Synthesis Y. Ochi et al. Paper

Total Synthesis of Lycopalhine A

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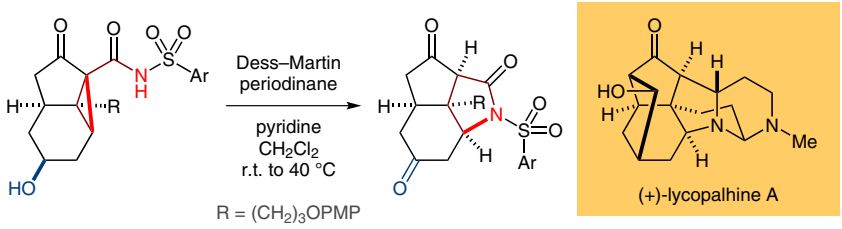
Dedicated to Professor Dieter Enders on the occasion of his 70th birthday



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Abstract The total synthesis of lycopalhine A featuring the construction of a tricyclic system via cleavage of a cyclopropane ring and an ensuing intramolecular Michael addition, stereoselective introduction of a 2-aminoethyl moiety via a reaction of allyltrimethylsilane with a sulfonyliminium ion, and a stereoselective intramolecular aldol reaction is reported.

Key words alkaloid, aminal, cyclopropanation, Michael addition, polycyclic system

A variety of alkaloids have been isolated from the genus *Lycopodium*.[2] The lycopodium alkaloids are classified based on their core structures, with the fawcettimine-type lycopodium alkaloids constituting one of the major classes. These alkaloids have a hydrindane skeleton fused to a nine-membered ring containing a nitrogen atom (Figure 1). In fawcettimine (**1**), the nitrogen atom forms a hemiaminal moiety with a carbonyl group at C13, resulting in the formation of a tetracyclic skeleton. Additional bonds or functional groups generate a range of related alkaloids with more complicated structures,[3] rendering this structure an attractive target for synthetic studies.[4,5] Lycopalhine A (**2**) is just one of such fawcettimine-type alkaloids.

Lycopalhine A (**2**) was first isolated from *Palhinhaea cernua* (syn.: *Lycopodium cernuum*) by Zhao and co-workers.[6] As compared with fawcettimine, C16 is connected to C6 to form a β-hydroxy ketone moiety and a cyclopentane ring. An additional nitrogen atom participates in the formation of a pyrrolidine ring and an aminal moiety. The first total synthesis of lycopalhine A was reported by Williams and Trauner in 2016.[7] The densely functionalized hexacyclic structure was elegantly constructed via a Pauson–Khand reaction and an L-proline-mediated 5-*endo*-trig intramolecular Mannich reaction as the key reactions. Soon after the first total synthesis had been completed, we disclosed our own synthesis of (+)-lycopalhine A, featuring the construction of a tricyclic system via the cleavage of a cyclopropane ring and an ensuing intramolecular Michael addition.[8] Herein, we describe a detailed account of our synthesis.

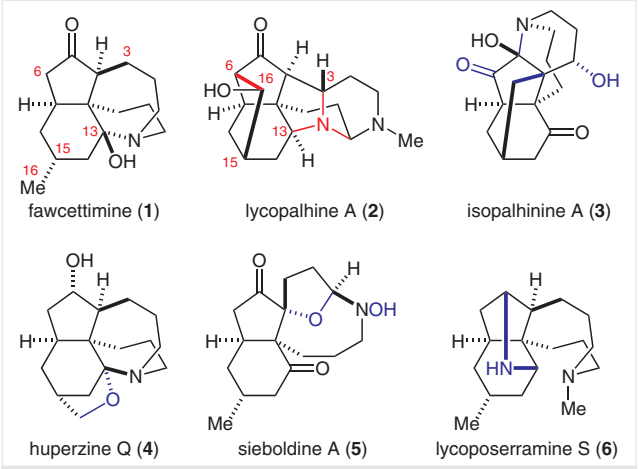
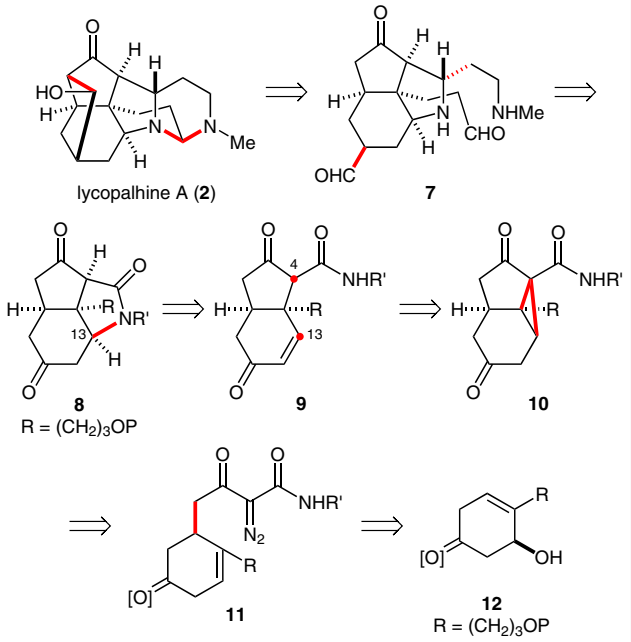


Figure 1 Structures of selected fawcettimine-type lycopodium alkaloids

Our retrosynthesis is shown in Scheme 1. Cleavage of the aminal and the β-hydroxy ketone moieties would generate the tricycle **7**. The 2-aminoethyl moiety and the formyl group were removed from **7**, leading to the tricarbonyl compound **8**. These carbonyl groups could be used both to install the carbon units and to construct the tricyclic system. The C13–N bond at the β-position of the carbonyl group could be easily formed via an intramolecular nucleophilic addition between the amide and enone moieties in **9**. A connection at C4–C13 would generate cyclo-

propane **10**, which could in turn be constructed via the intramolecular cyclopropanation of **11**.[9] The side chain on the cyclohexane ring in **11** could be introduced by means of a Claisen–Johnson rearrangement, which required cyclohexenol **12** as a substrate.

