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Diastereoselective cascade reactions toward substituted diazaindeno[2,1-α]phenanthrenes

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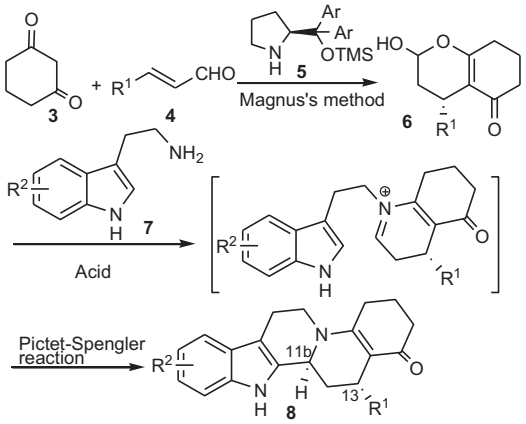
ABSTRACT

A cascade sequence between cyclic hemiacetals and tryptamines was developed, which provided efficient access to highly substituted diazaindeno[2,1-α]phenanthrenes in moderate to good yields with high diastereoselectivities and good to excellent enantioselectivities. Hemiacetals were prepared by asymmetric organocatalyzed conjugate addition of cyclic 1,3-diketones to α,β-unsaturated aldehydes. Hemiacetals with various R^1, both aromatic and aliphatic, were examined for the cascade sequence.

1. Introduction

Polycyclic indole moieties are present in many bioactive natural or synthetic products.[1–2] Traditionally, time consuming sequential multi-step syntheses were required to build up this type of framework.[3] In contrast, cascade reactions, which often proceed via highly reactive intermediates that allow a series of intramolecular reactions to take place, provide an efficient entry to polycyclic skeletons in a time-saving and atom-economic fashion.[4] Pictet–-Spengler (PS) reaction is a powerful classic tool for the assembly of nitrogen-containing heterocyclic ring systems from β-arylethylamine, such as tryptamine and aldehyde.[5] The incorporation of a PS reaction into a cascade sequence would result in an elegant strategy for the one-pot production of natural product-like and drug-like hetero-polycyclic derivatives.[6,7]

Recently, our group reported organocatalyzed enantioselective cascade reactions employing α,β-unsaturated aldehydes, active methylene compounds (e.g., ethyl acetylacetate, dialkyl malonate) and β-arylethylamine as substrates, leading to highly functionalized quinolizidines.[7] Functionalized tricyclic benzoquinolizidines and tetracyclic indoloquinolizidines were prepared efficiently by this strategy featuring the incorporation of PS reaction into the cascade sequence. We speculated that this strategy might well be extended to construction of pentacyclic diazaindeno[2,1-α]phenanthrene moieties (Scheme 1). Hemiacetal **6** was prepared enantioselectively according to previously reported methods from the Rueping group and Jørgensen group.[8] By applying a similar strategy as in our previous report,[7a–c] the reaction between hemiacetal **6** and tryptamine **7** promoted by some acid would provide pentacyclic product **8** stereoselectively via an iminium intermediate.



Scheme 1. Concept of a cascade sequence for preparing pentacycle diazaindeno[2,1-α]phenanthrenes.

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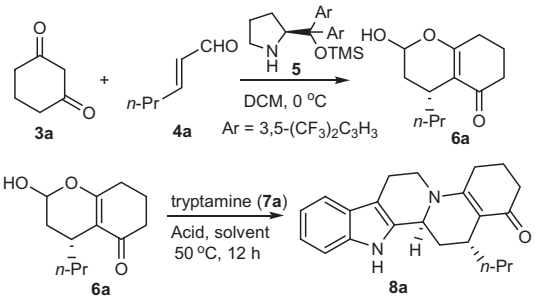
2. Results and discussion

Initially, a model reaction between **6a** and tryptamine **7a** was examined under a broad set of conditions (Table 1). Hemiacetal **6a** was prepared from diketone **3a** and enal **4a** employing prolinol TMS ether **5** as the catalyst.[9] The reaction mixture was diluted, filtered through a short pad of silica gel and then concentrated to afford crude **6a**, which was used directly in the second step. Cyclic hemiacetal **6a** was redissovled in DCM, followed by addition of tryptamine **7a** and a stoichiometric amount of TFA. After heating at 50 °C for 12 h, **8a** was obtained in 93% yield with 95% ee (entry 1). A brief screen of solvents revealed that the reaction was quite solvent dependent. DCM proved to be the best (entry 1). Polar solvent DMSO provided the product in a moderate yield (entry 6). While no formation of **8a** was observed when DMF or H_2O was employed (entries 7–8). In all cases (entries 1–6), the formation of minor cis isomer of **8a** was observed (dr>10:1). Among the acids screened, TFA proved to be the best one in terms of yield (entry 2, entries 9–11).

Table 1
Screening studies of cascade reaction conditions[a]



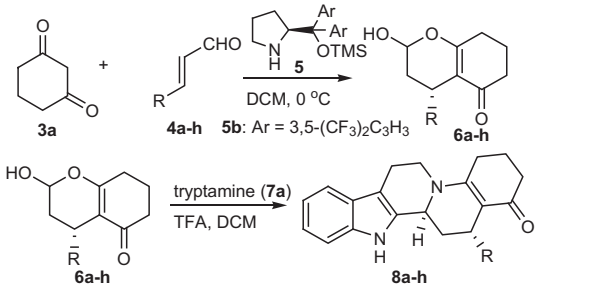
Entry	Acid[b]	Solvent	Yield[c] (%)	ee[d] (%)
1	**A1**	DCM	93	95
2	**A1**	$CHCl_3$	80	94
3	**A1**	$PhCH_3$	66	95
4	**A1**	THF	93	92
5	**A1**	CH_3CN	72	94
6	**A1**	DMSO	48	96
7	**A1**	DMF	—	—
8	**A1**	H_2O	—	—
9	**A2**	DCM	12	96
10	**A3**	DCM	19	97
11	**A4**	DCM	81	97

[a] See Experimental section for details.
[b] **A1**: TFA; **A2**: acetic acid; **A3**: benzoic acid; **A4**: 4-NO_2–$C_6H_4CO_2H$.
[c] Yield referred to isolated pure product over two steps.
[d] Enantiomeric excess of **8** was determined by chiral HPLC analysis.

Since DCM was the optimal solvent for both conjugate addition and subsequent PS cyclization as demonstrated in our preliminary study, attempt to simplify the reaction conditions was carried out. The reaction mixture in the first step was used directly in next step without work-up. Then, the mixture was diluted with DCM, and followed by addition of tryptamine and TFA. The formation of the desired product was observed on TLC. However, we found it difficult to separate the cyclized product from side products by column chromatography. Therefore work-up procedure in the first step was included in further studies.

