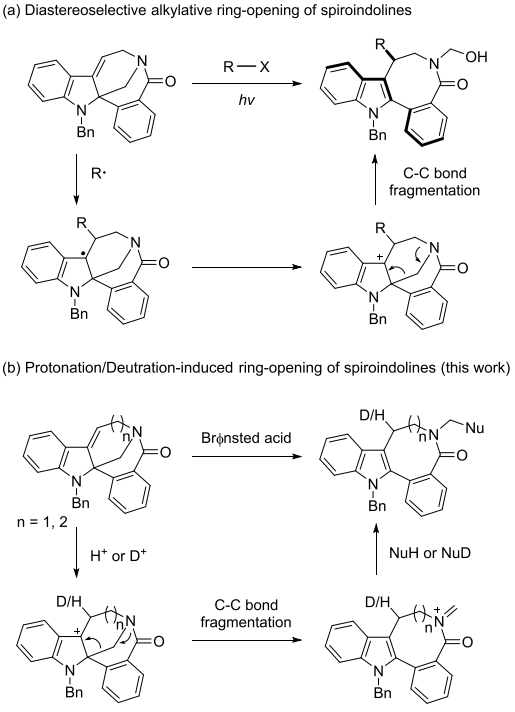


INTRODUCTION

Indole-annulated medium-sized nitrogen-containing heterocyclic rings are core structures embedded in bioactive natural alkaloids, including balasubramide,[1] deoxyisoaustamide,[2] okaramine,[3] lundurine A−D,[4] and vinblastine.[5] Generally, the construction of medium-sized compounds has been challenging in organic synthesis due to unfavorable entropy and transannular interactions.[6] It is impressive that significant strategies including cycloaddition,[7] cycloisomerization,[8] and ring expansion[9] have been invented for the generation of eight- and nine-membered nitrogen-containing heterocycles.

Recently, we have developed a diastereoselective protocol to prepare indole-annulated eight-membered lactams through light-driven alkylative ring-opening of spiroindolines, a type of dearomative Heck product of easily available β-carbolines.[10] DFT calculations and mechanistic experiments support that a cationic C−C fragmentation should be favorable rather than a homolytic C−C fragmentation, in which a tertiary cation intermediate might be involved (Scheme 1a).[11] Because a tertiary carbon cation could be formed regioselectively through direct protonation of an alkene, we envisioned an alternative to indole-annulated medium-sized lactams by protonation-induced ring-opening of the spiroindolines (Scheme 1b). The key issues of the transformation include the choice of Brønsted acids, the tolerance of the indole ring, and the nucleophile to trap the iminium intermediate. Furthermore, if this can be realized, a deuterative ring-opening would be feasible by employing deuterated acids and deuterated nucleophiles, which provides an unprecedented protocol to prepare deuterated indole-containing medium-sized hetero-

Scheme 1. Reaction Design



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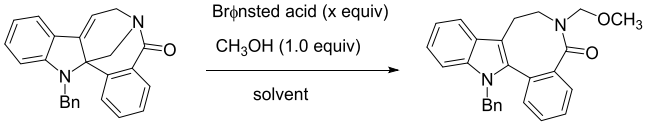
cycles.[12] Here, we report our experimental results on the reaction design.

RESULTS AND DISCUSSION

We commenced the study by reacting spiroindole **1a** with methanol using acetic acid as a promoter. The anticipated ring-opening reaction did not take place even after heating in 1,2-dichloroethane at 60 °C for 12 h, probably due to the relatively weak acidity (Table 1, entry 1). However, in the presence of stronger Brønsted acids such as trifluoroacetic acid, hydrochloride, and methanesulfonic acid, the spiroindoline was converted successfully to eight-membered lactam **2a** (Table 1, entries 2−4). The structure of **2a** was confirmed unequivocally by single-crystal X-ray diffraction (Figure 1). It was impressive that **2a** was isolated in 89% yield under the promotion of methanesulfonic acid even when the ring-opening reaction was performed at room temperature. Control experiments showed that 0.2 equiv of methanesulfonic acid is appropriate for the transformation (entries 5 and 6). Further screenings of solvents by fixing methanesulfonic acid and methanol demonstrated that lower yields were obtained in dichloromethane, chloroform, 1,4-dioxane, tetrahydrofuran, and toluene, while the reaction was completely inhibited in acetonitrile, *N*,*N*-dimethylformamide, and dimethyl sulfoxide (Table 1, entries 9−14).

Table 1. Optimization of the Protonation-Induced Ring-Opening of Spiroindoline 1a[a]



1a **2a**

entry	acid	*x*	solvent	temp. (°C)	time (h)	yield (%)[b]
1	HOAc	1.0	DCE	60	12	
2	TFA	1.0	DCE	60	2	68
3[c]	HCl	1.0	DCE	60	2	80
4	MsOH	1.0	DCE	rt	2	89
5	MsOH	0.2	DCE	rt	2	85
6	MsOH	0.1	DCE	rt	12	70
7	MsOH	0.2	DCM	rt	2	81
8	MsOH	0.2	$CHCl_3$	rt	2	63
9	MsOH	0.2	dioxane	rt	2	25
10	MsOH	0.2	THF	rt	2	24
11	MsOH	0.2	toluene	rt	2	58
12	MsOH	0.2	MeCN	rt	2	
13	MsOH	0.2	DMF	rt	2	
14	MsOH	0.2	DMSO	rt	2	

[a]Reaction conditions: spiroindoline **1a** (0.05 mmol), acid (*x* equiv), methanol (0.05 mmol), and degassed solvent (0.25 mL) were stirred in a sealed vial. [b]Isolated yield after column purification. [c]20% HCl in water.

The scope of the protonation-induced C−C bond fragmentation was next examined (Scheme 2). Like spiroindoline **1a**, spiroindolines with electron-donating and electron-withdrawing substituents (Me, MeO, F, Cl) located at ortho, meta, and para positions of the benzamide ring, participated in the ring-opening reaction with methanol smoothly, affording indole-annulated eight-membered lactams **2b−2k** in yields ranging from 76 to 90%. It seems that the electron-donating group might be more favorable than the electron-withdrawing group for the transformation. Different substituents (MeO, Cl, Me) on the indole ring were also compatible, affording lactams **2l−2n** in a comparable efficiency. Replacing the benzyl group on the nitrogen of the indole ring by a methyl group did not interfere with the conversion, affording lactam **2o** in 91% yield. Spiroindoline **1a** reacted with heteroatom-containing nucleophiles with increasing steric hindrance such as ethanol, benzyl alcohol, isopropanol, and 4-methylbenzenethiol in a similar manner, affording lactams **2p−2s** in good yields. Carbon nucleophiles including 2-naphthol and indole engaged in the ring-opening reaction to afford lactams **2t** and **2u** in 82 and 70% yields, respectively.

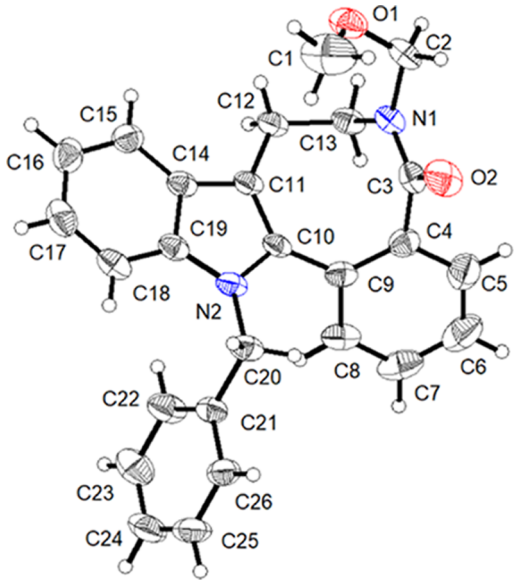


Figure 1. X-ray crystal structure of **2a** (30% probability levels).

We further tested the feasibility of deuteration-induced ring-opening of spiroindolines by employing commercially available deuterated Brønsted acid and deuterated nucleophile. To our delight, the ring-opening of spiroindoline **1a** was observed at 60 °C under the promotion of deuterated trifluoroacetic acid and deuterated methanol, affording indole-annulated eight-membered lactam **3a** in 70% yield (Table 2, entry 1). The assignment of different hydrogens of lactam **3a** was identified by a series of NMR studies. Further NOE experiments of lactam **3a** supported that hydrogens *a*, *d*, and *e* are close in space, in which the cross-peaks of hydrogen *a* and *e*, *a* and *d* had strong intensities (Figure 2). Based on the integration of peaks on the ^{1}H NMR spectra of **3a**, we found that hydrogens *c* and *d* were partially deuterated with 49 and 48% deuterium installation. When deuterated hydrochloride was employed as Brønsted acid, the medium-sized lactam was isolated in 83% yield of 49 and 46% deuterium contents (Table 2, entry 2). It is worth mentioning that the competitive nucleophilic addition of D_2O toward the iminium intermediate did not happen, highlighting that deuterated methanol performed as a benign nucleophile. Inferior results were obtained in dichloromethane, chloroform, toluene, 1,4-dioxane, and THF, and no conversions were observed in acetonitrile, DMF, and DMSO (Table 1, entries 3−10), which are consistent with those encountered in the protonation-induced ring-opening reaction.

By fixing the combination of deuterated hydrochloride and deuterated methanol, the deuteration-induced ring-opening of

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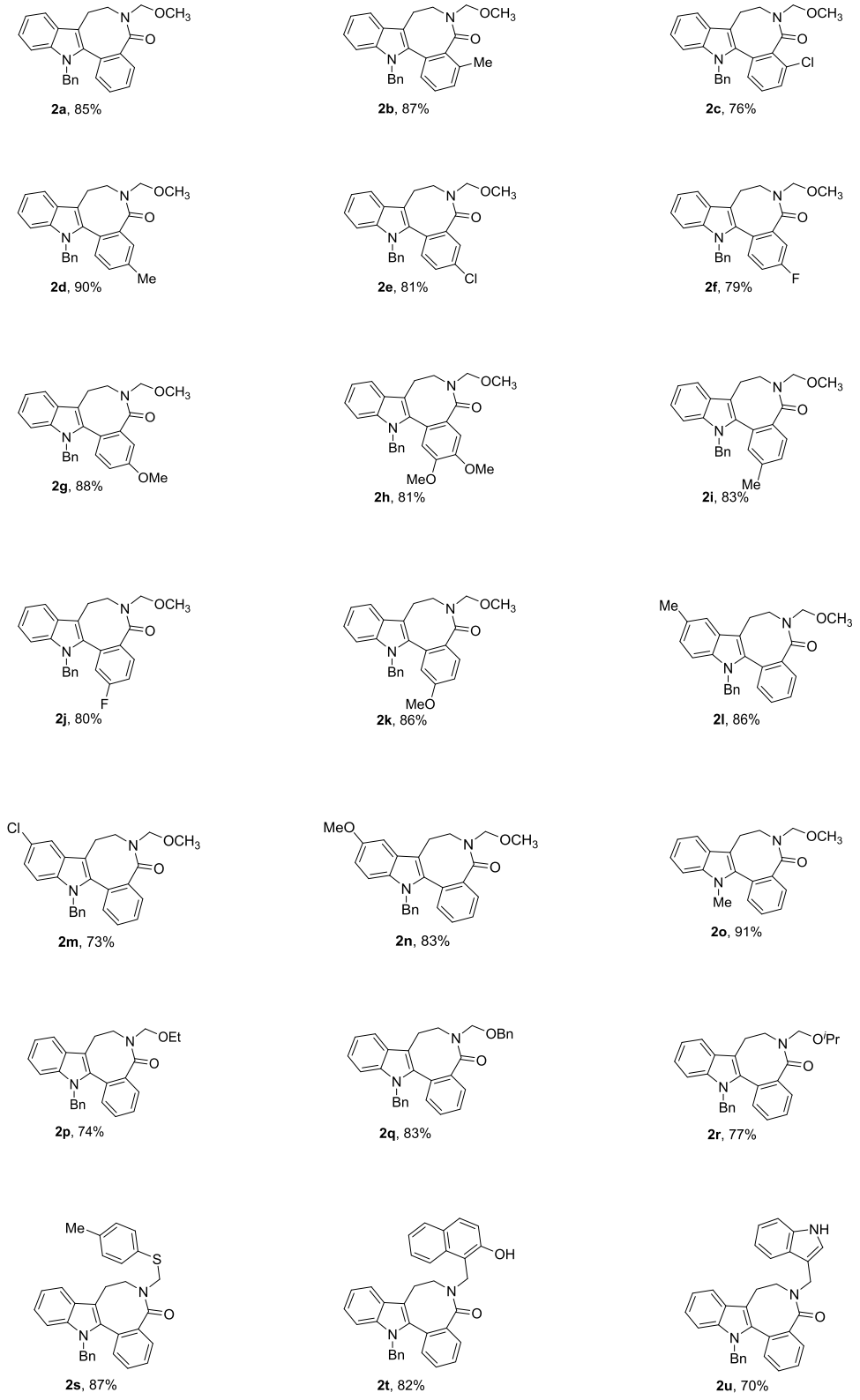
Scheme 2. Scope of Indole-Annulated Eight-Membered Lactams[a]