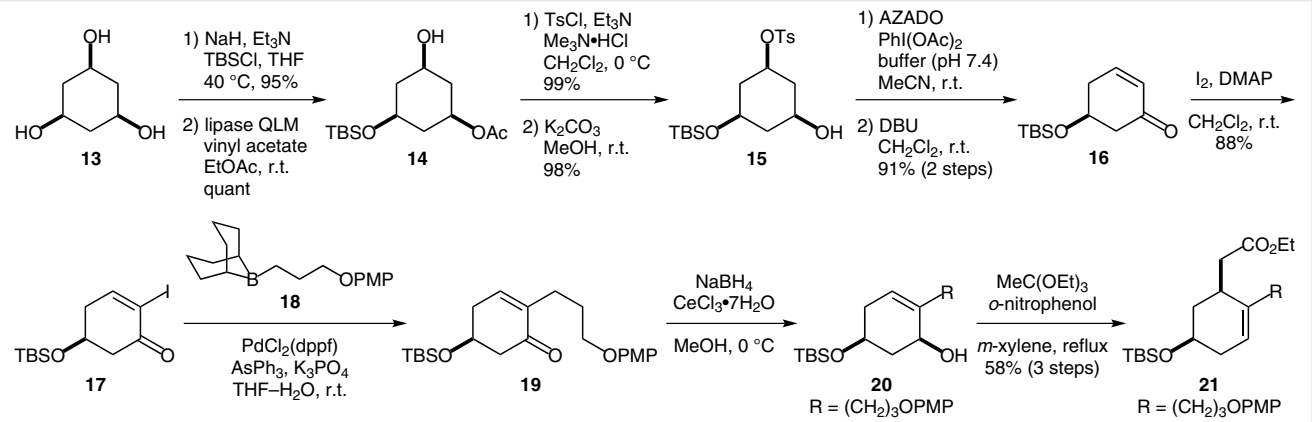


Scheme 1 Retrosynthesis of lycopalhine A

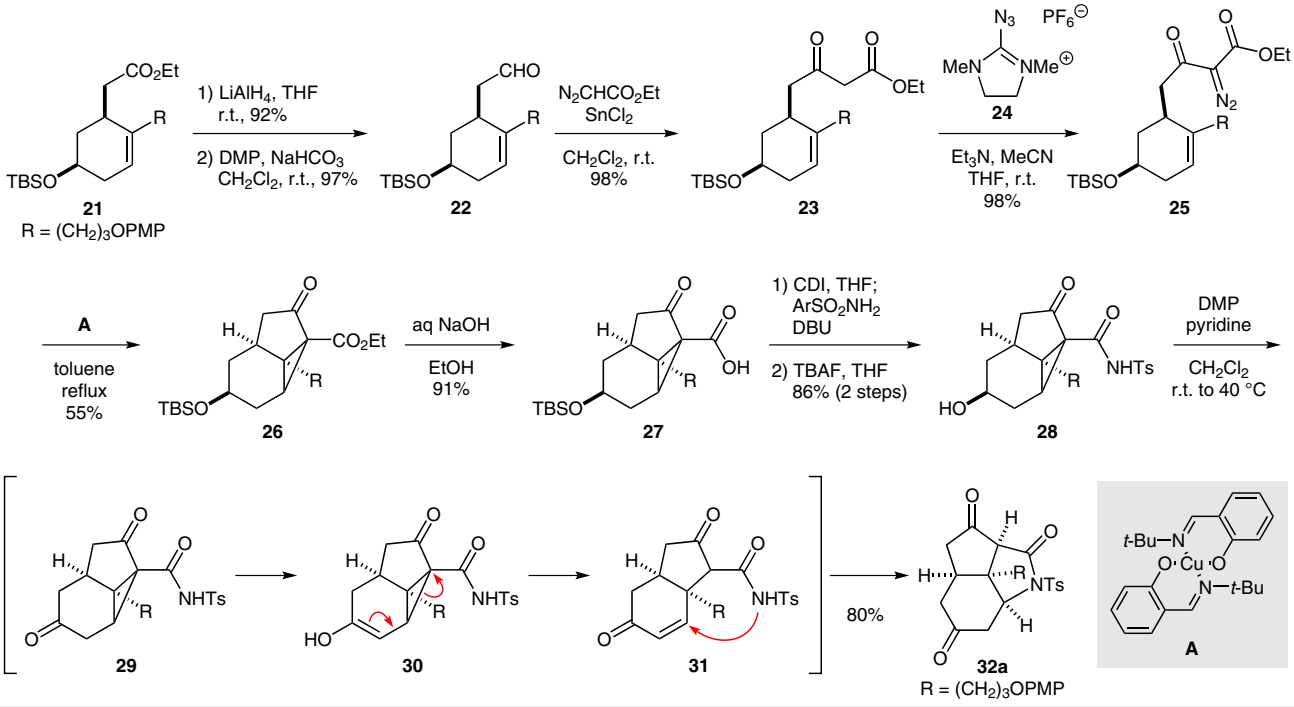
Our synthesis began with the preparation of the cyclohexenol **20** for use in the Claisen–Johnson rearrangement (Scheme 2). Protection of a hydroxy group in cyclohexane-1,3,5-triol (**13**) with a TBS group, followed by enzymatic acetylation with vinyl acetate and lipase QLM, generated **14** in >99% ee.[10] After tosylation of the remaining hydroxy group in **14**,[11] the acetyl group was removed by basic methanolysis. The resulting alcohol **15** was oxidized with 2-azaadamantane-*N*-oxyl (AZADO) and (diacetoxyiodo)benzene,[12] and subsequent treatment with DBU afforded enone **16**. Iodination at the α-position of the carbonyl group proceeded without incident, and the side chain unit was introduced by means of the Suzuki–Miyaura coupling with **18**.[13] 1,2-Reduction of enone **19** gave cyclohexenol **20**,[14] which was subjected to the Claisen–Johnson rearrangement to yield **21**.