Next the scope of this method was examined under the optimal reaction condition (Table 1, entry 2). A series of α,β-unsaturated aldehydes **4** with different substituents together with **3a** and tryptamine **7a** were employed. As shown in Table 2, both aromatic and aliphatic substituted α,β-unsaturated aldehydes served as appropriate substrates, providing diverse diazaindeno[2,1-α]phenanthrenes in moderate to excellent yields and good to excellent enantioselectivities with good diastereoselectivities. In general, aldehydes with aliphatic substituents delivered the cyclized product with much higher yields and diastereoselectivities than those with aromatic substituents (entries 1–4 vs entries 5–8).

Table 2
Cyclization reaction of tryptamine **7a** and hemiacetals **6a**–**h**[a]



Entry	R, **6**	**8**	Yield[b] (%)	dr	ee[c] (%)
1	*n*-C_3H_7, **6a**	**8a**	93	19:1	95
2	*n*-C_2H_5, **6b**	**8b**	89	15:1	92
3	*n*-C_5H_{11}, **6c**	**8c**	88	11:1	88
4	*n*-C_7H_{15}, **6d**	**8d**	89	12:1	73
5	4-Br–C_6H_4, **6e**	**8e**	55	6:1	86
6	4-F–C_6H_4, **6f**	**8f**	71	6:1	97
7	4-Me–C_6H_4, **6g**	**8g**	65	6:1	88
8	4-MeO–C_6H_4, **6h**	**8h**	63	6:1	90

[a] See Experimental section for details.
[b] Yield referred to isolated pure product over two steps.
[c] Enantiomeric excess of **8** was determined by chiral HPLC analysis.

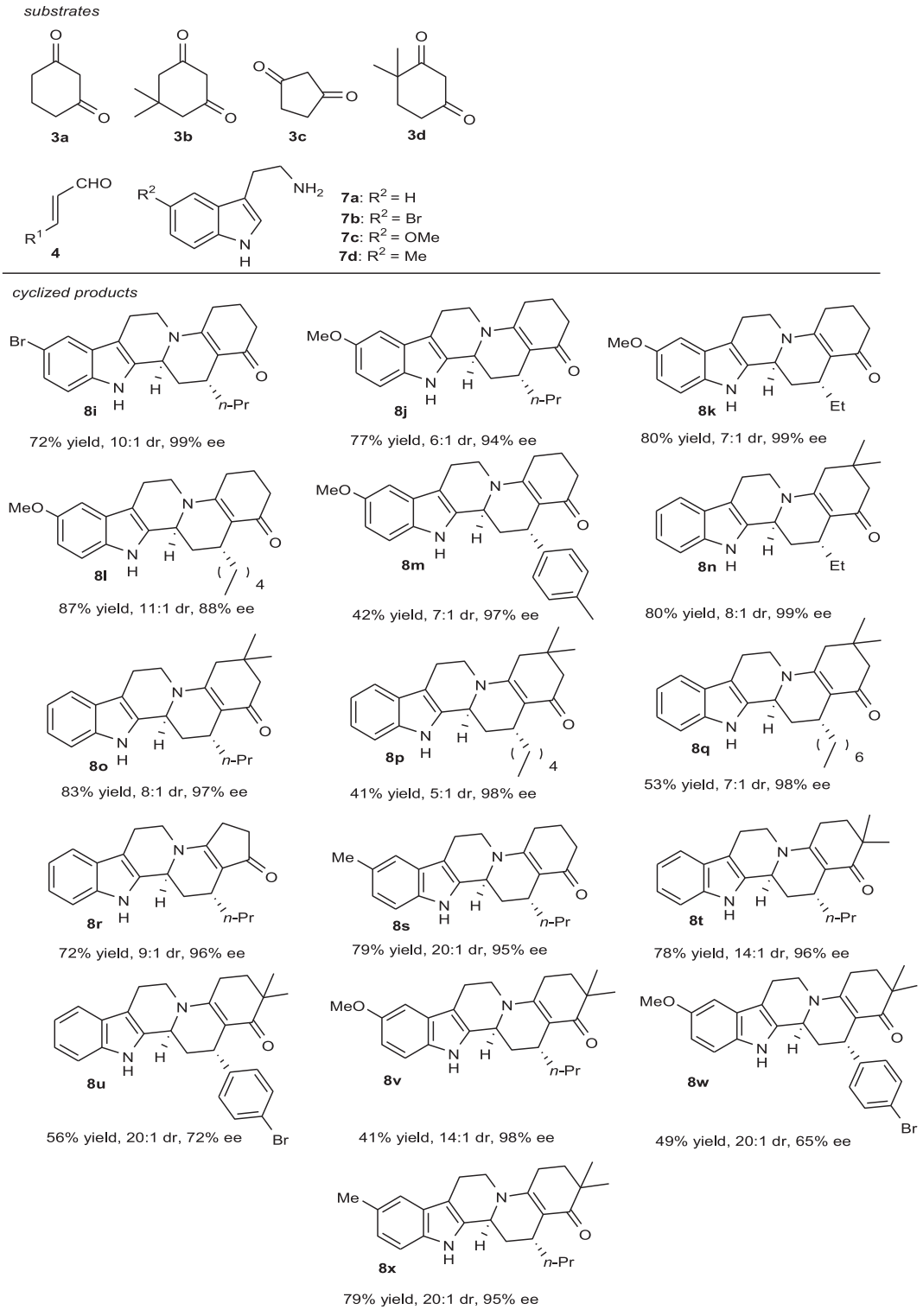
The scope of the reaction was further expanded to several 1,3-cyclodiketones **3a**–**d** and substituted tryptamines **7a**–**d**. As shown in Scheme 2, a small combinatorial library of penta-heterocyclic compounds was prepared in moderate to good yields (41–87% yield) and moderate to excellent enantioselectivities (65–99% ee) with dr from 5:1 to 20:1. The yields for compound **8m**, **8p**, and **8v** were quite lower as compared with others, which may be ascribed to their poor solubility in eluting solvents during column chromatography. 4,4-Dimethyl-1,3-cyclohexanedione **3d** led to exclusive formation of cyclized products **8t**–**x** with α,α-dimethyl ketone moiety. Steric factor is likely to play a role in this regioselectivity.

The trans H13/H11b relative configuration of the isolated major diastereomer was assigned on the basis of the X-ray crystal structure of **8a** (Fig. 1).[10] The absolute configuration of **8a** is determined to be 13*R*,11b*S* based on previous work by Rueping et al. and Jørgensen et al.[8] Thus, the stereochemistry at C13 of **8a** was originated from hemiacetal **6a** obtained from asymmetric conjugate addition of diketone **3a** to unsaturated aldehyde **4a** catalyzed by (*S*)-prolinol TMS ether. The selective formation of C11b stereochemistry was induced by C13 chirality through the condensation of tryptamine **7a** with hemiacetal **6a** and subsequent PS cyclization. The absolute configuration of other cyclized products could be assigned by analogy.