[a]Reaction conditions: a mixture containing spiroindoline **1** (0.05 mmol), methanesulfonic acid (0.01 mmol), nucleophile (0.05 mmol), and degassed 1,2-dichloroethane (0.25 mL) was stirred in a sealed vial at room temperature for 2 h. Isolated yield after column purification.

spiroindoline **1a** was extended (Scheme 3). Other candidates with methoxy, methyl, chlorine, and fluorine groups located at different positions on the benzamide and indoline rings as well as the nitrogen of the indoline afforded lactams **3b**−**3o** in good to excellent yields. The deuterium content ratio of two hydrogens on the eight-membered ring is close to 1:1, except for that of compounds **3b** and **3c**. It was suggested that in most cases, nondiastereoselective deuteration of the alkene in

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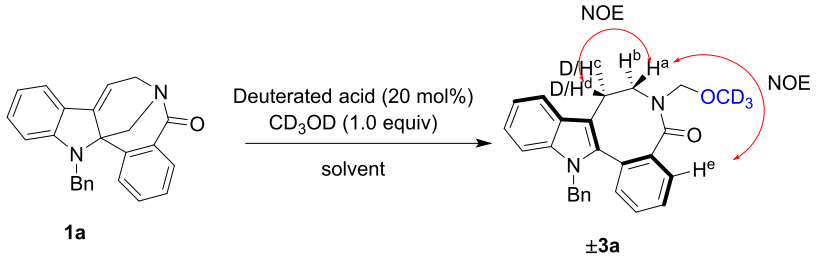
Table 2. Optimization of the Deuteration-Induced Ring-Opening of Spiroindoline 1a[a]



						deuterium content	
entry	deuterated acid	solvent	temp. (°C)	t (h)	yield (%)[b]	H^c (%)[c]	H^d (%)[c]
1	CF_3COOD	DCE	60	2	70	49	48
2	DCl (20% in D_2O)	DCE	60	2	83	49	46
3	DCl (20% in D_2O)	DCM	40	8	72	48	45
4	DCl (20% in D_2O)	$CHCl_3$	60	2	61	45	41
5	DCl (20% in D_2O)	toluene	60	2	50	45	40
6	DCl (20% in D_2O)	dioxane	60	2	28	43	41
7	DCl (20% in D_2O)	THF	60	2	29	42	39
8	DCl (20% in D_2O)	MeCN	60	2			
9	DCl (20% in D_2O)	DMF	60	2			
10	DCl (20% in D_2O)	DMSO	60	2			

[a]Reaction conditions: spiroindoline **1a** (0.05 mmol), deuterated acid (0.01 mmol), CD_3OD (0.05 mmol), 1,2-dichloroethane (degassed, 0.25 mL), 60 °C, 2 h. [b]Isolated yields after column purification. [c]The deuterium content was calculated by the integration of peaks shown on the ^1H NMR spectra.

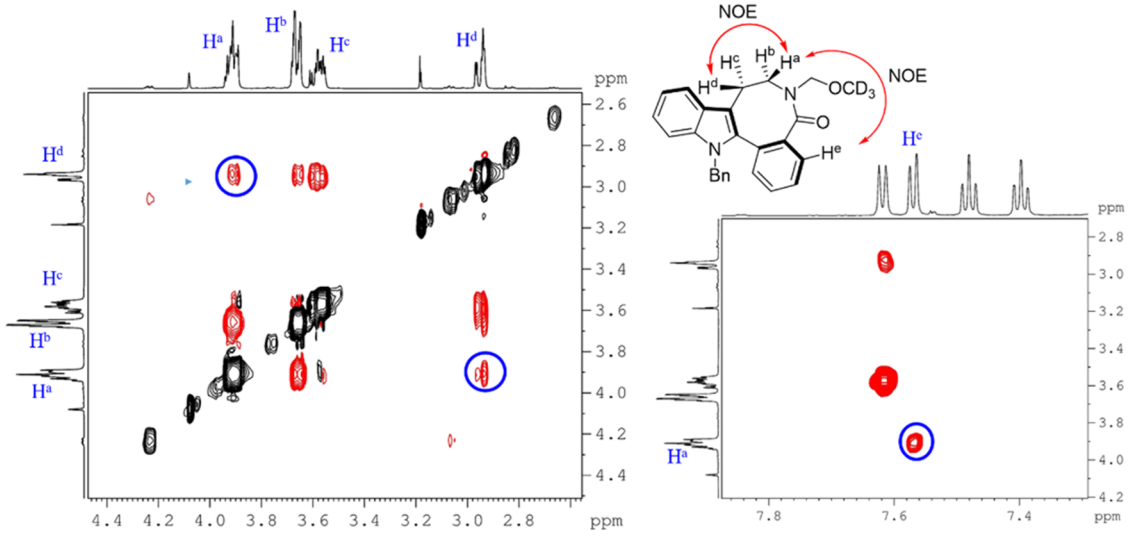


Figure 2. ^2D NOESY spectra of compound **3a** with a mixing time of 700 ms.

spiroindolines is predominant, while the ortho substituent on the benzamide ring leads to a diastereoselective deuteration, which makes one diastereomer of **3b** or **3c** excess.

Based on the protonation/deuteration-promoted ring-opening reaction, indole-annulated nine-membered lactams **5a−5d** can be prepared from spiroindoline **4** (Scheme 4). As illustrated, under the promotion of methanesulfonic acid, spiroindoline **4** reacted with oxygen and carbon nucleophiles to afford lactams **5a−5c** in excellent yields, in which methoxy, 2-naphthol, and indole were installed to the side chain of the nine-membered lactams. In the presence of deuterated hydrochloride and methanol, lactam **5d** was obtained in 88% yield with 58 and 41% deuterium installation.

CONCLUSIONS

In summary, we have established a protocol to prepare indole-annulated eight- and nine-membered lactams by taking advantage of protonation-induced ring-opening of spiroindolines. Under the promotion of methanesulfonic acid, spiroindolines reacted with different hetero and carbon nucleophiles to afford medium-sized lactams with side chains containing alkoxy, thiol ether, 2-naphthol, and indole groups. In the presence of deuterated hydrochloride and deuterated methanol, a deuterative ring-opening of spiroindolines proceeded smoothly to afford deuterated medium-sized lactams. Further investigations on the diastereoselective deuteration-induced ring-opening of spiroindolines are underway.

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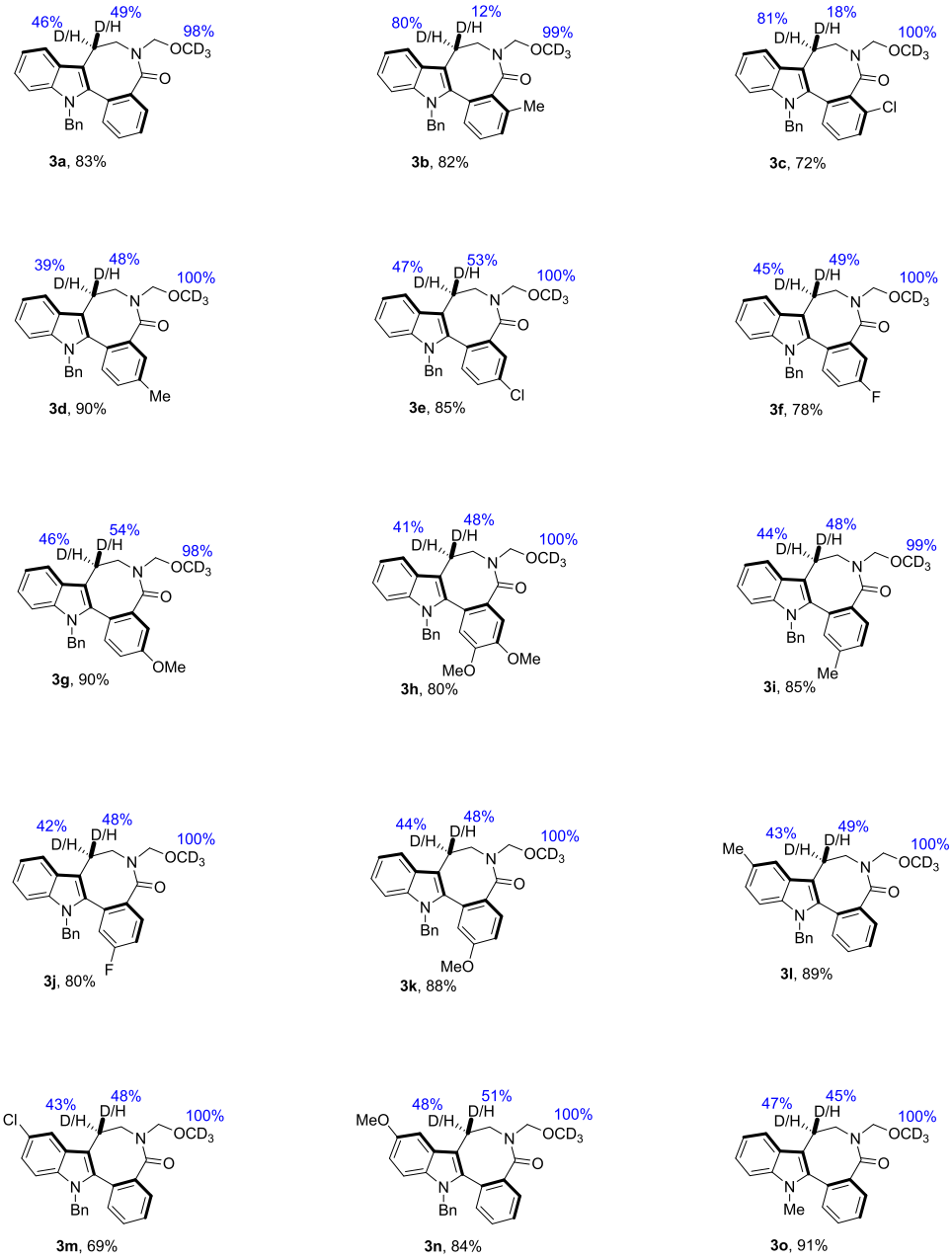
Scheme 3. Scope of Deuterated Indole-Annulated Eight-Membered Lactams[a]



[a]Reaction conditions: a mixture containing spiroindoline **1** (0.05 mmol), deuterated hydrochloride (20% in D_2O, 0.01 mmol), deuterated methanol (0.05 mmol), degassed 1,2-dichloroethane (0.25 mL) was stirred at 60 °C for 2 h. Isolated yield after column purification.