The next task was to construct the tricyclic system via cyclopropanation (Scheme 3). Ester **21** was converted into aldehyde **22** via reduction with lithium aluminum hydride, followed by oxidation with Dess–Martin periodinane (DMP).[15] The Roskamp reaction was applied to aldehyde **22** to give the β-keto ester,[16] which was subjected to a diazo transfer reaction involving 2-azido-1,3-dimethylimidazolinium hexafluorophosphate (ADMP, **24**).[17] Refluxing the resulting diazoester **25** in the presence of the catalyst **A** in toluene induced cyclopropanation to give **26** in 55% yield.[18] After basic hydrolysis of the ester moiety in **26**, the resulting carboxylic acid **27** was condensed with tosylamide, and the TBS group was removed by treatment with TBAF, giving alcohol **28**. Oxidation of **28** with DMP[15] facilitated the cleavage of the cyclopropane at the β-position of the carbonyl group, and an ensuing intramolecular Michael addition of the imide moiety generated tricycle **32a** in 80% yield. The entire process was so fast that we could not isolate ketone **29** or enone **31**.

Having succeeded in constructing the tricyclic system, we next focused on introducing a one-carbon unit at C15 (Scheme 4). Reduction of the three carbonyl groups in **32a** using diisobutylaluminum hydride (DIBAL-H) afforded triol **33a**, two hydroxy groups in which were tied up as an acetonide. While mesylation of **34a** followed by an S_N2 reaction with potassium cyanide gave **35a** in good yield, the yields of DIBAL-H reduction of **32a** and the acetonide formation of **33a** were not good (32% and 50%, respectively). Since the lability of the hemiaminal moiety appeared to be the main reason for the poor result, we decided to replace the Ts group with a more strongly electron-withdrawing



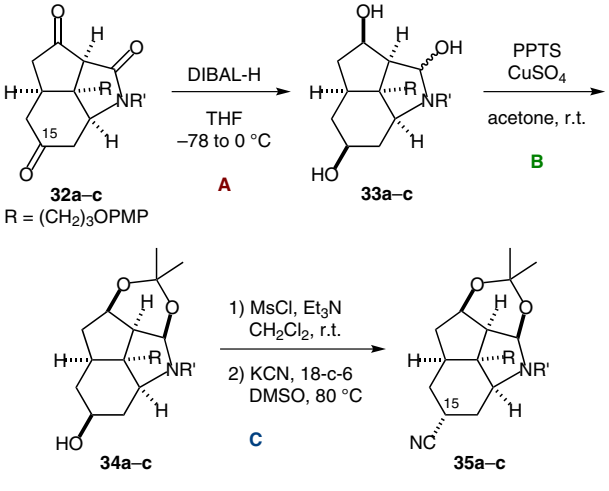
Scheme 2 Preparation of cyclohexene **21** via a Claisen–Johnson rearrangement