On the basis of the observed stereochemistries of the cyclized products and the previous reported chiral induction during Pictet–Spengler cyclization,[7] we propose the following mechanism to rationalize the substrate controlled formation of 11b-position chirality (Fig. 2). Diastereoisomer *anti*-**8a** formed exclusively due to less steric interaction between the equatorial β-proton and the indole moiety in **TS1**, as compared to that between the axial α-proton and the indole moiety in **TS2**.

3. Conclusions

In summary, we have developed a practical diastereoselective cascade sequence leading to highly substituted pentacyclic diazaindeno[2,1-α]phenanthrenes. Tryptamines **7** first condensed



Scheme 2. Further expanding of substrate scope.

with cyclic hemiacetals **6** obtained from asymmetric organocatalyzed conjugate addition of 1,3-diketones to unsaturated aldehydes **4**, and then delivered the cyclized products via acid-catalyzed PS cyclization. The *trans* products were obtained as major diastereomers from a broad spectrum of readily available reagents in moderate to good yields and good to excellent enantioselectivities.

4. Experimental

4.1. General information

Thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates visualized with UV light and/or by staining with ethanolic phosphomolybdic acid (PMA) or iodine. Flash column

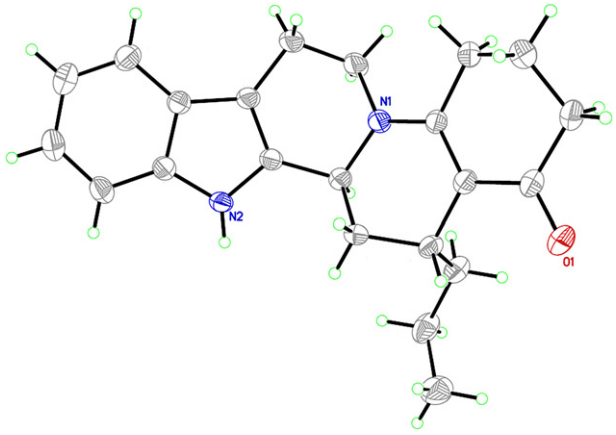


Fig. 1. X-ray structure of **8a**.

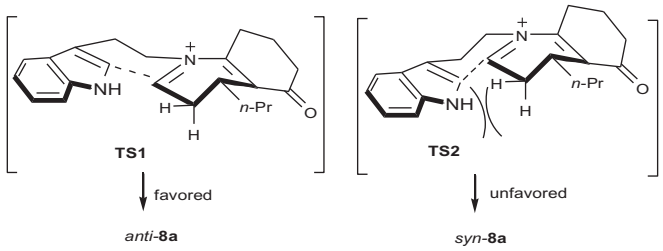


Fig. 2. Proposed transition state for PS cyclization.

chromatography was performed on silica gel H (10–40 μ). NMR spectra were recorded on Bruker AM500 (500 MHz). Chemical shifts (δ) are given in parts per million relative to TMS, coupling constants (J) in hertz. Optical rotations were taken on JASCO P1030. High-resolution mass spectra were recorded on Bruker ApeXIII 7.0 TESLA FTMS. Enantiomeric excesses were determined by chiral HPLC using a Waters or Shimadzu instrument.

4.2. Preparation of compounds 8a–r

General procedure for asymmetric organocatalyzed addition of diketone to α,β-unsaturated aldehydes. Chiral secondary amine catalyst **5** (0.02 mmol, 0.1 equiv) was added to a solution of α,β-unsaturated aldehyde **4** (0.3 mmol, 1.5 equiv) in DCM (0.2 mL) at 0 °C while stirring, followed by the addition of diketone **3** (0.2 mmol, 1 equiv). The reaction was stirred for 48 h at 0 °C, and filtered through a short pad of silica gel. After concentration under reduced pressure, the crude product **6a** was obtained and used directly in the next step.

General procedure for cascade reaction. Tryptamine **7** (0.3 mmol, 1.5 equiv) was added to a solution of crude hemiacetal **6** (0.2 mmol, 1 equiv) in DCM (2 mL) in a sealed tube followed by the addition of TFA (0.2 mol, 1 equiv). The reaction mixture was heated in an oil bath at 50 °C for 12 h. After cooling to room temperature, the reaction mixture was diluted with DCM (10 mL) and quenched with saturated $NaHCO_3$ (5 mL). The organic layer was separated and washed with brine (5 mL). After drying over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography on silica gel using petroleum ether–ethyl acetate as eluents to give the desired product **8**.

*4.2.1. (13R,11bS)-13-Propyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8a**).* Pale yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.90 (br, 1H), 7.48 (d, J=7.6 Hz, 1H), 7.35 (d, J=7.6 Hz, 1H), 7.16 (t, J=7.6 Hz, 1H), 7.10 (t, J=7.6 Hz, 1H), 4.69 (d, J=11.1 Hz, 1H), 4.23 (dd, J=13.2 Hz and 3.0 Hz, 1H), 3.22–3.30 (m, 1H), 3.09–3.12 (m, 1H), 2.79–2.95 (m, 2H), 2.60–2.67 (m, 1H), 2.43–2.53 (m, 2H), 2.32–2.38 (m, 2H), 1.96–2.05 (m, 3H), 1.50–1.66 (m, 2H), 1.23–1.38 (m, 2H), 0.93 (t, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.9, 158.2, 136.4, 134.5, 126.8, 121.8, 119.6, 118.0, 111.6, 111.3, 108.2, 50.5, 45.1, 36.7, 36.1, 31.1, 27.7, 27.3, 22.5, 22.3, 20.5, 14.4; $[\alpha]_D^{25}$ −62.11 (c 1.13, $CHCl_3$). HRMS (ESI) calcd for $(C_{22}H_{27}N_2O)^+$ 335.2118, found 335.2111; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.7 mL/min, λ=220 nm): t_R=10.81 min (major enantiomer), t_R=15.37 min (minor enantiomer).

*4.2.2. (13R,11bS)-13-Ethyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8b**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.00 (s, 1H), 7.40 (d, J=7.6 Hz, 1H), 7.33 (d, J=7.6 Hz, 1H), 7.06 (t, J=7.6 Hz, 1H), 6.98 (t, J=7.6 Hz, 1H), 4.61 (d, J=10.8 Hz, 1H), 4.21 (dd, J=13.2 Hz and 3.2 Hz, 1H), 3.12–3.20 (m, 1H), 2.47–2.81 (m, 6H), 2.05–2.21 (m, 2H), 1.76–1.93 (m, 2H), 1.54–1.59 (m, 1H), 1.16–1.40 (m, 2H), 0.98 (t, J=7.3 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.9, 157.7, 136.1, 134.8, 126.3, 120.8, 118.5, 117.5, 111.1, 110.0, 106.8, 49.5, 44.3, 35.7, 29.6, 29.5, 26.5, 26.4, 21.8, 11.7; $[\alpha]_D^{25}$ −119.64 (c 1.07, $CHCl_3$); HRMS (ESI) calcd for $(C_{21}H_{25}N_2O)^+$ 321.1961, found 321.1950; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.5 mL/min, λ=220 nm): t_R=14.08 min (major enantiomer), t_R=20.56 min (minor enantiomer).