EXPERIMENTAL SECTION

General Information. ^1H NMR spectra was obtained at 400 MHz. ^2H NMR spectra were recorded at a frequency of 92 MHz. ^{13}C NMR spectra were obtained at 100 MHz, and ^{19}F NMR spectra were obtained at 376 MHz. Spectra were recorded in a $CDCl_3$ solution using the residual protonated solvent as the internal standard, and *J* values are given in hertz. IR spectra were recorded on a Fourier transform infrared spectrometer and listed in cm^{-1}. High-resolution mass spectral analyses (HRMS) were performed on a Q-TOF-MS spectrometer. All air moisture-sensitive reactions were conducted in oven-dried glassware under a nitrogen atmosphere using dry and degassed solvents. Flash column chromatography was performed over silica gel (300−400 mesh). All commercially available reagents were used without further purification. Spiroindolines were prepared according to the known procedure.[10]

General Procedure A for the Synthesis of Indole-Annulated Medium-Sized Lactams. To a dry 1.5 mL glass bottle, spiroindoline **1** or **4** (0.05 mmol) and degassed DCE (0.25 mL) were added successively. Then, a nucleophile (50 μL, 0.05 mmol, 1 mol/L DCE solution) and MsOH (10 μL, 0.01 mmol, 1 mol/L DCE solution) were added. The reaction mixture was stirred at room temperature for 2 h. The solution was concentrated under vacuum to afford a residue, which was purified by column chromatography on silica gel to afford lactam **2** or **5a**−**5c**.

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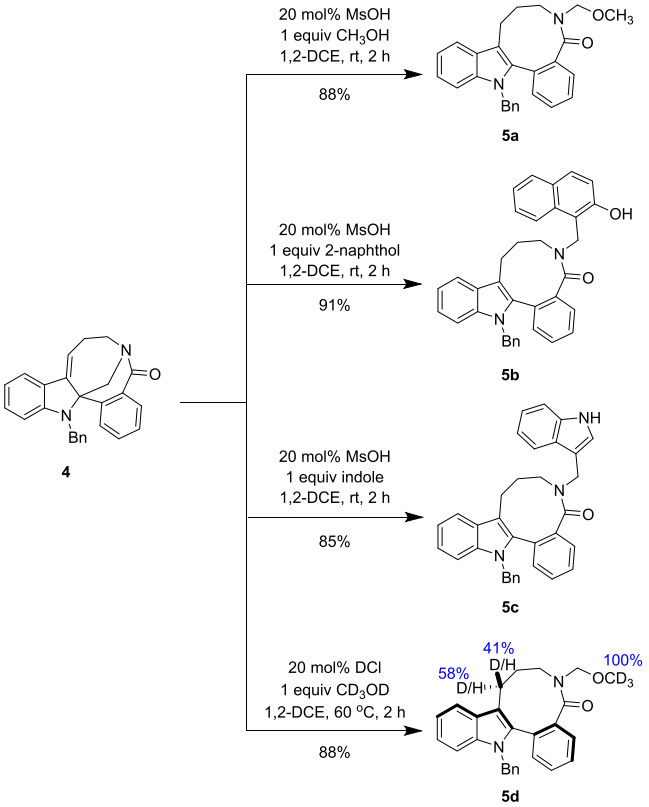
Scheme 4. Access to Indole-Annulated Nine-Membered Lactams from Spiroindoline 4



General Procedure B for the Synthesis of Deuterated Indole-Annulated Medium-Sized Lactams. To a dry 1.5 mL glass bottle, spiroindoline **1** or **4** (0.05 mmol) and degassed DCE (0.25 mL) were added successively. Then, CD_3OD (50 μL, 0.05 mmol, 1 mol/L DCE solution) and DCl (20% in D_2O, 2 μL, 0.01 mmol) were added. The reaction mixture was stirred at 60 °C for 2 h. The solution was concentrated under vacuum to afford a residue, which was purified by chromatography on silica gel to afford lactam **3** or **5d**.

*13-Benzyl-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2a**).* According to procedure A, lactam **2a** was obtained from spiroindoline **1a** (18.2 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (16.3 mg, 85% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 101−103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.50 (m, 2H), 7.44 (td, J = 7.5, 1.3 Hz, 1H), 7.36 (td, J = 7.6, 1.5 Hz, 1H), 7.28−7.11 (m, 7H), 6.99−6.94 (m, 2H), 5.17 (d, J = 16.9 Hz, 1H), 5.10−4.98 (m, 2H), 4.88 (d, J = 10.3 Hz, 1H), 3.88 (td, J = 14.2, 4.6 Hz, 1H), 3.68−3.49 (m, 2H), 3.15 (s, 3H), 2.92 (ddd, J = 16.5, 4.4, 1.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 138.0, 137.6, 137.5, 134.0, 130.6, 129.3, 129.2, 129.0, 128.7, 128.6, 128.2, 127.2, 126.1, 122.7, 119.9, 118.4, 110.6, 109.4, 75.6, 56.2, 47.6, 44.9, 24.4 ppm. IR (film) ν_{max} 1644, 1460, 1442, 1346, 1178, 1081, 1015, 962, 906, 727, 698 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{24}N_2NaO_2$ 419.1730 [M + Na]$^+$, found 419.1732.

*13-Benzyl-6-(methoxymethyl)-4-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2b**).* According to procedure A, lactam **2b** was obtained from spiroindoline **1b** (18.9 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (17.8 mg, 87% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 166−168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59−7.53 (m, 1H), 7.29−7.17 (m, 5H), 7.16−7.09 (m, 3H), 7.05−6.98 (m, 3H), 5.23 (d, J = 16.9 Hz, 1H), 5.16−5.07 (m, 2H), 4.79 (d, J = 10.4 Hz, 1H), 3.88−3.79 (m, 1H), 3.68−3.47 (m, 2H), 3.19 (s, 3H), 2.91−2.80 (m, 1H), 2.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 138.1, 137.4, 137.0, 135.5, 134.6, 130.8, 129.2, 128.7, 128.7, 128.5, 128.0, 127.1, 126.2, 122.5, 119.7, 118.2, 110.7, 109.0, 74.9, 56.3, 47.7, 44.4, 24.0, 19.8 ppm. IR (film) ν_{max} 1645, 1451, 1421, 1349, 1180, 1195, 1078, 1024, 907, 727, 699 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{26}N_2O_2$ 433.1886 [M + Na]$^+$, found 433.1883.

*13-Benzyl-4-chloro-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2c**).* According to procedure A, lactam **2c** was obtained from spiroindoline **1c** (20.0 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (16.4 mg, 76% yield, eluent: petroleum ether/ethyl acetate = 2/1). Mp 182−184 °C. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.60−7.56 (m, 1H), 7.52−7.41 (m, 3H), 7.29−7.24 (m, 1H), 7.23−7.06 (m, 5H), 6.93−6.83 (m, 2H), 5.22 (d, J = 16.8 Hz, 1H), 5.11 (d, J = 16.9 Hz, 1H), 4.97 (dd, J = 10.2, 1.1 Hz, 1H), 4.86 (d, J = 10.2 Hz, 1H), 3.86 (td, J = 14.2, 4.4 Hz, 1H), 3.67−3.45 (m, 2H), 3.12 (s, 3H), 2.96−2.80 (m, 1H) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2) δ 172.4, 138.4, 138.1, 137.8, 134.4, 131.0, 129.6, 129.5, 129.3, 129.1, 128.9, 128.4, 127.4, 126.5, 122.8, 120.1, 118.8, 110.9, 110.1, 76.0, 56.3, 47.7, 45.3, 24.8 ppm. IR (film) ν_{max} 1653, 1469, 1443, 1418, 1360, 1095, 1017, 726, 661, 648 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{23}ClN_2NaO_2$ 453.1340 [M + Na]$^+$, found 453.1337.

*13-Benzyl-6-(methoxymethyl)-3-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocin[5,4-b]indol-5-one (**2d**).* According to procedure A, lactam **2d** was obtained from spiroindoline **1d** (18.9 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (18.5 mg, 90% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 73−75 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.52 (m, 1H), 7.35 (d, J = 1.8 Hz, 1H), 7.27−7.12 (m, 7H), 7.07 (d, J = 7.9 Hz, 1H), 7.00−6.95 (m, 2H), 5.17 (d, J = 16.9 Hz, 1H), 5.11−4.99 (m, 2H), 4.86 (d, J = 10.3 Hz, 1H), 3.90 (td, J = 14.3, 4.6 Hz, 1H), 3.67−3.46 (m, 2H), 3.16 (s, 3H), 2.91 (ddd, J = 16.5, 4.4, 1.2 Hz, 1H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 139.1, 138.1, 137.5, 137.3, 134.2, 130.5, 130.1, 128.7, 128.7, 128.6, 127.1, 126.2, 126.1, 122.5, 119.8, 118.3, 110.6, 109.1, 75.5, 56.2, 47.6, 44.8, 24.3, 21.2 ppm. IR (film) ν_{max} 1643, 1464, 1440, 1349, 1174, 1092, 1015, 907, 727, 699 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{26}N_2NaO_2$ 433.1886 [M + Na]$^+$, found 433.1885.

*13-Benzyl-3-chloro-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2e**).* According to procedure A, lactam **2a** was obtained from spiroindoline **1e** (20.0 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (17.5 mg, 81% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 65−67 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.56 (m, 1H), 7.52 (d, J = 2.3 Hz, 1H), 7.33 (dd, J = 8.3, 2.2 Hz, 1H), 7.28−7.13 (m, 6H), 7.10 (d, J = 8.3 Hz, 1H), 6.98−6.91 (m, 2H), 5.17 (d, J = 17.0 Hz, 1H), 5.09−4.97 (m, 2H), 4.86 (d, J = 10.3 Hz, 1H), 3.87 (td, J = 14.4, 4.3 Hz, 1H), 3.71−3.48 (m, 2H), 3.14 (s, 3H), 2.92 (ddd, J = 16.6, 4.4, 1.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 138.9, 137.8, 137.8, 135.1, 132.8, 131.9, 129.4, 128.8, 128.4, 128.3, 127.7, 127.3, 126.0, 123.0, 120.0,

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118.5, 110.6, 109.9, 75.6, 56.3, 47.6, 44.9, 24.3 ppm. IR (film) ν_{max} 1651, 1464, 1441, 1350, 1180, 1093, 1015, 910, 732, 698 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{26}H_{23}ClN_2NaO_2$ 453.1340 $[M + Na]^+$, found 453.1338.