Scheme 3 Construction of the tricyclic system

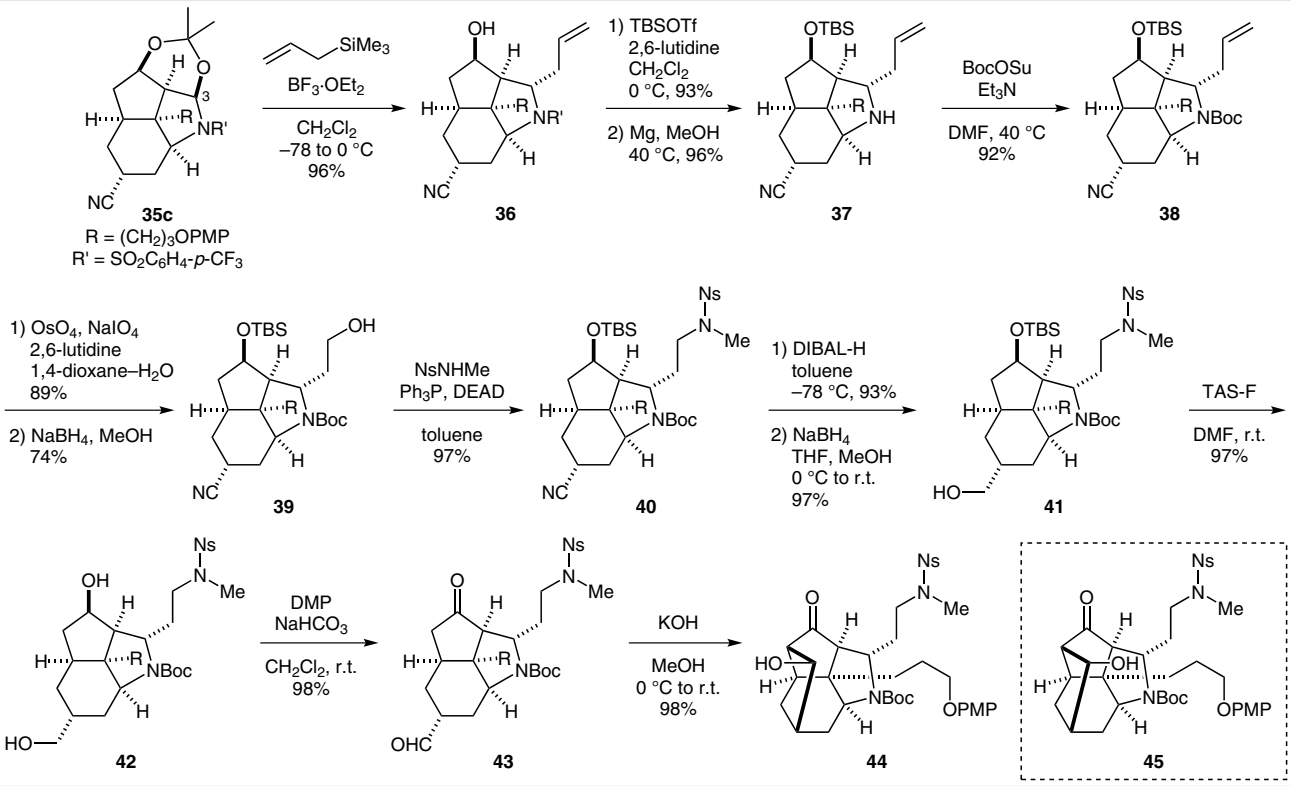
sulfonyl group [i.e., 2-nitrobenzensulfonyl (Ns) group].[19] To our delight, the use of **32b** as a substrate improved the yields of the reduction with DIBAL-H and the formation of the acetonide to give **33b** and **34b** in 71% and 68% yield, respectively. Although the subsequent mesylation proceeded without problems, the S_N2 reaction of the mesylate with potassium cyanide did not give the desired product. Investigation of the crude reaction mixture suggested that the Ns group decomposed during the reaction. The cyanide ion might have attacked the electron-deficient benzene ring of the Ns group. A 4-(trifluoromethyl)benzenesulfonyl group was next chosen to construct the tricycle **32c**. Reduction with DIBAL-H and the subsequent formation of acetonide proceeded in 88% and 80% yields, respectively. After mesylation of the remaining hydroxy group, the crucial S_N2 reaction with potassium cyanide proceeded smoothly, giving **35c** in 90% yield. Thus, we have established a robust route for the introduction of a single carbon unit at C15.

We next turned our attention to the introduction of a 2-aminoethyl moiety at C3 (Scheme 5). Treatment of **35c** with $BF_3{\cdot}OEt_2$ activated the hemiaminal moiety to generate a sulfonyliminium ion, which was attacked by allyltrimethylsilane from the convex face, giving **36** in 96% yield as a single diastereomer. After protecting the liberated hydroxy group with a TBS group, reductive cleavage of the sulfonyl group, followed by protection of the resulting secondary amine with a Boc group, afforded **38**.[20] The Lemieux–Johnson oxidation of **38** gave an aldehyde, which was reduced with sodium borohydride to furnish alcohol **39**. The Mitsunobu reaction of **39** with *N*-methylnosylamide proceeded smoothly to give **40** in 97% yield.[21,22]



compound	R'	yield A (dr)	yield B	yield C
a	Ts	32% (2:1)	50%	83%
b	Ns	71% (1:1)	68%	–
c	*p*-$CF_3C_6H_4SO_2$	88% (3:1)	80%	90%

Scheme 4 Introduction of one carbon unit at C16



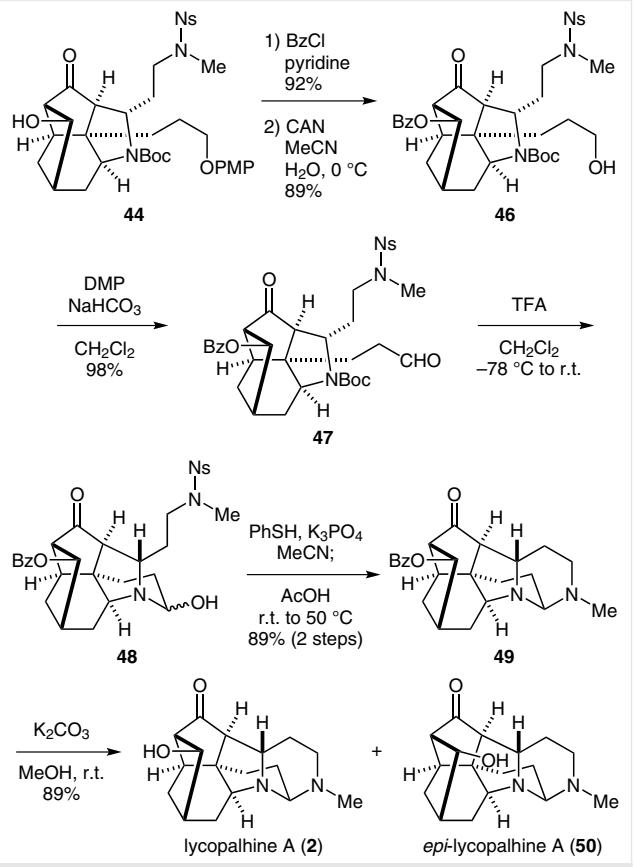
Scheme 5 Introduction of a 2-aminoethyl moiety and construction of the β-hydroxy ketone moiety

Having installed all the units required for the synthesis of lycopalhine A, the remaining task was to construct the ring system including the β-hydroxy ketone and the aminal. It should be emphasized that the order of the ring formation was critical to the completion of the total synthesis. Since we realized that the aminal moiety could not be constructed prior to the formation of the β-hydroxy ketone moiety, the β-hydroxy ketone moiety was constructed in the following manner. A 2-step reduction of the cyano group afforded alcohol **41**, and the TBS group was cleaved with TAS-F. The resulting diol **42** was oxidized with DMP,[15] giving ketoaldehyde **43** in 98% yield. Upon treatment with potassium hydroxide in methanol, **43** underwent an intramolecular aldol reaction to afford β-hydroxy ketone **44** in 98% yield as a single isomer. It should be noted that conducting the aldol reaction in tetrahydrofuran in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base provided a 2:5 mixture of **44** and its diastereomer **45**,[23] and the diastereomer **45** could be completely converted into **44** by treatment with potassium hydroxide in methanol.