*4.2.3. (13R,11bS)-13-Pentyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8c**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.97 (s, 1H), 7.40 (d, J=7.6 Hz, 1H), 7.32 (d, J=7.6 Hz, 1H), 7.05 (t, 7.6 Hz, 1H), 6.97 (t, 7.6 Hz, 1H), 4.62 (d, J=11.2 Hz, 1H), 4.22 (dd, J=13.2 Hz and 2.8 Hz, 1H), 3.13–3.22 (m, 1H), 2.48–2.80 (m, 5H), 2.02–2.20 (m, 2H), 1.76–1.93 (m, 2H), 1.45–1.55 (m, 2H), 1.18–1.40 (m, 8H), 0.91 (t, J=7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.7, 157.5, 136.0, 134.8, 126.3, 120.7, 118.4, 117.5, 111.0, 110.1, 106.8, 49.6, 44.3, 35.7, 33.7, 31.5, 30.0, 27.6, 26.4, 26.2, 22.2, 21.8, 14.0; $[\alpha]_D^{25}$ +44.82 (c 0.50, CH_3OH); HRMS (ESI) calcd for $(C_{24}H_{31}N_2O)^+$ 363.2431, found 363.2443; HPLC (Daicel Chiralpak ODH, hexane–isopropanol=4:1, flow rate=0.7 mL/min, λ=220 nm): t_R=13.29 min (major enantiomer), t_R=9.52 min (minor enantiomer).

*4.2.4. (13R,11bS)-13-Heptyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8d**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.98 (s, 1H), 7.40 (d, J=8.0 Hz, 1H), 7.32 (d, J=8.0 Hz, 1H), 7.05 (t, J=8.0 Hz, 1H), 6.97 (t, J=8.0 Hz, 1H), 4.62 (d, J=11.6 Hz, 1H), 4.22 (dd, J=13.6 Hz and 3.2 Hz, 1H), 3.13–3.20 (m, 1H), 2.46–2.82 (m, 5H), 2.04–2.20 (m, 2H), 1.76–1.93 (m, 2H), 1.46–1.55 (m, 2H), 1.13–1.38 (m, 12H), 0.88 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.7, 157.5, 136.0, 134.8, 126.3, 120.7, 118.4, 117.5, 111.0, 110.1, 106.8, 49.6, 44.3, 35.7, 33.8, 31.3, 30.0, 29.2, 28.8, 27.6, 26.6, 26.4, 22.1, 21.8, 13.9; $[\alpha]_D^{25}$ −38.13 (c 0.80, $CHCl_3$); HRMS (ESI) calcd for $(C_{26}H_{35}N_2O)^+$ 391.2744, found 391.2756; HPLC (Daicel Chiralpak ODH, hexane–isopropanol=4:1, flow rate=0.7 mL/min, λ=220 nm): t_R=14.76 min (major enantiomer), t_R=9.76 min (minor enantiomer).

*4.2.5. (13S,11bS)-13-(4-Bromophenyl)-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8e**).* Pale yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.89 (s, 1H), 7.48 (d, J=8.4 Hz, 2H), 7.40 (d, J=8.0 Hz, 1H), 7.25 (d, J=8.0 Hz, 1H), 7.16 (d, J=8.4 Hz, 2H), 7.04 (d, J=8.0 Hz, 1H), 6.96 (d, J=8.0 Hz, 1H), 4.30 (d, J=10.4 Hz, 1H), 4.23 (d, J=12.0 Hz, 1H), 4.10–4.17 (m, 1H), 3.11–3.21 (m, 1H), 2.64–2.83 (m, 5H), 2.06–2.30 (m, 2H), 1.98–2.05 (m, 1H), 1.84–1.96 (m, 1H), 1.73–1.83 (m, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz)

δ 191.7, 159.5, 145.6, 136.1, 134.0, 131.4, 130.7, 130.0, 128.3, 126.2, 120.8, 118.6, 118.5, 117.6, 111.0, 107.1, 106.3, 49.4, 44.4, 35.5, 34.6, 33.4, 26.5, 21.7, 14.0; $[\alpha]_D^{25}$ +100.24 (*c* 1.00, $CHCl_3$); HRMS (ESI) calcd for $(C_{25}H_{24}N_2OBr)^+$ 447.1067, found 447.1071; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.7 mL/min, λ=220 nm): t_R=28.63 min (major enantiomer), t_R=15.16 min (minor enantiomer).

*4.2.6. (13S,11bS)-13-(4-Fluorophenyl)-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8f**).* Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.45–8.55 (br, 1H), 7.46 (d, *J*=7.6 Hz, 1H), 7.20 (d, *J*=7.6 Hz, 1H), 7.03–7.16 (m, 4H), 6.86–6.95 (m, 2H), 4.27–4.30 (m, 3H), 3.19–3.26 (m, 1H), 2.76–2.93 (m, 3H), 2.64–2.68 (m, 1H), 2.34–2.40 (m, 3H), 2.11–2.17 (m, 1H), 1.85–1.97 (m, 1H), 1.22–1.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.7, 160.3, 159.6, 141.1, 136.4, 133.5, 129.2, 129.1, 126.7, 122.0, 119.7, 118.0, 115.2, 115.0, 111.2, 108.5, 108.1, 50.0, 45.0, 36.0, 35.8, 33.4, 27.5, 22.5, 22.4; $[\alpha]_D^{25}$ +108.84 (*c* 0.47, $CHCl_3$); HRMS (ESI) calcd for $(C_{25}H_{23}N_2OFNa)^+$ 409.1687, found 409.1695; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.7 mL/min, λ=220 nm): t_R=16.91 min (major enantiomer), t_R=12.77 min (minor enantiomer).

*4.2.7. (13S,11bS)-13-(p-Tolyl)-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8g**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.88 (br, 1H), 7.39 (d, *J*=8.0 Hz, 1H), 7.25 (d, *J*=8.0 Hz, 1H), 7.06–7.12 (m, 4H), 7.03 (t, *J*=8.0 Hz, 1H), 6.96 (t, *J*=8.0 Hz, 1H), 4.31 (dd, *J*=14 Hz and 3.2 Hz, 1H), 4.22 (d, *J*=11.2 Hz, 1H), 4.10–4.15 (m, 1H), 3.11–3.17 (m, 1H), 2.77–2.87 (m, 2H), 2.63–2.71 (m, 3H), 2.27 (s, 3H), 2.19–2.24 (m, 1H), 2.08–2.13 (m, 1H), 1.85–2.04 (m, 2H), 1.75 (td, *J*=12.8 Hz and 5.2 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.7, 159.2, 143.0, 136.1, 134.4, 134.2, 128.5, 127.6, 126.2, 120.8, 118.5, 117.5, 111.0, 107.1, 106.9, 49.6, 44.5, 35.6, 34.9, 33.2, 26.5, 21.9, 21.8, 20.5; $[\alpha]_D^{25}$ +88.49 (*c* 0.93, $CHCl_3$); HRMS (ESI) calcd for $(C_{26}H_{27}N_2O)^+$ 383.2118, found 383.2110; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.7 mL/min, λ=220 nm): t_R=15.62 min (major enantiomer), t_R=13.11 min (minor enantiomer).