*13-Benzyl-3-fluoro-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2f**).* According to procedure A, lactam **2f** was obtained from spiroindoline **1f** (19.1 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (16.4 mg, 79% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 76−77 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.54 (m, 1H), 7.28−7.12 (m, 8H), 7.06 (td, *J* = 8.3, 2.7 Hz, 1H), 6.99−6.92 (m, 2H), 5.17 (d, *J* = 17.0 Hz, 1H), 5.09−4.99 (m, 2H), 4.86 (d, *J* = 10.3 Hz, 1H), 3.86 (td, *J* = 14.5, 4.4 Hz, 1H), 3.71−3.48 (m, 2H), 3.14 (s, 3H), 2.92 (ddd, *J* = 16.5, 4.5, 1.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.87, 163.98, 161.49, 139.46 (d, *J* = 8.1 Hz), 137.73 (d, *J* = 19.2 Hz), 132.96, 132.57 (d, *J* = 8.1 Hz), 128.75, 128.42, 127.26, 125.97, 125.32 (d, *J* = 3.0 Hz), 122.82, 119.96, 118.39, 116.52 (d, *J* = 12.1 Hz), 115.36 (d, *J* = 23.2 Hz), 110.55, 109.53, 75.65, 56.27, 47.55, 44.93, 24.27. ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.48 (s, 1F) ppm. IR (film) ν_{max} 1647, 1464, 1441, 1347, 1306, 1270, 1201, 1175, 1088, 1015, 962, 908, 728, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{26}H_{23}FN_2NaO_2$ 437.1636 $[M + Na]^+$, found 437.1633.

*13-Benzyl-3-methoxy-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2g**).* According to procedure A, lactam **2g** was obtained from spiroindoline **1g** (19.7 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (18.8 mg, 88% yield, eluent: petroleum ether/ethyl acetate = 3/2). Mp 66−68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.50 (m, 1H), 7.28−7.11 (m, 6H), 7.10−7.04 (m, 2H), 7.01−6.95 (m, 2H), 6.89 (dd, *J* = 8.6, 2.7 Hz, 1H), 5.17 (d, *J* = 17.0 Hz, 1H), 5.09−4.99 (m, 2H), 4.85 (d, *J* = 10.2 Hz, 1H), 3.91 (td, *J* = 14.5, 4.6 Hz, 1H), 3.85 (s, 3H), 3.69−3.46 (m, 2H), 3.15 (s, 3H), 2.91 (ddd, *J* = 16.4, 4.5, 1.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 160.0, 138.7, 138.1, 137.4, 134.0, 131.9, 128.7, 128.6, 127.1, 126.1, 122.4, 121.4, 119.7, 118.2, 115.8, 112.7, 110.5, 108.9, 75.6, 56.2, 55.5, 47.5, 45.0, 24.3 ppm. IR (film) ν_{max} 1644, 1464, 1452, 1431, 1349, 1315, 1293, 1229, 1182, 1083, 1032, 1014, 908, 727, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{27}H_{26}N_2NaO_3$ 449.1836 $[M + Na]^+$, found 449.1833.

*13-Benzyl-2,3-dimethoxy-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2h**).* According to procedure A, lactam **2h** was obtained from spiroindoline **1h** (21.2 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (18.5 mg, 81% yield, eluent: petroleum ether/ethyl acetate = 1/1). Mp 89−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dt, *J* = 6.9, 1.4 Hz, 1H), 7.33−7.13 (m, 6H), 7.10−7.00 (m, 3H), 6.53 (s, 1H), 5.21 (d, *J* = 17.5 Hz, 1H), 5.05 (dd, *J* = 10.1, 1.1 Hz, 1H), 4.96 (d, *J* = 17.5 Hz, 1H), 4.82 (d, *J* = 10.1 Hz, 1H), 3.99 (dd, *J* = 14.8, 4.2 Hz, 1H), 3.93 (s, 3H), 3.70−3.47 (m, 2H), 3.19 (s, 3H), 3.18 (s, 3H), 2.94 (ddd, *J* = 16.6, 4.3, 1.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 149.3, 149.2, 138.8, 137.9, 134.2, 129.2, 128.9, 128.4, 127.1, 125.8, 122.7, 121.8, 119.9, 118.4, 113.1, 110.9, 110.1, 108.9, 75.7, 56.2, 56.1, 55.1, 47.7, 45.0, 24.2 ppm. IR (film) ν_{max} 1641, 1604, 1515, 1465, 1429, 1350, 1267, 1249, 1222, 1205, 1167, 1082, 1043, 910, 729, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{28}H_{28}N_2NaO_4$ 479.1941 $[M + Na]^+$, found 479.1939.

*13-Benzyl-6-(methoxymethyl)-2-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2i**).* According to procedure A, lactam **2i** was obtained from spiroindoline **1i** (18.9 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (17.0 mg, 83% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 57−58 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.54 (m, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.26−7.11 (m, 7H), 7.02−6.95 (m, 2H), 6.92−6.87 (m, 1H), 5.20 (d, *J* = 16.8 Hz, 1H), 5.06−4.94 (m, 2H), 4.86 (d, *J* = 10.2 Hz, 1H), 3.90 (td, *J* = 14.3, 4.4 Hz, 1H), 3.68−3.46 (m, 2H), 3.14 (s, 3H), 2.90 (ddd, *J* = 16.4, 4.4, 1.2 Hz, 1H), 2.19 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 139.2, 138.3, 137.8, 134.5, 134.3, 131.4, 129.6, 129.1, 128.6, 128.5, 128.2, 127.1, 126.2, 122.6, 119.8, 118.4, 110.4, 109.4, 75.6, 56.1, 47.7, 44.9, 24.3, 21.1 ppm. IR (film) ν_{max} 1643, 1465, 1453, 1428, 1349, 11178, 1091, 1022, 908, 828, 727, 707 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{27}H_{26}N_2NaO_2$ 433.1886 $[M + Na]^+$, found 433.1885.

*13-Benzyl-2-fluoro-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2j**).* According to procedure A, lactam **2j** was obtained from spiroindoline **1j** (19.1 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (16.6 mg, 80% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 194−196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.52 (dd, *J* = 8.5, 5.7 Hz, 1H), 7.29−7.09 (m, 7H), 6.98−6.91 (m, 2H), 6.87 (dd, *J* = 9.5, 2.6 Hz, 1H), 5.20 (d, *J* = 16.9 Hz, 1H), 5.07 (d, *J* = 16.9 Hz, 1H), 5.00 (dd, *J* = 10.3, 1.0 Hz, 1H), 4.88 (d, *J* = 10.3 Hz, 1H), 3.87 (td, *J* = 14.3, 4.4 Hz, 1H), 3.68−3.49 (m, 2H), 3.13 (s, 3H), 2.93 (ddd, *J* = 16.5, 4.3, 1.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.45, 163.85, 161.36, 137.81, 137.63, 133.63 (d, *J* = 3.0 Hz), 132.67 (d, *J* = 2.0 Hz), 131.65 (d, *J* = 8.1 Hz), 130.36 (d, *J* = 9.1 Hz), 128.77, 128.37, 127.34, 126.02, 123.08, 120.05, 118.56, 117.46 (d, *J* = 22.2 Hz), 116.12 (d, *J* = 22.2 Hz), 110.62, 110.19, 75.74, 56.22, 47.70, 44.91, 24.36 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.52 (td, *J* = 8.7, 5.8 Hz, 1F) ppm. IR (film) ν_{max} 1647, 1606, 1465, 1453, 1431, 1346, 1179, 1090, 1021, 909, 729, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{26}H_{23}FN_2NaO_2$ 437.1636 $[M + Na]^+$, found 437.1634.

*13-Benzyl-2-methoxy-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2k**).* According to procedure A, lactam **2k** was obtained from spiroindoline **1k** (19.7 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (18.3 mg, 86% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 67−69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dt, *J* = 7.1, 1.4 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 1H), 7.30−7.13 (m, 6H), 7.06−6.99 (m, 2H), 6.95 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.62 (d, *J* = 2.5 Hz, 1H), 5.21 (d, *J* = 17.2 Hz, 1H), 5.07−4.97 (m, 2H), 4.85 (d, *J* = 10.3 Hz, 1H), 3.98−3.87 (m, 1H), 3.67−3.48 (m, 2H), 3.34 (s, 3H), 3.16 (s, 3H), 2.93 (ddd, *J* = 16.5, 4.4, 1.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 159.9, 138.5, 137.9, 134.1, 130.7, 129.9, 129.5, 128.8, 128.4, 127.1, 125.9, 122.8, 119.9, 118.5, 116.0, 114.5, 110.4, 109.5, 75.6, 56.1, 54.8, 47.6, 44.8, 24.3 ppm. IR (film) ν_{max} 1639, 1602, 1465, 1431, 1348, 1307, 1239, 1121, 1177, 1090, 1048, 1022, 907, 727, 698 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{27}H_{26}N_2NaO_3$ 449.1836 $[M + Na]^+$, found 449.1834.

*13-Benzyl-6-(methoxymethyl)-10-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2l**).* According to procedure A, lactam **2l** was obtained from spiroindoline **1l** (19.1 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (17.6 mg, 86% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 62−64 °C. ^{1}H NMR (400

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MHz, $CDCl_3$) δ 7.56−7.50 (m, 1H), 7.43 (td, J = 7.5, 1.3 Hz, 1H), 7.39−7.31 (m, 2H), 7.27−7.14 (m, 4H), 7.07−6.92 (m, 4H), 5.14 (d, J = 16.9 Hz, 1H), 5.08−4.99 (m, 2H), 4.86 (d, J = 10.2 Hz, 1H), 3.96−3.79 (m, 1H), 3.68−3.43 (m, 2H), 3.17 (s, 3H), 2.89 (ddd, J = 16.5, 4.4, 1.3 Hz, 1H), 2.46 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 138.1, 137.4, 136.0, 134.1, 130.5, 129.4, 129.2, 129.1, 128.9, 128.8, 128.7, 128.2, 127.1, 126.1, 124.2, 118.1, 110.3, 108.9, 75.5, 56.2, 47.7, 44.8, 24.3, 21.5 ppm. IR (film) ν_{max} 1644, 1466, 1442, 1420, 1349, 1309, 1180, 1091, 1036, 1014, 907, 790, 774, 727, 699 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{26}N_2NaO_2$ 433.1886 $[M + Na]^+$, found 433.1884.

*13-Benzyl-10-chloro-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2m**).* According to procedure A, lactam **2m** was obtained from spiroindoline **1m** (20.0 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (15.7 mg, 73% yield, eluent: petroleum ether/ethyl acetate = 2/1). Mp 63−65 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dt, J = 4.4, 1.8 Hz, 2H), 7.47 (td, J = 7.5, 1.3 Hz, 1H), 7.38 (td, J = 7.5, 1.5 Hz, 1H), 7.28−7.16 (m, 4H), 7.11 (dd, J = 8.7, 2.0 Hz, 1H), 7.05 (d, J = 8.7 Hz, 1H), 6.93 (dd, J = 7.6, 1.8 Hz, 2H), 5.15 (d, J = 16.9 Hz, 1H), 5.09−4.96 (m, 2H), 4.91 (d, J = 10.3 Hz, 1H), 3.86 (td, J = 14.5, 4.4 Hz, 1H), 3.62 (ddd, J = 15.0, 6.1, 1.4 Hz, 1H), 3.47 (ddd, J = 16.5, 13.9, 6.2 Hz, 1H), 3.14 (s, 3H), 2.88 (ddd, J = 16.5, 4.5, 1.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 137.5, 137.5, 135.9, 135.4, 130.4, 129.6, 129.4, 129.3, 128.8, 128.7, 128.2, 127.3, 126.0, 125.6, 122.9, 117.9, 111.7, 109.1, 75.7, 56.3, 47.7, 45.0, 24.4 ppm. IR (film) ν_{max} 1644, 1466, 1440, 1420, 1179, 1091, 1036, 1013, 908, 729, 700 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{23}ClN_2NaO_2$ 453.1340 $[M + Na]^+$, found 453.1340.