Having succeeded in forming the β-hydroxy ketone moiety, the characteristic aminal moiety was next constructed (Scheme 6). Protection of the hydroxy group in **44** with a benzoyl group, followed by oxidative cleavage of the PMP group,[24] afforded alcohol **46**, which was oxidized with DMP to give aldehyde **47**. Cleavage of the Boc group using trifluoroacetic acid (TFA) afforded hemiaminal **48**. Removal of the Ns group from **48** was effected by treatment with benzenethiol and potassium phosphate. Addition of acetic acid followed by heating promoted the formation of the aminal moiety to give **49** in good yield. Finally, the benzoyl group was cleaved by basic methanolysis to afford lycopalhine A (**2**) and its C16 epimer **50**.[7,25]

In conclusion, we have achieved the total synthesis of (+)-lycopalhine A (**2**) in 41 steps and 2.1% overall yield. The features of our synthesis include the construction of the tricyclic system via cleavage of a cyclopropane ring and an ensuing intramolecular Michael addition, stereoselective introduction of a 2-aminoethyl moiety via a reaction of allyltrimethylsilane with a sulfonyliminium ion, and a stereoselective intramolecular aldol reaction.

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)) spectra were recorded on a JEOL-ECS400 instrument, unless otherwise noted. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm) downfield from TMS (δ) or relative to the singlet for residual $CHCl_3$ at 7.26 ppm or pyridine at 7.19 ppm as the internal standard. Coupling constants are reported in hertz (Hz). Standard abbreviations are used for spin multiplicity. Chemical shifts for ^{13}C NMR were reported in ppm relative to the center line of a triplet at 77.0 ppm for $CDCl_3$ or a triplet at 123.4 ppm for pyridine-d_5. IR spectra were recorded on a JASCO



Scheme 6 Completion of the synthesis

FT/IR-4100 Fourier Transform Infrared Spectrophotometer and were reported in wavenumbers (cm^{-1}). High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100LP AccuTOF LC-plus either in positive electrospray ionization (ESI) method or in positive direct analysis in real time (DART) ionization method, using PEG as the internal standard. Melting points were determined on a Yanaco Micro Melting Point Apparatus. Analytical TLC was performed on Merck precoated analytical plates, silica gel 60 F_{254}, 0.25 mm thick. Preparative TLC separations were performed on Merck analytical plates (0.25 or 0.50 mm thick) precoated with silica gel 60 F_{254}. Flash chromatography separations were performed on Kanto Chemical Silica Gel 60 (spherical, 40–100 mesh), unless otherwise noted. Reagents were commercial grades and were used without any purification. Anhyd THF, Et_2O, toluene, and CH_2Cl_2 were purchased from Kanto Chemicals Co., Inc., and were purified using a Glass Contour Solvent System. Anhyd benzene and DMF were purchased from Kanto Chemicals Co., Inc. and stored over activated MS. Anhyd MeOH, EtOH, and MeCN were also purchased from Kanto Chemicals Co., Inc. and stored over activated 3Å MS. (1*R*,3*S*,5*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxycyclohexyl acetate (**14**),[10] 1-allyloxy-4-methoxybenzene,[26] and bis(*N*-*tert*-butylsalicylaldiminato)copper(II)[27] were prepared according to the literature. All reactions sensitive to oxygen or moisture were conducted under an argon atmosphere.

(1*R*,3*S*,5*S*)-1-Acetoxy-3-(*p*-toluenesulfonyloxy)-5-(*tert*-butyldimethylsilyloxy)cyclohexane (51)

To a solution of **14** (29.7 g, 102 mmol), Et_3N (35.4 mL, 254 mmol), and $Me_3N{\cdot}HCl$ (9.7 g, 102 mmol) in CH_2Cl_2 (300 mL) was added TsCl (29.0 g, 152 mmol) at 0 °C. The mixture was stirred for 1 h. To decompose the remaining TsCl, *N*,*N*-dimethylethylenediamine (ca. 18.0 mL) was added to the reaction mixture. After stirring for another 10 min, H_2O was added to the mixture. The resulting solution was extracted with CH_2Cl_2 (3 ×). The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 10:1) to give **51** (44.9 g, 99%) as a colorless oil; $[\alpha]_D^{24}$ –1.88 (*c* = 1.00, $CHCl_3$).