*4.2.8. (13S,11bS)-13-(4-Methoxyphenyl)-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8h**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.88 (br, 1H), 7.39 (d, *J*=7.6 Hz, 1H), 7.25 (d, *J*=7.6 Hz, 1H), 7.10 (d, *J*=8.5 Hz, 2H), 7.03 (t, *J*=7.6 Hz, 1H), 6.96 (t, *J*=7.6 Hz, 1H), 6.86 (d, *J*=8.5 Hz, 2H), 4.31 (dd, *J*=9.2 Hz and 2.8 Hz, 1H), 4.23 (d, *J*=11.2 Hz, 1H), 4.10–4.14 (m, 1H), 3.72 (s, 3H), 3.11–3.19 (m, 1H), 2.77–2.88 (m, 2H), 2.63–2.73 (m, 3H), 2.08–2.30 (m, 2H), 1.99–2.04 (m, 1H), 1.86–1.94 (m, 1H), 1.72 (td, *J*=12.6 Hz and 4.8 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.6, 159.1, 157.3, 137.9, 136.0, 134.2, 128.5, 126.2, 120.7, 118.4, 117.5, 113.4, 111.0, 107.0, 54.9, 49.5, 44.4, 35.6, 34.9, 32.7, 26.5, 21.9, 21.8; $[\alpha]_D^{25}$ +103.79 (*c* 0.35, $CHCl_3$); HRMS (ESI) calcd for $(C_{26}H_{27}N_2O_2)^+$ 399.2067, found 399.2061; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.7 mL/min, λ=220 nm): t_R=33.03 min (major enantiomer), t_R=16.25 min (minor enantiomer).

*4.2.9. (13R,11bS)-8-Bromo-13-propyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8i**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.22 (br, 1H), 7.59 (s, 1H), 7.28 (d, *J*=8.6 Hz, 1H), 7.15 (d, *J*=8.6 Hz, 1H), 4.63 (d, *J*=10.8 Hz, 1H), 4.21 (d, *J*=13.0 Hz, 1H), 3.11–3.19 (m, 1H), 2.52–2.82 (m, 5H), 2.04–2.20 (m, 2H), 1.81–1.93 (m, 2H), 1.17–1.61 (m, 6H), 0.93 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.8, 157.5, 136.6, 134.7, 128.1, 123.1, 119.9, 112.9, 111.0, 110.1, 106.8, 49.5, 44.2, 36.1, 35.7, 30.0, 27.3, 26.3, 21.8, 21.6, 19.7, 14.0; $[\alpha]_D^{25}$ +23.35 (*c* 0.60, $CHCl_3$); HRMS (ESI) calcd for $(C_{22}H_{26}N_2OBr)^+$ 413.1223, found 413.1221; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.5 mL/min, λ=220 nm): t_R=12.28 min (major enantiomer), t_R=20.40 min (minor enantiomer).

*4.2.10. (13R,11bS)-8-Methoxyl-13-propyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8j**).* Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.01 (br, 1H), 7.23 (d, *J*=8.4 Hz, 1H), 6.93 (d, *J*=2.0 Hz, 1H), 6.80 (dd, *J*=8.4 Hz and 2.0 Hz, 1H), 4.66 (d, *J*=11.0 Hz, 1H), 4.22 (dd, *J*=13.4 Hz and 3.3 Hz, 1H), 3.85 (s, 3H), 3.21–3.29 (m, 1H), 3.02–3.10 (m, 1H), 2.74–2.89 (m, 2H), 2.59–2.67 (m, 1H), 2.42–2.53 (m, 2H), 2.34 (t, *J*=4.9 Hz, 2H), 1.93–2.05 (m, 2H), 1.46–1.64 (m, 2H), 1.20–1.35 (m, 3H), 0.89 (t, *J*=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.9, 158.3, 154.1, 135.4, 131.5, 127.1, 112.0, 111.5, 107.8, 100.3, 56.1, 50.6, 45.2, 36.6, 36.1, 30.9, 27.7, 27.3, 22.5, 22.3, 20.4, 14.4; $[\alpha]_D^{25}$ +5.25 (*c* 0.27, $CHCl_3$); HRMS (ESI) calcd for $(C_{23}H_{29}N_2O_2)^+$ 365.2224, found 365.2237; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.5 mL/min, λ=220 nm): t_R=18.96 min (major enantiomer), t_R=38.58 min (minor enantiomer).

*4.2.11. (13R,11bS)-8-Methoxyl-13-ethyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8k**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.80 (br, 1H), 7.20 (d, *J*=8.4 Hz, 1H), 6.90 (d, *J*=2.4 Hz, 1H), 6.69 (dd, *J*=8.4 Hz and 2.4 Hz, 1H), 4.58 (d, *J*=11.2 Hz, 1H), 4.21 (dd, *J*=13.6 Hz and 3.2 Hz, 1H), 3.75 (s, 3H), 3.12–3.20 (m, 1H), 2.55–2.77 (m, 6H), 2.04–2.21 (m, 2H), 1.77–1.94 (m, 2H), 1.51–1.59 (m, 1H), 1.33 (td, *J*=12.4 Hz and 4.4 Hz, 1H), 1.16–1.20 (m, 1H), 0.97 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.8, 157.5, 153.1, 135.5, 131.1, 126.6, 111.5, 110.4, 110.0, 106.7, 99.9, 55.3, 49.6, 44.3, 35.7, 29.6, 29.4, 26.5, 26.4, 21.9, 21.8, 11.7; $[\alpha]_D^{25}$ −21.70 (*c* 1.00, $CHCl_3$); HRMS (ESI) calcd for $(C_{22}H_{27}N_2O_2)^+$ 351.2067, found 351.2078; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.5 mL/min, λ=220 nm): t_R=20.14 min (major enantiomer), t_R=37.41 min (minor enantiomer).