*13-Benzyl-10-methoxy-6-(methoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2n**).* According to procedure A, lactam **2n** was obtained from spiroindoline **1n** (19.7 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (17.7 mg, 83% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 60−62 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.49 (m, 1H), 7.44 (td, J = 7.5, 1.3 Hz, 1H), 7.37 (td, J = 7.5, 1.5 Hz, 1H), 7.28−7.15 (m, 4H), 7.06−6.99 (m, 2H), 6.99−6.93 (m, 2H), 6.83 (dd, J = 8.8, 2.4 Hz, 1H), 5.13 (d, J = 16.9 Hz, 1H), 5.07−4.99 (m, 2H), 4.91 (d, J = 10.3 Hz, 1H), 3.93−3.84 (m, 4H), 3.62 (ddd, J = 15.0, 6.1, 1.4 Hz, 1H), 3.49 (ddd, J = 16.4, 13.9, 6.1 Hz, 1H), 3.16 (s, 3H), 2.89 (ddd, J = 16.5, 4.4, 1.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 154.4, 138.0, 137.4, 134.7, 132.9, 130.5, 129.3, 129.3, 128.9, 128.7, 128.2, 127.1, 126.1, 112.6, 111.4, 109.0, 100.3, 75.7, 56.2, 55.9, 47.7, 44.9, 24.5 ppm. IR (film) ν_{max} 1647, 1483, 1466, 1442, 1291, 1208, 1172, 1091, 1046, 1028, 909, 774, 729, 700 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{26}N_2NaO_3$ 449.1836 $[M + Na]^+$, found 449.1833.

*6-(Methoxymethyl)-13-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2o**).* According to procedure A, lactam **2o** was obtained from spiroindoline **1o** (14.4 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (14.6 mg, 85% yield, eluent: petroleum ether/ethyl acetate = 2/1). Mp 55−57 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.45 (m, 4H), 7.34−7.23 (m, 3H), 7.15 (ddd, J = 7.9, 6.7, 1.3 Hz, 1H), 5.07 (dd, J = 10.2, 1.2 Hz, 1H), 4.78 (d, J = 10.2 Hz, 1H), 3.90−3.82 (m, 1H), 3.62 (ddd, J = 15.0, 6.0, 1.5 Hz, 1H), 3.55−3.45 (m, 4H), 3.19 (s, 3H), 2.88 (ddd, J = 16.6, 4.3, 1.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 138.0, 137.2, 133.8, 131.0, 129.4, 129.3, 128.8, 128.2, 128.1, 122.5, 119.5, 118.3, 109.5, 108.8, 75.3, 56.2, 44.6, 31.0, 24.1 ppm. IR (film) ν_{max} 1644, 1467, 1444, 1421, 1359, 1089, 1036, 1011, 910, 737, 648 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{20}N_2NaO_2$ 343.1417 $[M + Na]^+$, found 343.1415.

*13-Benzyl-6-(ethoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2p**).* According to procedure A, lactam **2p** was obtained from spiroindoline **1a** (18.2 mg, 0.05 mmol) and ethanol (2.3 mg, 0.05 mmol) as a pale yellow solid (15.3 mg, 74% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 56−58 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.56 (m, 1H), 7.53 (dd, J = 7.6, 1.5 Hz, 1H), 7.44 (td, J = 7.5, 1.3 Hz, 1H), 7.36 (td, J = 7.6, 1.5 Hz, 1H), 7.27−7.10 (m, 7H), 6.99−6.92 (m, 2H), 5.17 (d, J = 16.9 Hz, 1H), 5.13−5.02 (m, 2H), 4.96 (d, J = 10.5 Hz, 1H), 3.89 (td, J = 14.3, 4.4 Hz, 1H), 3.70−3.50 (m, 2H), 3.41 (dq, J = 9.5, 7.0 Hz, 1H), 3.27 (dq, J = 9.5, 7.0 Hz, 1H), 2.92 (ddd, J = 16.5, 4.4, 1.2 Hz, 1H), 1.00 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 138.0, 137.6, 137.5, 134.0, 130.6, 129.2, 128.9, 128.7, 128.5, 128.1, 127.1, 126.1, 122.7, 119.8, 118.4, 110.6, 109.5, 74.2, 64.2, 47.6, 45.0, 24.4, 15.0 ppm. IR (film) ν_{max} 2973, 2925, 1644, 1464, 1443, 1420, 1386, 1349, 1319, 1182, 1089, 1036, 1014, 909, 729, 698 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{26}N_2NaO_2$ 433.1886 $[M + Na]^+$, found 433.1890.

*13-Benzyl-6-((benzyloxy)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2q**).* According to procedure A, lactam **2q** was obtained from spiroindoline **1a** (18.2 mg, 0.05 mmol) and benzyl alcohol (5.4 mg, 0.05 mmol) as a pale yellow solid (19.5 mg, 83% yield, eluent: petroleum ether/ethyl acetate = 2/1). Mp 61−63 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, J = 7.7, 1.4 Hz, 2H), 7.44 (td, J = 7.5, 1.3 Hz, 1H), 7.41−7.34 (m, 1H), 7.27−7.14 (m, 9H), 7.14−7.03 (m, 3H), 7.00−6.91 (m, 2H), 5.25−5.00 (m, 4H), 4.39 (d, J = 11.6 Hz, 1H), 4.28 (d, J = 11.6 Hz, 1H), 3.91 (td, J = 14.4, 4.4 Hz, 1H), 3.73−3.48 (m, 2H), 2.92 (ddd, J = 16.5, 4.4, 1.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 137.9, 137.8, 137.6, 137.4, 134.0, 130.6, 129.3, 129.3, 128.9, 128.7, 128.5, 128.3, 128.2, 127.9, 127.6, 127.2, 126.1, 122.7, 119.9, 118.6, 110.63, 109.6, 74.6, 71.1, 65.4, 47.7, 45.4, 24.5 ppm. IR (film) ν_{max} 2923, 1645, 1464, 1442, 1420, 1378, 1349, 1319, 1071, 1017, 908, 728, 696 cm^{-1}. HRMS (ESI) m/z calcd for $C_{32}H_{28}N_2NaO_2$ 495.2043 $[M + Na]^+$, found 495.2045.

*13-Benzyl-6-(isopropoxymethyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2r**).* According to procedure A, lactam **2r** was obtained from spiroindoline **1a** (18.2 mg, 0.05 mmol) and 2-propanol (3.0 mg, 0.05 mmol) as a pale yellow solid (16.3 mg, 77% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 67−69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dt, J = 6.8, 1.4 Hz, 1H), 7.52 (dd, J = 7.6, 1.5 Hz, 1H), 7.44 (td, J = 7.5, 1.3 Hz, 1H), 7.36 (td, J = 7.6, 1.5 Hz, 1H), 7.28−7.10 (m, 7H), 7.00−6.88 (m, 2H), 5.22−4.99 (m, 2H), 4.84 (d, J = 10.6 Hz, 1H), 3.94−3.79 (m, 1H), 3.77−3.44 (m, 3H), 2.92 (ddd, J = 16.5, 4.2, 1.5 Hz, 1H), 1.15 (d, J = 6.1 Hz, 3H), 1.00 (d, J = 6.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 138.0, 137.6, 137.5, 134.0, 130.6, 129.2, 128.9, 128.6, 128.5, 128.1, 127.1, 126.1, 122.6, 119.7, 118.5, 110.6, 109.5, 71.7, 69.4, 47.6, 44.4, 24.1, 22.3, 22.2 ppm. IR (film) ν_{max} 2970, 2924, 1644, 1464, 1443, 1420, 1367, 1180, 1065, 1036, 1015, 908, 731, 699 cm^{-1}. HRMS (ESI) m/z calcd for $C_{28}H_{28}N_2NaO_2$ 447.2043 $[M + Na]^+$, found 447.2046.

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*13-Benzyl-6-((p-tolylthio)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2s**).* According to procedure A, lactam **2s** was obtained from spiroindoline **1a** (18.2 mg, 0.05 mmol) and methyl *p*-tolyl sulfide (6.9 mg, 0.05 mmol) as a pale yellow solid (21.0 mg, 87% yield, eluent: petroleum ether/ethyl acetate = 1/1). Mp 67−69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59−7.50 (m, 1H), 7.40−7.27 (m, 4H), 7.26−7.04 (m, 10H), 6.99−6.92 (m, 2H), 5.61 (dd, *J* = 13.4, 1.1 Hz, 1H), 5.13 (d, *J* = 17.0 Hz, 1H), 5.00 (d, *J* = 17.0 Hz, 1H), 4.21 (d, *J* = 13.3 Hz, 1H), 3.89−3.71 (m, 2H), 3.45 (ddd, *J* = 16.7, 12.3, 7.5 Hz, 1H), 2.88 (ddd, *J* = 16.7, 3.7, 2.0 Hz, 1H), 2.33 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 137.9, 137.6, 137.6, 137.2, 134.0, 132.5, 130.4, 129.8, 129.2, 129.1, 128.8, 128.7, 128.5, 128.0, 127.1, 126.1, 122.7, 119.8, 118.4, 110.7, 109.0, 48.6, 47.6, 43.9, 23.3, 21.2 ppm. IR (film) ν_{max} 2919, 1640, 1493, 1464, 1443, 1419, 1349, 1274, 1249, 1182, 1142, 1022, 908, 870, 730, 698 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{32}H_{28}N_2NaOS$ 511.1815 $[M + Na]^+$, found 511.1816.

*13-Benzyl-6-((2-hydroxynaphthalen-1-yl)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2t**).* According to procedure A, lactam **2t** was obtained from spiroindoline **1a** (18.2 mg, 0.05 mmol) and 2-hydroxynaphthalene (7.2 mg, 0.05 mmol) as a white solid (20.8 mg, 82% yield, eluent: petroleum ether/ethyl acetate = 1/2). Mp 231−233 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 8.07 (d, *J* = 8.6 Hz, 1H), 7.81 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.72 (d, *J* = 8.9 Hz, 1H), 7.65−7.54 (m, 2H), 7.53−7.47 (m, 1H), 7.46−7.32 (m, 3H), 7.30−7.11 (m, 8H), 7.01−6.90 (m, 2H), 5.20 (dd, *J* = 16.2, 12.2 Hz, 2H), 5.05 (d, *J* = 17.0 Hz, 1H), 4.85 (d, *J* = 15.4 Hz, 1H), 3.93−3.54 (m, 3H), 2.99 (dd, *J* = 15.7, 3.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 155.7, 137.9, 137.7, 135.7, 134.0, 133.9, 130.7, 130.6, 129.9, 129.7, 129.2, 129.0, 128.9, 128.8, 128.2, 127.2, 127.2, 126.0, 122.9, 122.7, 120.8, 120.0, 119.9, 118.3, 113.0, 110.7, 108.7, 47.7, 46.0, 38.5, 23.1 ppm. IR (film) ν_{max} 3067, 1598, 1582, 1514, 1465, 1452, 1438, 1360, 1348, 1317, 1294, 1273, 1212, 1182, 1042, 815, 758, 747, 729 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{35}H_{28}N_2NaO_2$ 531.2043 $[M + Na]^+$, found 531.2042.