IR (film): 2954, 2930, 2857, 1738, 1598, 1471, 1365, 1241, 1178, 1099, 1036, 935, 861, 813, 778 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.2 Hz, 2 H), 7.34 (d, *J* = 8.2 Hz, 2 H), 4.61 (dddd, *J* = 11.5, 11.5, 4.6, 4.6 Hz, 1 H), 4.36 (dddd, *J* = 11.5, 11.5, 4.6, 4.6 Hz, 1 H), 3.53 (dddd, *J* = 11.5, 11.5, 4.6, 4.6 Hz, 1 H), 2.43 (s, 3 H), 2.18 (ddd, *J* = 11.5, 4.6, 4.6 Hz, 1 H), 2.15–2.03 (m, 2 H), 2.00 (s, 3 H), 1.48 (ddd, *J* = 11.5, 11.5, 11.5 Hz, 1 H), 1.43 (ddd, *J* = 11.5, 11.5, 11.5 Hz, 1 H), 1.29 (ddd, *J* = 11.5, 11.5, 11.5 Hz, 1 H), 0.82 (s, 9 H), –0.01 (s, 3 H), –0.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0 (C), 144.8 (C), 134.1 (C), 129.9 (CH), 127.6 (CH), 75.2 (CH), 66.6 (CH), 65.3 (CH), 41.4 (CH_2), 40.2 (CH_2), 37.1 (CH_2), 25.6 (CH_3), 21.6 (CH_3), 21.0 (CH_3), 17.9 (C), –4.9 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{21}H_{34}O_6SSiNa$: 465.1743; found: 465.1744.

(1*R*,3*S*,5*S*)-1-Hydroxy-3-(*p*-toluenesulfonyloxy)-5-(*tert*-butyldimethylsilyloxy)cyclohexane (15)

To a solution of **51** (44.9 g, 101 mmol) in MeOH (1.00 L) was added K_2CO_3 (21.4 g, 152 mmol) at r.t. and stirring was continued at r.t. for 2 h. The solution was evaporated and the residue was partitioned between EtOAc and H_2O. The aqueous phase was further extracted with EtOAc and the combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 5:1 → 2:1) to afford **15** (39.6 g, 98%, >99.5% ee) as a colorless oil. The enantiomeric excess was determined by HPLC analysis with a chiral HPLC column (DAICEL CHIRALCEL AD-H, 4% *i*-PrOH in *n*-hexane, 1.0 mL/min at 25 °C, 210 nm). The retention times corresponding to **15** and its enantiomer are 30.9 and 27.1 min, respectively; $[\alpha]_D^{25}$ –1.32 (*c* = 1.00, $CHCl_3$).

IR (film): 2953, 2930, 2857, 1598, 1470, 1360, 1256, 1176, 1099, 1049, 956, 931, 873, 836, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.2 Hz, 2 H), 7.33 (d, *J* = 8.2 Hz, 2 H), 4.42 (dddd, *J* = 10.5, 10.5, 4.6, 4.6 Hz, 1 H), 3.57 (dddd, *J* = 10.5, 10.5, 4.6, 4.6 Hz, 1 H), 3.57 (dddd, *J* = 10.5, 10.5, 4.6, 4.6 Hz, 1 H), 2.44 (s, 3 H), 2.18–2.08 (m, 1 H), 2.08–1.94 (m, 2 H), 1.91 (d, *J* = 5.0 Hz, 1 H), 1.50 (ddd, *J* = 12.0, 10.5, 10.5 Hz, 1 H), 1.48 (ddd, *J* = 12.2, 10.5, 10.5 Hz, 1 H), 1.33 (ddd, *J* = 12.0, 10.5, 10.5 Hz, 1 H), 0.83 (s, 9 H), 0.00 (s, 3 H), –0.01 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7 (C), 134.3 (C), 129.8 (CH), 127.6 (CH), 75.8 (CH), 65.7 (CH), 65.1 (CH), 43.4 (CH_2), 40.8 (CH_2), 40.5 (CH_2), 25.7 (CH_3), 21.6 (CH_3), 18.0 (C), –4.9(CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{19}H_{32}O_5SSiNa$: 423.1637; found: 423.1622.

(5*S*)-5-*tert*-Butyldimethylsilyloxycyclohex-2-enone (16)

To a solution of **15** (56.0 g, 140 mmol) and $PhI(OAc)_2$ (98.0 g, 304 mmol) in MeCN (580 mL) and phosphate buffer (pH 7.4, 580 mL) was added AZADO (1.58 g, 10.4 mmol) at 0 °C. The reaction mixture was allowed to warm to r.t. After stirring for 2 h at r.t., the reaction was quenched with aq $Na_2S_2O_3$. The resulting solution was extracted with EtOAc (3 ×). The combined organic phases were washed with brine, dried (Na_2SO_4) and filtered. The filtrate was concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (1.00 L), and DBU (25.5 mL, 171 mmol) was added at 0 °C. After stirring for 1.5 h at 0 °C, aq NH_4Cl was added. The resulting mixture was extracted with CH_2Cl_2 (3 ×). The combined organic phases were washed with brine, dried (Na_2SO_4) and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:0 → 10:1) to give **16** (28.5 g, 91%) as a pale yellow oil; $[\alpha]_D^{25}$ +10.4 (*c* = 1.00, $CHCl_3$).

IR (film): 2955, 2930, 2894, 2857, 1682, 1472, 1389, 1253, 1103, 939, 836, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.85 (ddd, *J* = 10.1, 5.0, 3.2 Hz, 1 H), 6.03 (d, *J* = 10.1 Hz, 1 H), 4.22 (dddd, *J* = 9.6, 7.5, 4.7, 4.1 Hz, 1 H), 2.64 (dd, *J* = 16.0, 4.1 Hz, 1 H), 2.58 (ddd, *J* = 18.3, 5.0, 4.7 Hz, 1 H), 2.46 (dd, *J* = 16.0, 9.6 Hz, 1 H), 2.36 (dddd, *J* = 18.3, 7.5, 3.2, 2.7 Hz 1 H), 0.86 (s, 9 H), 0.05 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.6 (C), 146.8 (CH), 130.0 (CH), 67.5 (CH), 48.0 (CH_2), 35.5 (CH_2), 25.7 (CH_3), 17.9 (C), –4.8 (CH_3), –4.9 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{12}H_{22}O_2SiNa$: 249.1287; found: 249.1284.