*4.2.12. (13R,11bS)-8-Methoxyl-13-pentyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8l**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.81 (br, 1H), 7.20 (d, *J*=8.4 Hz, 1H), 6.90 (d, *J*=2.0 Hz, 1H), 6.69 (dd, *J*=8.4 Hz and 2.0 Hz, 1H), 4.60 (d, *J*=11.2 Hz, 1H), 4.20 (dd, *J*=14.4 Hz and 2.8 Hz, 1H), 3.75 (s, 3H), 3.12–3.19 (m, 1H), 2.53–2.77 (m, 5H), 2.03–2.19 (m, 2H), 1.81–1.93 (m, 2H), 1.45–1.56 (m, 2H), 1.17–1.38 (m, 8H), 0.90 (t, *J*=6.7 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.8, 157.6, 153.1, 135.5, 131.1, 126.6, 111.6, 110.5, 110.1, 106.7, 99.9, 55.3, 49.6, 44.4, 35.8, 33.8, 31.5, 30.0, 27.6, 26.4, 26.3, 22.2, 21.9, 21.8, 14.0; $[\alpha]_D^{25}$ +10.46 (*c* 0.70, $CHCl_3$); HRMS (ESI) calcd for $(C_{25}H_{33}N_2O_2)^+$ 393.2537, found 393.2543; HPLC (Daicel Chiralpak OD, hexane–isopropanol=9:1, flow rate=0.7 mL/min, λ=220 nm): t_R=48.64 min (major enantiomer), t_R=42.41 min (minor enantiomer).

*4.2.13. (13S,11bS)-8-Methoxyl-13-p-tolyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8m**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.69 (br, 1H), 7.05–7.14 (m, 5H), 6.88 (d, *J*=2.0 Hz, 1H), 6.66 (dd, *J*=8.7 Hz and 2.0 Hz, 1H), 4.31 (dd, *J*=11.9 Hz and 3.0 Hz, 1H), 4.20 (d, *J*=11.6 Hz, 1H), 4.108–4.14 (m, 1H), 3.73 (s, 3H), 3.10–3.16 (m, 1H), 2.80–2.88 (m, 1H), 2.60–2.77 (m, 4H), 2.27 (s, 3H), 2.17–2.25 (m, 1H), 2.08–2.13 (m, 1H), 1.99–2.05 (m, 1H), 1.89–1.94 (m, 1H), 1.73 (td, *J*=12.6 Hz and 5.0 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.6, 159.1, 153.1, 143.0, 134.9, 134.3, 131.1, 128.5, 127.5, 126.5, 111.5, 110.5, 106.9, 106.8, 99.9, 55.3, 49.6, 44.5, 35.6, 34.8, 33.2, 26.5, 21.8, 20.5; $[\alpha]_D^{25}$ +185.07 (*c* 0.30, $CHCl_3$); HRMS (ESI) calcd for $(C_{27}H_{29}N_2O_2)^+$ 413.2223, found 413.2226; HPLC (Daicel Chiralpak ODH,

hexane–isopropanol=4:1, flow rate=0.5 mL/min, λ=220 nm): t_R=29.89 min (major enantiomer), t_R=41.95 min (minor enantiomer).

*4.2.14. (13R,11bS)-3,3-Dimethyl-13-ethyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8n**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.98 (br, 1H), 7.41 (d, J=7.6 Hz, 1H), 7.32 (d, J=7.6 Hz, 1H), 7.06 (t, J=7.6 Hz, 1H), 6.98 (t, J=7.6 Hz, 1H), 4.63 (d, J=11.2 Hz, 1H), 4.23 (d, J=12.6 Hz, 1H), 3.14–3.21 (m, 1H), 2.73–2.79 (m, 3H), 2.62 (d, J=11.6 Hz, 1H), 2.52–2.562 (m, 1H), 2.33 (d, J=16.3 Hz, 1H), 2.12 (d, J=15.5 Hz, 1H), 1.93 (d, J=15.5 Hz, 1H), 1.48–1.58 (m, 1H), 1.36 (td, J=12.7 Hz and 4.6 Hz, 1H), 1.21–1.28 (m, 1H), 1.05 (s, 3H), 0.94–1.00 (m, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 192.0, 156.2, 136.5, 135.4, 126.8, 121.3, 119.0, 118.0, 111.5, 109.2, 107.4, 50.3, 49.9, 44.9, 32.5, 30.3, 30.2, 29.7, 27.3, 27.2, 22.5, 12.2; $[\alpha]_D^{25}$ −82.56 (c 0.50, $CHCl_3$); HRMS (ESI) calcd for $(C_{23}H_{28}N_2ONa)^+$ 371.2094, found 371.2104; HPLC (Daicel Chiralpak ASH, hexane–sopropanol=9:1, flow rate=0.6 mL/min, λ=220 nm): t_R=51.24 min (major enantiomer), t_R=78.43 min (minor enantiomer).

*4.2.15. (13R,11bS)-3,3-Dimethyl-13-propyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8o**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.97 (br, 1H), 7.39 (d, J=7.6 Hz, 1H), 7.31 (d, J=7.6 Hz, 1H), 7.04 (t, J=7.6 Hz, 1H), 6.96 (t, J=7.6 Hz, 1H), 4.64 (d, J=11.0 Hz, 1H), 4.22 (d, J=12.6 Hz, 1H), 3.13–3.18 (m, 1H), 2.84 (s, 1H), 2.68–2.76 (m, 2H), 2.50–2.63 (m, 1H), 2.31 (d, J=16.4 Hz, 1H), 2.09 (d, J=15.6 Hz, 1H), 1.94 (t, J=15.6 Hz, 1H), 1.54–1.58 (m, 1H), 1.22–1.45 (m, 4H), 1.04 (s, 3H), 0.92 (s, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.3, 155.6, 136.0, 134.9, 126.3, 120.7, 118.5, 117.5, 111.0, 108.7, 106.8, 79.1, 49.8, 49.3, 44.4, 36.3, 32.0, 30.3, 29.7, 27.1, 26.8, 22.0, 19.8, 14.1; $[\alpha]_D^{25}$ −78.99 (c 0.60, $CHCl_3$); HRMS (ESI) calcd for $(C_{24}H_{31}N_2O)^+$ 363.2431, found 363.2437; HPLC (Daicel Chiralpak ASH, hexane–isopropanol=9:1, flow rate=0.6 mL/min, λ=220 nm): t_R=38.38 min (major enantiomer), t_R=61.97 min (minor enantiomer).

*4.2.16. (13R,11bS)-3,3-Dimethyl-13-pentyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8p**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.97 (br, 1H), 7.40 (d, J=8.0 Hz, 1H), 7.32 (d, J=8.0 Hz, 1H), 7.05 (t, J=8.0 Hz, 1H), 6.97 (t, J=8.0 Hz, 1H), 4.64 (d, J=11.2 Hz, 1H), 4.24 (d, J=12.4 Hz, 1H), 3.14–3.21 (m, 1H), 2.56–2.81 (m, 4H), 2.32 (d, J=16.0 Hz, 1H), 2.10 (d, J=16.0 Hz, 1H), 1.92 (d, J=16.0 Hz, 1H), 1.23–1.55 (m, 10H), 1.05 (s, 3H), 0.89–0.94 (m, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.3, 155.6, 136.0, 134.8, 126.3, 120.7, 118.4, 117.5, 111.0, 108.7, 106.8, 49.8, 49.3, 44.4, 33.9, 32.0, 31.4, 30.2, 29.6, 27.2, 26.8, 26.2, 22.1, 22.0, 14.0; $[\alpha]_D^{25}$ −117.02 (c 0.35, $CHCl_3$); HRMS (ESI) calcd for $(C_{26}H_{35}N_2O)^+$ 391.2744, found 391.2751; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.5 mL/min, λ=220 nm): t_R=12.39 min (major enantiomer), t_R=9.50 min (minor enantiomer).