*6-((1H-Indol-3-yl)methyl)-13-benzyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one (**2u**).* According to procedure A, lactam **2u** was obtained from spiroindoline **1a** (18.2 mg, 0.05 mmol) and indole (5.9 mg, 0.05 mmol) as a white solid (16.8 mg, 70% yield, eluent: petroleum ether/ethyl acetate = 1/2). Mp 164−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.14 (m, 1H), 7.77 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.57 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.47−6.86 (m, 16H), 5.35 (d, *J* = 14.8 Hz, 1H), 5.15 (d, *J* = 17.0 Hz, 1H), 5.04 (d, *J* = 17.0 Hz, 1H), 4.37 (d, *J* = 14.8 Hz, 1H), 3.84−3.65 (m, 1H), 3.52−3.28 (m, 2H), 2.87−2.68 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 138.1, 138.1, 137.5, 136.3, 134.2, 130.4, 129.3, 128.9, 128.9, 128.7, 128.6, 128.0, 127.1, 127.0, 126.2, 124.1, 122.5, 122.3, 121.9, 121.8, 119.9, 119.6, 119.6, 119.2, 119.1, 118.2, 111.8, 111.2, 111.1, 110.6, 109.2, 47.6, 44.6, 38.8, 23.4 ppm. IR (film) ν_{max} 3271, 3057, 2923, 1613, 1495, 1464, 1450, 1423, 1350, 1279, 1183, 1024, 907, 729, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{33}H_{27}N_3NaO$ 504.2046 $[M + Na]^+$, found 504.2048.

*(±)-aS-13-Benzyl-6-((methoxy-d3)methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3a**).* According to procedure B, lactam **3a** was obtained from spiroindoline **1a** (18.2 mg, 0.05 mmol) as a pale yellow solid (16.6 mg, 83% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 108−109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.56 (m, 1H), 7.53 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.45 (td, *J* = 7.5, 1.3 Hz, 1H), 7.36 (td, *J* = 7.6, 1.5 Hz, 1H), 7.26−7.12 (m, 7H), 7.01−6.93 (m, 2H), 5.17 (d, *J* = 17.0 Hz, 1H), 5.10−4.96 (m, 2H), 4.88 (dd, *J* = 10.3, 2.0 Hz, 1H), 3.94−3.81 (m, 1H), 3.62 (ddd, *J* = 14.9, 3.7, 2.3 Hz, 1H), 3.53 (dd, *J* = 13.8, 6.1 Hz, 0.51H), 2.96−2.87 (m, 0.54H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 138.0, 137.6, 137.5, 134.1, 130.6, 129.3, 129.2, 129.0, 128.7, 128.6 (q, *J* = 3.0 Hz), 128.2, 127.2, 126.1, 122.7 119.9, 118.4, 110.6, 109.4, 75.5, 47.6, 44.8, 24.1 (q, *J* = 18.2 Hz) ppm. IR (film) ν_{max} 1648, 1463, 1448, 1350, 1183, 1089, 1008, 967, 906, 728, 700 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{26}H_{20}D_4N_2NaO_2$ 423.1981 $[M + Na]^+$, found 423.1983.

*(±)-aS-13-Benzyl-6-((methoxy-d3)methyl)-4-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3b**).* According to procedure B, lactam **3b** was obtained from spiroindoline **1b** (18.9 mg, 0.05 mmol) as a pale yellow solid (17.0 mg, 82% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 171−173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.53 (m, 1H), 7.29−7.17 (m, 5H), 7.17−7.09 (m, 3H), 7.06−6.97 (m, 3H), 5.23 (d, *J* = 16.9 Hz, 1H), 5.16−5.05 (m, 2H), 4.79 (d, *J* = 10.4 Hz, 1H), 3.91−3.75 (m, 1H), 3.62 (dd, *J* = 14.9, 6.4 Hz, 1H), 3.52 (dd, *J* = 13.8, 6.4 Hz, 0.88H), 2.86 (dd, *J* = 16.1, 4.3 Hz, 0.2H), 2.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 138.1, 137.4, 137.0, 135.5, 134.7, 130.8, 129.2, 128.8, 128.7, 128.5, 128.0, 127.1, 126.2, 122.5, 119.7, 118.2, 110.7, 109.0 (d, *J* = 6.1 Hz), 74.9, 47.7, 44.3 (d, *J* = 5.1 Hz), 23.8 (q, *J* = 19.2 Hz), 19.8 ppm. IR (film) ν_{max} 1645, 1451, 1423, 1346, 1098, 1025, 907, 728, 698 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{27}H_{22}D_4N_2NaO_2$ 437.2138 $[M + Na]^+$, found 437.2136.

*(±)-aS-13-Benzyl-4-chloro-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3c**).* According to procedure B, lactam **3c** was obtained from spiroindoline **1c** (20.0 mg, 0.05 mmol) as a pale yellow solid (15.6 mg, 72% yield, eluent: petroleum ether/ethyl acetate = 2/1). Mp 195−196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dt, *J* = 7.3, 1.4 Hz, 1H), 7.47 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.30−7.21 (m, 4H), 7.21−7.11 (m, 3H), 7.08 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.05−7.00 (m, 2H), 5.24 (d, *J* = 17.0 Hz, 1H), 5.19−5.07 (m, 2H), 4.77 (d, *J* = 10.5 Hz, 1H), 3.80 (ddd, *J* = 15.0, 13.8, 1.1 Hz, 1H), 3.69 (dd, *J* = 15.1, 6.5 Hz, 1H), 3.54 (dd, *J* = 13.8, 6.5 Hz, 0.82H), 2.88 (ddd, *J* = 16.6, 4.7, 1.5 Hz, 0.19H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 137.8, 137.6, 136.5, 133.2, 131.4, 131.3, 130.0, 129.5, 128.9, 128.8, 128.7, 127.3, 126.1, 123.0, 120.0, 118.4, 110.7, 109.9 (d, *J* = 5.1 Hz), 74.7, 47.8, 44.1 (d, *J* = 5.1 Hz), 23.8 (q, *J* = 19.2 Hz) ppm. IR (film) ν_{max} 1655, 1440, 1419, 1345, 1229, 1099, 1018, 910, 729, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{26}H_{19}D_4ClN_2NaO_2$ 457.1591 $[M + Na]^+$, found 457.1590.

*(±)-aS-13-Benzyl-6-((methoxy-d3)methyl)-3-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3d**).* According to procedure B, lactam **3d** was obtained from spiroindoline **1d** (18.9 mg, 0.05 mmol) as a pale yellow solid (18.6 mg, 90% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 88−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.53 (m, 1H), 7.35 (d, *J* = 1.8 Hz, 1H), 7.27−7.10 (m, 7H), 7.07 (d, *J* = 7.9 Hz, 1H), 7.00−6.94 (m, 2H), 5.17 (d, *J* = 16.9 Hz, 1H), 5.12−4.99 (m, 2H), 4.86 (dd, *J* = 10.3, 2.0 Hz, 1H), 3.90 (ddd, *J* = 14.4, 9.1, 4.8 Hz, 1H), 3.62 (ddd, *J* = 14.9, 3.7, 2.3 Hz, 1H), 3.55−3.46 (m, 0.52 H), 2.92 (dd, *J* = 19.0, 4.0 Hz, 0.61H), 2.40 (s, 3H) ppm. ^{13}C NMR

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(100 MHz, $CDCl_3$) δ 172.6, 148.9, 139.1, 138.1, 137.5, 137.3, 130.5, 130.1, 129.9 (d, J = 6.1 Hz), 128.7, 128.7, 128.6, 127.1, 126.7, 126.2, 126.1 (d, J = 2.0 Hz), 125.2, 122.5, 119.8, 118.3, 110.6, 109.1 (t, J = 3.0 Hz), 76.7, 75.5 (d, J = 2.0 Hz), 47.5, 44.8 (t, J = 5.1 Hz), 24.1 (q, J = 18.2 Hz), 21.2 ppm. IR (film) ν_{max} 1644, 1464, 1437, 1348, 1307, 1097, 1022, 908, 830, 730, 698 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{22}D_4N_2NaO_2$ 437.2138 $[M + Na]^+$, found 437.2137.

(±)-aS-13-Benzyl-3-chloro-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3e**). According to procedure B, lactam **3e** was obtained from spiroindoline **1e** (20.0 mg, 0.05 mmol) as a pale yellow solid (18.5 mg, 85% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 72−73 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dt, J = 6.7, 1.6 Hz, 1H), 7.52 (d, J = 2.2 Hz, 1H), 7.32 (dd, J = 8.3, 2.3 Hz, 1H), 7.30−7.06 (m, 7H), 7.04−6.88 (m, 2H), 5.17 (d, J = 17.0 Hz, 1H), 5.10−4.95 (m, 2H), 4.87 (dd, J = 10.3, 1.9 Hz, 1H), 3.86 (ddd, J = 14.5, 9.2, 4.8 Hz, 1H), 3.64 (ddd, J = 15.0, 3.8, 2.3 Hz, 1H), 3.59−3.48 (m, 0.47H), 2.92 (ddd, J = 15.3, 4.4, 1.5 Hz, 0.53H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 138.9, 137.8, 135.1, 132.8, 132.8, 131.9, 129.4, 128.8, 128.5 (d, J = 3.0 Hz), 128.3, 127.7, 127.3, 126.0, 123.0, 120.0, 118.5, 110.6, 109.9, 109.9 (t, J = 3.0 Hz), 75.6 (d, J = 2.0 Hz), 47.6, 44.8 (t, J = 5.1 Hz), 24.2 (q, J = 19.2 Hz) ppm. IR (film) ν_{max} 1648, 1463, 1437, 1348, 1223, 1098, 1020, 908, 832, 730, 697 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{19}D_4ClN_2NaO_2$ 457.1591 $[M + Na]^+$, found 457.1591.

(±)-aS-13-Benzyl-3-fluoro-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3f**). According to procedure B, lactam **3f** was obtained from spiroindoline **1f** (19.7 mg, 0.05 mmol) as a pale yellow solid (16.3 mg, 78% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 87−89 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.64−7.49 (m, 1H), 7.30−7.10 (m, 8H), 7.06 (td, J = 8.3, 2.7 Hz, 1H), 7.00−6.89 (m, 2H), 5.17 (d, J = 17.0 Hz, 1H), 5.09−4.95 (m, 2H), 4.87 (dd, J = 10.3, 1.9 Hz, 1H), 3.86 (ddd, J = 14.4, 9.2, 4.7 Hz, 1H), 3.65 (ddd, J = 15.0, 3.8, 2.3 Hz, 1H), 3.59−3.49 (m, 0.51H), 2.92 (dd, J = 15.5, 3.7 Hz, 0.55H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 164.0, 161.5, 139.5 (d, J = 8.1 Hz), 137.7 (d, J = 20.2 Hz), 133.0, 132.6 (d, J = 8.1 Hz), 128.8, 128.4 (d, J = 3.0 Hz), 127.3, 126.0, 125.3 (d, J = 3.0 Hz), 122.8, 120.0, 118.4, 116.5 (d, J = 21.2 Hz), 115.4 (d, J = 23.2 Hz), 110.6, 109.5, 75.6, 47.6, 44.9, 24.1 (q, J = 19.2 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.48 (s, 1F) ppm. IR (film) ν_{max} 1648, 1464, 1439, 1346, 1298, 1270, 1202, 197, 1021, 908, 833, 730, 698 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{19}D_4FN_2NaO_2$ 441.1887 $[M + Na]^+$, found 441.1885.