(5*S*)-2-Iodo-5-*tert*-butyldimethylsilyloxycyclohex-2-enone (17)

To a solution of **16** (16.4 g, 72.4 mmol) and DMAP (17.7 g, 145 mmol) in CH_2Cl_2 (40.0 mL) was added I_2 (20.5 g, 80.8 mmol) in CH_2Cl_2 (500 mL) slowly at 0 °C. The reaction mixture was allowed to warm to r.t. After stirring for 2 h at r.t., the reaction was quenched with aq $Na_2S_2O_3$. The resulting solution was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 50:1) to afford **17** (22.5 g, 88%) as a pale yellow oil; $[\alpha]_D^{26}$ +11.0 (*c* = 1.00, $CHCl_3$).

IR (film): 2953, 2929, 2893, 2856, 1690, 1591, 1471, 1322, 1254, 1106, 962, 837, 776 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.61 (dd, *J* = 5.3, 3.8 Hz, 1 H), 4.27 (dddd, *J* = 9.2, 6.9, 5.0, 3.7 Hz, 1 H), 2.85 (dd, *J* = 15.6, 5.0 Hz, 1 H), 2.67 (dd, *J* = 15.6, 9.2 Hz, 1 H), 2.63 (ddd, *J* = 18.3, 5.3, 3.7 Hz, 1 H), 2.45 (ddd, *J* = 18.3, 6.9, 3.8 Hz, 1 H), 0.85 (s, 9 H), 0.05 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.2 (C), 155.1 (CH), 103.5 (C), 67.2 (CH), 46.7 (CH_2), 39.3 (CH_2), 25.6 (CH_3), 17.9 (C), –4.8 (CH_3), –4.9 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{12}H_{21}IO_2SiNa$: 375.0253; found: 375.0249.

(*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]-2-[3-(4-methoxyphenoxy)propyl]cyclohex-2-enone (19)

To a solution of 1-allyloxy-4-methoxybenzene (14.2 g, 86.5 mmol) in THF (120 mL) was added 9-BBN (0.5 M solution in THF, 152 mL, 76.0 mmol) at r.t. and the solution was heated at reflux for 2 h. In another flask **17** (20.6 g, 58.5 mmol) was dissolved in THF (240 mL). To this solution were added the above solution containing boron reagent **18**, $PdCl_2(dppf)\cdot CH_2Cl_2$ (4.74 g, 5.80 mmol), K_3PO_4 (24.0 g 113 mmol), $AsPh_3$ (1.81 g, 5.91 mmol), and H_2O (120 mL) at 0 °C. After stirring for 2 h at r.t., the reaction was quenched with aq NH_4Cl. The resulting solution was extracted with EtOAc. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified roughly by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 50:1 → 10:1) to afford a 5:1 mixture of **19** and **16** (20.86 g) as a yellow oil, which was used in the next step without further purification. The spectroscopic data for **19** were collected after purification by PTLC (SiO_2; toluene–acetone, 100:1); $[\alpha]_D^{26}$ +1.98 (*c* = 1.00, $CHCl_3$).

IR (film): 2953, 2929, 2896, 2856, 1676, 1508, 1471, 1380, 1231, 1106, 1041, 866, 835, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.85 (s, 4 H), 6.61 (dd, *J* = 4.6, 3.2 Hz, 1 H), 4.17 (dddd, *J* = 9.6, 7.3, 4.6, 4.1 Hz, 1 H), 3.88 (t, *J* = 6.4 Hz, 2 H), 3.75 (s, 3 H), 2.66 (dd, *J* = 16.0, 4.1 Hz, 1 H), 2.57 (ddd, *J* = 17.8, 4.6, 4.6 Hz, 1 H), 2.47 (dd, *J* = 16.0, 9.6 Hz, 1 H), 2.42–2.30 (m, 3 H), 1.86 (tt, *J* = 7.6, 6.4 Hz, 2 H), 0.86 (s, 9 H), 0.05 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0 (C), 153.7 (C), 153.0 (C), 141.9 (CH), 139.3 (C), 115.4 (CH), 114.6 (CH), 67.8 (CH_2), 67.7 (CH), 55.7 (CH_3), 48.2 (CH_2), 35.9 (CH_2), 28.1 (CH_2), 26.0 (CH_2), 25.8 (CH_3), 17.9 (C), –4.8 (CH_3), –4.9 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{22}H_{34}O_4SiNa$: 413.2124; found: 413.2112.

(1*S*,5*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]-2-[3-(4-methoxyphenoxy)propyl]cyclohex-2-enol (20)

To a solution of **19** containing a small amount of **16** in MeOH (500 mL) was added $CeCl_3\cdot 7H_2O$ (28.3 g, 76.0 mmol) and $NaBH_4$ (2.43 g, 64.3 mmol) at 0 °C. After stirring for 2 h at 0 °C, the reaction was quenched with aq NH_4Cl. The solution was evaporated and the residue was partitioned between EtOAc and H_2O. The aqueous phase was further extracted with EtOAc and the combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified roughly by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 20:1 → 0:1) to afford a 5:1 mixture of **20** and an alcohol derived from **16** (20.4 g) as a yellow oil, which was used in the next step without further purification. The spectroscopic data for **20** were collected after purification by PTLC (SiO_2; toluene–acetone, 100:1); $[\alpha]_D^{26}$ –3.04 (*c* = 1.00, $CHCl_3$).