*4.2.17. (13R,11bS)-3,3-Dimethyl-13-heptyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8q**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.96 (br, 1H), 7.40 (d, J=7.6 Hz, 1H), 7.32 (d, J=7.6 Hz, 1H), 7.05 (t, J=7.6 Hz, 1H), 6.97 (t, J=7.6 Hz, 1H), 4.63 (d, J=11.1 Hz, 1H), 4.24 (d, J=12.7 Hz, 1H), 3.14–3.21 (m, 1H), 2.52–2.81 (m, 5H), 2.32 (d, J=16.0 Hz, 1H), 2.10 (d, J=15.2 Hz, 1H), 1.92 (d, J=15.2 Hz, 1H), 1.23–1.55 (m, 13H), 1.05 (s, 3H), 0.86–0.94 (m, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 191.3, 155.6, 136.0, 134.8, 126.3, 120.7, 118.4, 117.5, 111.0, 108.7, 106.8, 49.8, 49.3, 44.4, 33.9, 32.0, 31.3, 30.2, 29.6, 29.2, 28.8, 27.2, 26.8, 26.6, 22.1, 22.0, 13.9; $[\alpha]_D^{25}$ −63.59 (c 0.55, $CHCl_3$); HRMS (ESI) calcd for $(C_{28}H_{39}N_2O)^+$ 419.3057, found 419.3071; HPLC (Daicel Chiralpak ADH, hexane–isopropanol=4:1, flow rate=0.5 mL/min, λ=220 nm): t_R=12.34 min (major enantiomer), t_R=9.66 min (minor enantiomer).

*4.2.18. (12R,10bS)-12-Propyl-2,3,4,5,10b,11,12-heptahydro-1-oxo-10H-3b,10-diazaindeno[2,1-α]cyclopenta[α]phenanthrene (**8r**).* Yellow solid; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.04 (br, 1H), 7.42 (d, J=8.0 Hz, 1H), 7.33 (d, J=8.0 Hz, 1H), 7.07 (t, J=8.0 Hz, 1H), 6.98 (t, J=8.0 Hz, 1H), 4.64 (d, J=11.2 Hz, 1H), 4.03 (d, J=12.8 Hz, 1H), 3.44–3.46 (m, 1H), 2.74–2.83 (m, 2H), 2.62–2.71 (m, 2H), 2.50–2.53 (m, 1H), 2.11–2.25 (m, 2H), 1.16–1.64 (m, 6H), 0.94 (t, J=6.8 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 198.5, 170.5, 136.1, 133.6, 126.3, 120.9, 118.5, 117.6, 112.5, 110.9, 106.6, 49.4, 43.8, 37.3, 32.9, 31.6, 27.6, 24.4, 21.2, 19.7, 14.1; $[\alpha]_D^{25}$ −36.08 (c 0.20, CH_3OH); HRMS (ESI) calcd for $(C_{21}H_{24}N_2ONa)^+$ 343.1781, found 343.1787; HPLC (Daicel Chiralpak ODH, hexane–isopropanol=4:1, flow rate=0.7 mL/min, λ=220 nm): t_R=14.98 min (major enantiomer), t_R=25.09 min (minor enantiomer).

*4.2.19. (13R,11bS)-13-Propyl-8-methyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8s**).* White solid; ^{1}H NMR ($CDCl_3$, 400 MHz,): δ 8.28 (br, 1H), 7.22–7.27 (m, 2H), 6.97 (d, J=8.0 Hz, 1H), 4.62–4.69 (m, 1H,), 4.22 (dd, J=13.2 Hz and 3.2 Hz, 1H,), 3.20–3.27 (m, 1H,), 3.03–3.08 (m, 1H,), 2.81–2.89 (m, 1H), 2.74–2.81 (m, 1H), 2.58–2.66 (m, 1H), 2.47–2.53 (m, 1H), 2.44 (s, 3H), 2.37–2.39 (m, 1H), 2.30–2.36 (m, 2H), 1.91–2.06 (m, 2H,), 1.56–1.65 (m, 2H), 1.32–1.44 (m, 1H), 1.22–1.29 (m, 2H), 0.94 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 194.0, 158.0, 134.7, 134.5, 129.1, 127.2, 123.6, 117.9, 111.7, 110.9, 108.1, 50.5, 45.2, 36.8, 36.2, 31.2, 27.7, 27.4, 22.6, 22.4, 21.6, 20.6, 14.5; $[\alpha]_D^{25}$ −20.25 (c 1.10, $CHCl_3$); HRMS (ESI) calcd for $(C_{23}H_{29}N_2O)^+$ 349.2274, found 349.2287; HPLC conditions: AD-H column, hexane–isopropanol=4:1, flow rate=0.7 mL/min, t_R=12.24 min (major enantiomer), t_R=24.25 min (minor enantiomer).

*4.2.20. (13R,11bS)-2,2-Dimethyl-13-propyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8t**).* Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (br, 1H), 7.48 (d, J=8.0 Hz, 1H), 7.34 (d, J=8.0 Hz, 1H), 7.07–7.19 (m, 2H), 4.60–4.68 (m, 1H), 4.20–4.50 (dd, J=13.2 Hz and 3.6 Hz, 1H), 3.13–3.20 (m, 1H), 2.96–2.30 (m, 1H), 2.72–2.86 (m, 2H), 2.58–2.64 (m, 1H), 2.42–2.48 (m, 1H), 2.30–2.38 (m, 1H), 1.72–1.81 (m, 2H), 1.53–1.61 (m, 1H), 1.42–1.49 (m, 2H), 1.27–1.32 (m, 1H), 1.12–1.19 (m, 1H), 1.07 (s, 3H), 1.03 (s, 3H), 0.87 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.2, 155.8, 136.3, 134.5, 126.9, 122.1, 119.8, 118.1, 111.2, 109.6, 108.6, 50.1, 44.6, 38.4, 37.0, 35.9, 31.4, 27.9, 25.7, 24.9, 24.2, 22.6, 20.7, 14.2; $[\alpha]_D^{25}$ −46.59 (c 0.85, $CHCl_3$); HRMS (ESI) calcd for $(C_{24}H_{31}N_2O)^+$ 363.2431, found 363.2432; HPLC conditions: AD-H column, hexane–isopropanol=4:1, flow rate=0.7 mL/min, t_R=9.21 min (major enantiomer), t_R=11.31 min (minor enantiomer).