(±)-aS-13-Benzyl-3-methoxy-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3g**). According to procedure B, lactam **3g** was obtained from spiroindoline **1g** (19.7 mg, 0.05 mmol) as a pale yellow solid (19.4 mg, 90% yield, eluent: petroleum ether/ethyl acetate = 3/2). Mp 80−81 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 8.2, 1.8 Hz, 1H), 7.27−7.18 (m, 3H), 7.16−7.11 (m, 3H), 7.10−7.03 (m, 2H), 7.01−6.94 (m, 2H), 6.89 (dd, J = 8.6, 2.7 Hz, 1H), 5.17 (d, J = 16.9 Hz, 1H), 5.11−4.97 (m, 2H), 4.86 (dd, J = 10.2, 1.9 Hz, 1H), 3.90 (ddd, J = 14.5, 9.2, 4.8 Hz, 1H), 3.85 (s, 3H), 3.63 (ddd, J = 15.0, 3.8, 2.4 Hz, 1H), 3.56−3.45 (m, 0.46H), 2.96−2.85 (m, 0.54H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 160.0, 138.7, 138.1, 137.5, 134.0, 131.9, 128.7, 128.6 (d, J = 3.0 Hz), 127.1, 126.1, 122.4, 121.4, 119.7, 118.2, 115.8 (d, J = 3.0 Hz), 112.7, 110.5, 108.8 (t, J = 3.0 Hz), 75.6, 55.5, 47.5, 44.9 (d, J = 5.1 Hz), 24.1 (q, J = 18.2 Hz) ppm. IR (film) ν_{max} 1644, 1464, 1452, 1431, 1349, 1315, 1293, 1229, 1182, 1083, 1032, 1014, 908, 727, 699 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{22}D_4N_2NaO_3$ 453.2087 $[M + Na]^+$, found 453.2085.

(±)-aS-13-Benzyl-2,3-dimethoxy-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3h**). According to procedure B, lactam **3h** was obtained from spiroindoline **1h** (21.2 mg, 0.05 mmol) as a pale yellow solid (18.4 mg, 83% yield, eluent: petroleum ether/ethyl acetate = 1/1). Mp 101−103 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (dt, J = 6.9, 1.5 Hz, 1H), 7.34−7.25 (m, 3H), 7.25−7.14 (m, 4H), 7.12−6.97 (m, 3H), 6.53 (s, 1H), 5.21 (d, J = 17.5 Hz, 1H), 5.04 (ddd, J = 10.1, 2.7, 1.1 Hz, 1H), 4.96 (d, J = 17.5 Hz, 1H), 4.82 (dd, J = 10.1, 2.0 Hz, 1H), 4.00−3.93 (m, 4H), 3.64 (ddd, J = 14.9, 3.7, 2.3 Hz, 1H), 3.55−3.46 (m, 0.52H), 2.98−2.91 (m, 0.59H), 3.18 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 149.3, 149.2, 138.8, 137.9, 134.2, 134.2, 129.2, 128.9, 128.4 (d, J = 3.0 Hz), 127.1, 125.8, 122.7, 121.8, 119.9, 118.4, 113.1, 110.9, 110.1, 108.9 (t, J = 3.0 Hz), 75.6, 56.1, 55.1, 47.7, 44.9 (d, J = 6.1 Hz), 24.0 (q, J = 16.2 Hz) ppm. IR (film) ν_{max} 1640, 1604, 1515, 1465, 1432, 1262, 1247, 1206, 1183, 1096, 1025, 911, 729, 698 cm^{-1}. HRMS (ESI) m/z calcd for $C_{28}H_{24}D_4N_2NaO_4$ 483.2192 $[M + Na]^+$, found 483.2191.

(±)-aS-13-Benzyl-6-((methoxy-d3)methyl)-2-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3i**). According to procedure B, lactam **3i** was obtained from spiroindoline **1i** (18.9 mg, 0.05 mmol) as a pale yellow solid (17.6 mg, 85% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 68−70 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 7.3, 1.4 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.29−7.11 (m, 7H), 7.04−6.94 (m, 2H), 6.92−6.85 (m, 1H), 5.20 (d, J = 16.9 Hz, 1H), 5.07−4.95 (m, 2H), 4.86 (dd, J = 10.2, 2.0 Hz, 1H), 3.97−3.82 (m, 1H), 3.61 (ddd, J = 14.9, 3.7, 2.3 Hz, 1H), 3.55−3.47 (m, 0.52H), 2.90 (dd, J = 15.8, 3.8 Hz, 0.56H), 2.19 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 139.2, 138.3, 137.7, 134.5, 134.3, 131.4, 129.6, 129.1, 128.6, 128.5 (d, J = 3.0 Hz), 128.2, 127.1, 126.4, 122.6, 119.8, 118.4, 110.4, 109.3 (d, J = 3.0 Hz), 75.6 (d, J = 2.0 Hz), 47.7, 44.9 (d, J = 5.1 Hz), 24.1 (q, J = 18.2 Hz), 21.1 ppm. IR (film) ν_{max} 1642, 1464, 1452, 1432, 1348, 1095, 1023, 908, 829, 728, 699 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{22}D_4N_2NaO_2$ 437.2138 $[M + Na]^+$, found 437.2136.

(±)-aS-13-Benzyl-2-fluoro-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3j**). According to procedure B, lactam **3j** was obtained from spiroindoline **1j** (19.1 mg, 0.05 mmol) as a pale yellow solid (16.7 mg, 80% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 212−213 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 7.6, 1.3 Hz, 1H), 7.52 (dd, J = 8.5, 5.8 Hz, 1H), 7.29−7.09 (m, 7H), 6.98−6.91 (m, 2H), 6.87 (dd, J = 9.4, 2.5 Hz, 1H), 5.20 (d, J = 16.9 Hz, 1H), 5.07 (d, J = 16.9 Hz, 1H), 4.99 (ddd, J = 10.3, 2.7, 1.0 Hz, 1H), 4.88 (dd, J = 10.3, 2.0 Hz, 1H), 3.86 (ddd, J = 14.4, 9.1, 4.7 Hz, 1H), 3.64 (ddd, J = 15.0, 3.7, 2.3 Hz, 1H), 3.59−3.50 (m, 0.52H), 2.96−2.89 (m, 0.58H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 163.9, 161.4, 137.7 (d, J = 17.2 Hz), 133.6, 132.7, 131.7 (d, J = 8.1 Hz), 130.4 (d, J = 9.1 Hz), 128.8, 128.4 (d, J = 3.0 Hz), 127.3, 126.0, 123.1, 120.1, 118.6, 117.5 (d, J = 22.2 Hz), 116.1 (d, J = 22.2 Hz), 110.6, 110.2 (d, J = 3.0 Hz), 75.7, 47.7, 44.9, 24.2 (q, J = 18.2 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.52 (s, 1F) ppm. IR (film) ν_{max} 1644, 1605, 1464, 1453,

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1434, 1345, 1294, 1262, 1232, 1189, 1099, 1022, 909, 728, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{26}H_{19}D_4FN_2NaO_2$ 441.1887 $[M + Na]^+$, found 441.1887.

*(±)-aS-13-Benzyl-2-methoxy-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3k**).* According to procedure B, lactam **3k** was obtained from spiroindoline **1k** (19.7 mg, 0.05 mmol) as a pale yellow solid (18.9 mg, 88% yield, eluent: petroleum ether/ethyl acetate = 3/2). Mp 83−84 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (dt, *J* = 7.1, 1.4 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.32−7.13 (m, 6H), 7.07−6.99 (m, 2H), 6.95 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.62 (d, *J* = 2.5 Hz, 1H), 5.21 (d, *J* = 17.2 Hz, 1H), 5.09−4.96 (m, 2H), 4.85 (dd, *J* = 10.2, 2.1 Hz, 1H), 3.92 (ddd, *J* = 14.4, 9.1, 4.7 Hz, 1H), 3.62 (ddd, *J* = 14.9, 3.7, 2.2 Hz, 1H), 3.57−3.48 (m, 0.52H), 2.97−2.88 (m, 0.56H)], 3.34 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 159.9, 138.5, 137.9, 134.1, 130.7, 129.9, 129.5 (d, *J* = 1.0 Hz), 128.8, 128.4 (d, *J* = 3.0 Hz), 127.1, 125.9, 122.8, 119.9, 118.5 (d, *J* = 2.0 Hz), 116.0, 114.5, 110.4, 109.5 (t, *J* = 3.0 Hz), 75.6, 54.8, 47.8, 44.8 (t, *J* = 5.1 Hz), 24.1 (q, *J* = 19.2 Hz) ppm. IR (film) ν_{max} 1642, 1602, 1465, 1433, 1308, 1237, 1214, 1094, 1021, 909, 730, 700 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{27}H_{22}D_4N_2NaO_3$ 453.2087 $[M + Na]^+$, found 453.2085.

*(±)-aS-13-Benzyl-6-((methoxy-d3)methyl)-10-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3l**).* According to procedure B, lactam **3l** was obtained from spiroindoline **1l** (18.9 mg, 0.05 mmol) as a pale yellow solid (18.4 mg, 89% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 77−78 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.43 (td, *J* = 7.5, 1.3 Hz, 1H), 7.39−7.32 (m, 2H), 7.27−7.15 (m, 4H), 7.07−6.92 (m, 4H), 5.14 (d, *J* = 16.9 Hz, 1H), 5.09−4.99 (m, 2H), 4.86 (dd, *J* = 10.3, 1.9 Hz, 1H), 3.86 (ddd, *J* = 14.4, 9.2, 4.8 Hz, 1H), 3.62 (ddd, *J* = 15.0, 3.8, 2.3 Hz, 1H), 3.54−3.45 (m, 0.51H), 2.94−2.85 (m, 0.57H), 2.46 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 137.5, 136.0, 134.1 (d, *J* = 2.0 Hz), 130.5, 129.4, 129.2, 129.1, 128.9, 128.8 (d, *J* = 3.0 Hz), 128.6, 128.2, 127.1, 126.1, 124.2, 118.1, 108.9 (t, *J* = 3.0 Hz), 75.5 (d, *J* = 2.0 Hz), 47.6, 44.8 (d, *J* = 6.1 Hz), 24.1 (q, *J* = 18.2 Hz), 21.5 ppm. IR (film) ν_{max} 1648, 1466, 1443, 1421, 1351, 1306, 1098, 1019, 909, 791, 773, 729, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{27}H_{22}D_4N_2NaO_2$ 437.2138 $[M + Na]^+$, found 437.2135.

*(±)-aS-13-Benzyl-10-chloro-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3m**).* According to procedure B, lactam **3m** was obtained from spiroindoline **1m** (20.0 mg, 0.05 mmol) as a pale yellow solid (15.0 mg, 69% yield, eluent: petroleum ether/ethyl acetate = 2/1). Mp 73−74 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (td, *J* = 3.6, 2.8, 1.5 Hz, 2H), 7.47 (td, *J* = 7.5, 1.3 Hz, 1H), 7.38 (td, *J* = 7.6, 1.6 Hz, 1H), 7.28−7.16 (m, 4H), 7.11 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 1H), 6.93 (dd, *J* = 7.8, 1.7 Hz, 2H), 5.15 (d, *J* = 16.9 Hz, 1H), 5.09−4.95 (m, 2H), 4.91 (dd, *J* = 10.3, 2.0 Hz, 1H), 3.85 (ddd, *J* = 14.5, 9.2, 4.8 Hz, 1H), 3.61 (ddd, *J* = 15.1, 3.8, 2.4 Hz, 1H), 3.50−3.40 (m, 0.52H), 2.88 (ddd, *J* = 14.8, 4.4, 1.9 Hz, 0.57H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 137.5, 137.5, 135.9, 135.4 (d, *J* = 2.0 Hz), 129.6 (d, *J* = 3.0 Hz), 129.4, 129.3, 128.8, 128.7, 128.2, 127.3, 126.0, 125.6, 122.9, 117.9, 111.7, 109.1 (t, *J* = 3.0 Hz), 75.7, 47.7, 44.9 (d, *J* = 5.1 Hz), 24.2 (q, *J* = 18.2 Hz) ppm. IR (film) ν_{max} 1644, 1465, 1440, 1421, 1351, 1032, 1096, 1018, 908, 788, 765, 728, 699 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{26}H_{19}D_4ClN_2NaO_2$ 457.1591 $[M + Na]^+$, found 457.1592.