*4.2.21. (13S,11bS)-2,2-Dimethyl-13-(4-bromophenyl)-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8u**).* White solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.77 (br, 1H), 7.47 (d, J=7.6 Hz, 1H), 7.38 (d, J=8.4 Hz, 2H), 7.27 (d, J=7.6 Hz, 1H), 7.07–7.18 (m, 2H), 7.04 (d, J=8.4 Hz, 2H), 4.29–4.33 (m, 3H), 3.20–3.27 (m, 1H), 2.81–2.94 (m, 3H), 2.57–2.66 (m, 1H), 2.29–2.32 (m, 1H), 1.87–2.06 (m, 3H), 1.14 (s, 3H), 1.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.8, 157.5, 145.4, 136.3, 133.5, 131.6, 129.4, 126.9, 122.3, 119.9, 118.2, 111.1, 109.1, 105.9, 49.6, 44.5, 38.5, 36.2, 35.8, 34.4, 25.6, 24.6, 24.5, 22.5; $[\alpha]_D^{25}$ +58.72 (c 0.40, $CHCl_3$); HRMS (ESI) calcd for $(C_{27}H_{28}BrN_2O)^+$ 475.1380, found 475.1393; HPLC conditions: AD-H column, hexane–isopropanol=4:1, flow rate=0.7 mL/min, t_R=20.52 min (major enantiomer), t_R=10.87 min (minor enantiomer).

4.2.22. (13R,11bS)-2,2-Dimethyl-13-propyl-8-methoxyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]

*phenanthrene (**8v**).* Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.96 (br, 1H), 7.22 (d, J=8.8 Hz, 1H), 6.93 (d, J=2.0 Hz, 1H), 6.83 (dd, J=8.8 Hz and 2.0 Hz, 1H), 4.57–4.65 (m, 1H), 4.23 (dd, J=13.2 Hz and 3.6 Hz, 1H), 3.86 (s, 3H), 3.19–3.26 (m, 1H), 2.98–3.05 (m, 1H), 2.82–2.89 (m, 1H), 2.64–2.77 (m, 2H), 2.42–2.49 (m, 1H), 2.27–2.35 (m, 1H), 1.78–1.90 (m, 2H), 1.59–1.64 (m, 1H), 1.45–1.56 (m, 2H), 1.33–1.40 (m, 1H), 1.18–1.23 (m, 1H), 1.13 (s, 3H), 1.09 (s, 3H), 0.94 (t, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.2, 155.8, 154.4, 135.4, 131.4, 127.4, 111.8, 109.6, 108.5, 100.7, 56.2, 50.2, 44.7, 38.5, 37.0, 35.9, 31.3, 27.8, 25.7, 24.8, 24.2, 22.6, 20.6, 14.3; $[\alpha]_D^{25}$ −5.20 (c 0.80, $CHCl_3$); HRMS (ESI) calcd for $(C_{25}H_{33}N_2O_2)^+$ 393.2537, found 393.2539; HPLC conditions: AD-H column, hexane–isopropanol=4:1, flow rate=0.7 mL/min, t_R=13.67 min (major enantiomer), t_R=28.34 min (minor enantiomer).

*4.2.23. (13S,11bS)-2,2-Dimethyl-13-(4-bromophenyl)-8-methoxyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α] phenanthrene (**8w**).* White solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.91 (br, 1H), 7.34 (d, J=8.0 Hz, 2H), 7.12 (d, J=8.8 Hz, 1H), 6.98 (J=8.0 Hz, 2H), 6.92 (d, J=2.0 Hz, 1H), 6.79 (dd, J=8.8 Hz and 2.0 Hz, 1H), 4.23–4.32 (m, 3H), 3.84 (s, 3H), 3.16–3.27 (m, 1H), 2.75–2.90 (m, 3H), 2.58–2.63 (m, 1H), 2.28–2.31 (m, 1H), 1.86–1.99 (m, 3H), 1.14 (s, 3H), 1.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.8, 157.7, 154.4, 145.2, 131.5, 129.4, 127.3, 119.9, 111.8, 108.6, 105.8, 100.6, 92.8, 56.2, 49.7, 44.6, 38.5, 35.9, 35.8, 34.3, 25.6, 24.6, 24.5, 22.5; $[\alpha]_D^{25}$ +145.71 (c 1.03, $CHCl_3$); HRMS (ESI) calcd for $(C_{28}H_{30}BrN_2O_2)^+$ 505.1485, found 505.1497; HPLC conditions: AD-H column, hexane–isopropanol=4:1, flow rate=0.7 mL/min, t_R=10.83 min (major enantiomer), t_R=7.42 min (minor enantiomer).

*4.2.24. (13R,11bS)-2,2,8-Trimethyl-13-propyl-2,3,4,5,6,11b,12,13-octahydro-1-oxo-11H-4b,11-diazaindeno[2,1-α]phenanthrene (**8x**).* White solid; ^{1}H NMR ($CDCl_3$, 400M): δ 7.89 (br, 1H), 7.27 (s, 1H), 7.22 (d, J=8.8 Hz, 1H), 6.99 (d, J=8.8 Hz, 1H), 4.58–4.65 (m, 1H), 4.22 (dd, J=13.2 Hz, 4.0 Hz,, 1H), 3.17–3.25 (m, 1H), 2.98–3.07 (m, 1H), 2.81–2.88 (m, 1H), 2.74–2.78 (m, 1H), 2.63–2.71 (m, 1H), 2.46–2.48 (m, 1H), 2.44 (s, 3H), 2.28–2.33 (m, 1H), 1.77–1.90 (m, 2H), 1.57–1.62 (m,1H), 1.45–1.57 (m, 2H), 1.33–1.41 (m, 1H), 1.18–1.22 (m, 1H), 1.23 (s, 3H), 1.08 (s, 3H), 0.94 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.2, 155.8, 134.6, 129.2, 127.3, 123.6, 117.9, 110.8, 109.6, 108.3, 50.1, 44.7, 38.5, 37.0, 35.9, 31.4, 27.9, 25.8, 24.9, 24.2, 22.6, 21.6, 20.7, 14.2; $[\alpha]_D^{25}$ −20.71 (c 0.80, $CHCl_3$); HRMS (ESI) calcd for $(C_{25}H_{33}N_2O)^+$ 377.2587, found 377.2594; HPLC conditions: AD-H column, hexane–isopropanol=4:1, flow rate=0.7 mL/min, t_R=11.10 min (major enantiomer), t_R=19.35 min (minor enantiomer).

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Supplementary data

The original spectra of ^{1}H NMR, ^{13}C NMR, and HPLC of all products are supplied. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.07.050.

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