*(±)-aS-13-Benzyl-10-methoxy-6-((methoxy-d3)methyl)-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3n**).* According to procedure B, lactam **3n** was obtained from spiroindoline **1n** (19.7 mg, 0.05 mmol) as a pale yellow solid (18.1 mg, 84% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 80−81 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.37 (td, *J* = 7.5, 1.3 Hz, 1H), 7.29 (td, *J* = 7.5, 1.5 Hz, 1H), 7.20−7.09 (m, 5H), 7.00−6.92 (m, 1H), 6.91−6.86 (m, 2H), 6.75 (d, *J* = 8.9 Hz, 1H), 5.06 (d, *J* = 16.9 Hz, 1H), 5.01−4.91 (m, 2H), 4.84 (dd, *J* = 10.3, 2.1 Hz, 1H), 3.84−3.77 (m, 4H), 3.55 (ddd, *J* = 15.0, 3.8, 2.3 Hz, 1H), 3.43−3.35 (m, 0.49H), 2.87−2.77 (m, 0.52H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 154.3, 138.0, 137.4, 134.7, 132.9, 130.5, 129.3, 129.3, 128.9, 128.7, 128.2, 127.1, 126.1, 112.6, 111.4, 111.3, 109.0, 100.3, 75.6, 55.9, 47.7, 44.9, 24.3 (q, *J* = 17.2 Hz) ppm. IR (film) ν_{max} 1648, 1477, 1466, 1433, 1304, 1209, 1097, 1053, 1019, 911, 787, 772, 732, 700 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{27}H_{22}D_4N_2NaO_3$ 453.2087 $[M + Na]^+$, found 453.2086.

*(±)-aS-6-((Methoxy-d3)methyl)-13-methyl-6,7,8,13-tetrahydro-5H-benzo[6,7]azocino[5,4-b]indol-5-one-8-d (**3o**).* According to procedure B, lactam **3o** was obtained from spiroindoline **1o** (14.4 mg, 0.05 mmol) as a pale yellow solid (14.8 mg, 91% yield, eluent: petroleum ether/ethyl acetate = 2/1). Mp 61−63 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.61−7.44 (m, 4H), 7.36−7.22 (m, 3H), 7.15 (ddd, *J* = 7.9, 6.7, 1.2 Hz, 1H), 5.06 (ddd, *J* = 10.2, 2.7, 1.1 Hz, 1H), 4.78 (dd, *J* = 10.2, 1.8 Hz, 1H), 3.93−3.79 (m, 1H), 3.62 (ddd, *J* = 15.0, 3.7, 2.2 Hz, 1H), 3.51 (s, 3H), 3.50−3.46 (m, 0.55H), 2.92−2.82 (m, 0.53H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 138.0, 137.2, 133.9 (d, *J* = 2.0 Hz), 131.0, 129.4, 129.3, 128.8, 128.2, 128.1 (d, *J* = 3.0 Hz), 122.5, 119.5, 118.3, 109.5, 108.8 (t, *J* = 3.0 Hz), 75.3, 44.5, 31.0, 24.4 (q, *J* = 19.2 Hz) ppm. IR (film) ν_{max} 1643, 1467, 1444, 1422, 1358, 1232, 1097, 1031, 1012, 910, 734, 645 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{20}H_{16}D_4N_2NaO_2$ 347.1668 $[M + Na]^+$, found 347.1667.

*14-Benzyl-6-(methoxymethyl)-7,8,9,14-tetrahydrobenzo-[3,4]azonino[5,6-b]indol-5(6H)-one (**5a**).* According to procedure A, lactam **5a** was obtained from spiroindoline **4** (18.9 mg, 0.05 mmol) and methanol (1.65 mg, 0.05 mmol) as a pale yellow solid (18.1 mg, 88% yield, eluent: petroleum ether/ethyl acetate = 3/1). Mp 47−49 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62−7.56 (m, 1H), 7.48 (td, *J* = 7.6, 1.2 Hz, 1H), 7.39 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.29 (td, *J* = 7.6, 1.4 Hz, 1H), 7.24−7.17 (m, 3H), 7.16−7.07 (m, 4H), 7.00−6.91 (m, 2H), 5.23 (d, *J* = 16.9 Hz, 1H), 4.86 (d, *J* = 16.9 Hz, 1H), 4.72 (dd, *J* = 10.4, 1.0 Hz, 1H), 4.57 (d, *J* = 10.4 Hz, 1H), 3.53−3.30 (m, 2H), 3.12 (dddd, *J* = 14.5, 5.2, 2.3, 1.0 Hz, 1H), 2.81 (s, 3H), 2.36 (ddd, *J* = 14.5, 13.0, 2.5 Hz, 1H), 2.02 (dddt, *J* = 15.2, 13.2, 11.0, 2.2 Hz, 1H), 1.73−1.67 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 140.7, 138.6, 136.7, 134.7, 130.9, 129.52, 129.0, 128.5, 128.2, 127.1, 127.0, 126.3, 124.8, 122.0, 119.4, 118.1, 114.5, 110.2, 75.5, 55.8, 49.8, 47.5, 27.2, 24.5 ppm. IR (film) ν_{max} 2923, 1640, 1460, 1442, 1421, 1388, 1367, 1351, 1329, 1178, 1094, 1063, 1030, 762, 731, 696 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{27}H_{26}N_2NaO_2$ 433.1886 $[M + Na]^+$, found 433.1886.

*14-Benzyl-6-((2-hydroxynaphthalen-1-yl)methyl)-7,8,9,14-tetrahydrobenzo[3,4]azonino[5,6-b]indol-5(6H)-one (**5b**).* According to procedure A, lactam **5b** was obtained from spiroindoline **4** (18.9 mg, 0.05 mmol) and 2-

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hydroxynaphthalene (7.2 mg, 0.05 mmol) as a white solid (23.6 mg, 91% yield, eluent: petroleum ether/ethyl acetate = 1/1). Mp 258−260 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 7.82 (d, J = 8.6 Hz, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H), 7.53 (d, J = 7.7 Hz, 1H), 7.45 (q, J = 7.6 Hz, 2H), 7.36 (d, J = 7.5 Hz, 1H), 7.34−7.07 (m, 9H), 7.07−6.90 (m, 3H), 5.30 (d, J = 16.9 Hz, 1H), 5.01−4.75 (m, 2H), 4.55 (d, J = 15.5 Hz, 1H), 3.54−3.29 (m, 2H), 3.15 (dd, J = 13.9, 4.6 Hz, 1H), 2.45−2.30 (m, 1H), 2.20 (q, J = 12.8 Hz, 1H), 1.74 (t, J = 10.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 155.6, 139.2, 138.5, 136.8, 134.4, 134.0, 130.9, 130.5, 129.6, 129.3, 129.0, 128.7, 128.6, 128.5, 127.1, 126.9, 126.7, 126.2, 125.4, 122.5, 122.2, 121.0, 119.9, 119.6, 118.0, 114.0, 112.7, 110.4, 50.3, 47.6, 38.1, 25.8, 24.3 ppm. IR (film) ν_{max} 3141, 1590, 1579, 1507, 1497, 1461, 1435, 1409, 1368, 1347, 1272, 1251, 817, 743, 729 cm^{-1}. HRMS (ESI) m/z calcd for $C_{36}H_{30}N_2NaO_2$ 545.2199 [M + Na]$^+$, found 545.2200.

6-((1H-Indol-3-yl)methyl)-14-benzyl-7,8,9,14-tetrahydrobenzo[3,4]azonino[5,6-b]indol-5(6H)-one (**5c**). According to procedure A, lactam **5c** was obtained from spiroindoline **4** (18.9 mg, 0.05 mmol) and indole (5.9 mg, 0.05 mmol) as a white solid (21.0 mg, 85% yield, eluent: petroleum ether/ethyl acetate = 1/1). Mp 164−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.7 Hz, 1H), 7.86 (s, 1H), 7.34−7.19 (m, 5H), 7.19−7.02 (m, 4H), 6.92 (td, J = 7.5, 4.9 Hz, 2H), 6.65 (q, J = 8.0 Hz, 2H), 6.52 (d, J = 7.8 Hz, 1H), 6.34 (d, J = 8.3 Hz, 1H), 6.28 (d, J = 7.8 Hz, 1H), 6.15 (d, J = 2.7 Hz, 1H), 4.58 (td, J = 12.3, 7.1 Hz, 1H), 4.21 (d, J = 16.2 Hz, 1H), 4.03 (d, J = 16.2 Hz, 1H), 3.89 (d, J = 13.3 Hz, 1H), 3.47 (d, J = 13.3 Hz, 1H), 3.15 (dd, J = 13.1, 7.2 Hz, 1H), 2.64 (d, J = 13.2 Hz, 1H), 2.49 (dd, J = 15.6, 7.1 Hz, 1H), 2.35−2.15 (m, 1H), 2.07−1.89 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 150.7, 140.9, 138.3, 136.0, 133.1, 131.0, 128.7, 128.6, 128.4, 127.9, 126.7, 126.3, 126.1, 125.9, 124.3, 123.7, 121.0, 120.5, 120.2, 119.4, 119.3, 110.5, 110.2, 58.6, 48.7, 46.8, 46.5, 22.6 ppm. IR (film) ν_{max} 3306, 2928, 1641, 1602, 1481, 1459, 1421, 1348, 1296, 1236, 731, 707, 697 cm^{-1}. HRMS (ESI) m/z calcd for $C_{34}H_{29}N_3NaO$ 518.2203 [M + Na]$^+$, found 518.2205.

(±)-aS-14-Benzyl-6-((methoxy-d3)methyl)-7,8,9,14-tetrahydrobenzo[3,4]azonino[5,6-b]indol-5(6H)-one-9-d (**5d**). According to procedure B, lactam **5d** was obtained from spiroindoline **4** (18.9 mg, 0.05 mmol) as a pale yellow solid (18.6 mg, 90% yield, eluent: petroleum ether/ethyl acetate = 2/1). Mp 44−46 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.56 (m, 1H), 7.47 (td, J = 7.5, 1.2 Hz, 1H), 7.39 (dd, J = 7.7, 1.4 Hz, 1H), 7.29 (td, J = 7.6, 1.4 Hz, 1H), 7.25−7.16 (m, 3H), 7.15−7.09 (m, 4H), 7.00−6.92 (m, 2H), 5.22 (d, J = 16.9 Hz, 1H), 4.86 (d, J = 16.9 Hz, 1H), 4.71 (dd, J = 10.4, 0.9 Hz, 1H), 4.57 (d, J = 10.3 Hz, 1H), 3.56−3.32 (m, 2H), 3.18−3.06 (m, 0.41H), 2.36 (ddd, J = 15.4, 13.1, 2.5 Hz, 0.40H)], 2.09−1.92 (m, 1H), 1.77−1.56 (m, 1H). ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 140.7, 138.6, 136.7, 134.7, 134.6, 130.9, 129.5, 129.0, 128.5, 128.2, 127.1, 127.0, 126.3, 126.2, 124.8, 122.0, 119.4, 118.1, 114.4, 110.2, 75.5, 49.8, 49.7, 47.5, 27.1, 27.1 (t, J = 10.1 Hz), 24.2 (q, J = 19.2 Hz) ppm. IR (film) ν_{max} 2918, 1639, 1460, 1422, 1390, 1350, 1306, 1265, 1098 1056, 1028, 1013, 761, 730, 695 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{22}D_4N_2NaO_2$ 437.2138 [M + Na]$^+$, found 437.2138.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c04261.

Copies of ^{1}H and ^{13}C NMR spectra of all new compounds (PDF)

Accession Codes

CCDC 2087324 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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