IR (film): 3445, 2950, 2928, 2857, 1508, 1470, 1322, 1231, 1044, 962, 835, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.82 (s, 4 H), 5.38 (m, 1 H), 4.23 (d, *J* = 3.2 Hz, 1 H), 3.98 (m, 1 H), 3.91 (t, *J* = 6.4, Hz, 2 H), 3.75 (s, 3 H), 3.38 (d, *J* = 10.1 Hz, 1 H), 2.35–2.26 (m, 2 H), 2.23–2.16 (m, 2 H), 2.13 (ddd, *J* = 13.8, 4.1, 3.7 Hz, 1 H), 1.94 (m, 1 H), 1.82 (ddd, *J* = 13.8, 5.0, 1.8 Hz, 1 H), 0.88 (s, 9 H), 0.09 (s, 3 H), 0.07 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9 (C), 153.2 (C), 139.2 (C) 119.2 (CH), 115.5 (CH), 115.5 (CH), 114.6 (CH), 114.6 (CH), 68.3 (CH_2), 66.7 (CH), 66.7 (CH), 55.7 (CH_2), 37.5 (CH_2), 34.3 (CH_2), 30.7 (CH_2), 27.6 (CH_3), 25.8 (CH_3), 18.0 (C), –4.9 (CH_3), –5.1 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{22}H_{36}O_4SiNa$: 415.2281; found: 415.2264.

Ethyl 2-{(1*S*,5*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-2-[3-(4-methoxyphenoxy)propyl]cyclohex-2-en-1-yl}acetate (21)

To a solution of **20** containing a small amount of an impurity in *m*-xylene (200 mL) was added triethyl orthoacetate (200 mL) and *o*-nitrophenol (400 mg, 2.88 mmol) at r.t. and the solution was heated at reflux for 13.5 h. After cooling to r.t., the solvent was evaporated. The

residual oil was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:0 → 20:1) to afford **21** (16.4 g, 58% for 3 steps) as a pale yellow oil; $[\alpha]_D^{26}$ –34.8 (*c* = 1.00, $CHCl_3$).

IR (film): 2951, 2929, 2856, 1733, 1508, 1471, 1232, 1105, 1039, 835, 775 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.82 (s, 4 H), 5.38–5.37 (m, 1 H), 4.14 (q, *J* = 7.4 Hz, 2 H), 3.96–3.80 (m, 2 H), 3.76 (s, 3 H), 2.80–2.65 (m, 1 H), 2.61 (dd, *J* = 15.1, 4.1 Hz, 1 H), 2.28 (dd, *J* = 15.1, 9.6 Hz, 1 H), 2.25–2.15 (m, 1 H), 2.13 (t, *J* = 7.6 Hz, 1 H), 2.05–19.2 (m, 2 H), 1.90–1.85 (m, 1 H), 1.85–1.75 (m, 1 H), 1.46 (ddd, *J* = 12.4, 10.1, 10.1 Hz, 1 H), 1.25 (t, *J* = 7.4 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9 (C), 153.7 (C), 153.1 (C), 137.8 (C), 120.9 (CH), 115.4 (CH), 114.6 (CH), 68.0 (CH_2), 67.9 (CH), 60.2 (CH_2), 55.6 (CH_3), 38.4 (CH_2), 38.2 (CH_2), 35.3 (CH_2), 34.6 (CH), 30.5 (CH_2), 27.5 (CH_2), 25.9 (CH_3), 18.1 (C), 14.2 (CH_3), –4.7 (CH_3), –4.7 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{26}H_{42}O_5SiNa$: 485.2699; found: 485.2714.

2-{(1*R*,5*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-2-[3-(4-methoxyphenoxy)propyl]cyclohex-2-en-1-yl}ethanol (52)

To a solution of **21** (28.0 g, 60.5 mmol) in THF (900 mL) was added $LiAlH_4$ (2.53 g, 66.6 mmol) at 0 °C. After stirring for 2 h at 0 °C, H_2O (2.60 mL), 3 M aq NaOH (2.60 mL), and H_2O (7.80 mL) were successively added at the same temperature, and then the resulting mixture was filtered through a pad of Celite. The filtrate was concentrated *in vacuo*. The residual oil was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 5:1 → 2:1) to afford **52** (23.1 g, 92%) as a pale yellow oil; $[\alpha]_D^{27}$ –38.1 (*c* = 1.00, $CHCl_3$).

IR (film): 3409, 2950, 2929, 2856, 1508, 1231, 1105, 1041, 835, 775 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.82 (s, 4 H), 5.36 (d, *J* = 5.5 Hz, 1 H), 3.89 (dd, *J* = 9.2, 6.4 Hz, 2 H), 3.85–3.78 (m, 1 H), 3.76 (s, 3 H), 3.74–3.60 (m, 2 H), 2.50–2.35 (m, 1 H), 2.25–2.05 (m, 3 H), 2.05–1.85 (m, 4 H), 1.85–1.70 (m, 1 H), 1.56–1.44 (m, 2 H), 1.37 (ddd, *J* = 12.3, 11.0, 10.6 Hz, 1 H), 0.89 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.7 (C), 153.1 (C), 137.8 (C), 120.3 (CH), 115.4 (CH), 114.6 (CH), 68.4 (CH), 68.1 (CH_2), 60.5 (CH_2), 55.7 (CH_3), 38.4 (CH_2), 35.7 (CH_2), 35.5 (CH_2), 34.4 (CH), 30.6 (CH_2), 27.6 (CH_2), 26.0 (CH_3), 18.1 (C), –4.6 (CH_3), –4.7 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{24}H_{40}O_4SiNa$: 443.2594; found: 443.2584.

2-{(1*S*,5*R*)-5-[(*tert*-Butyldimethylsilyl)oxy)-2-[3-(4-methoxyphenoxy)propyl]cyclohex-2-en-1-yl}acetaldehyde (22)

To a solution of **52** (23.0 g, 54.7 mmol) in CH_2Cl_2 (600 mL) were added $NaHCO_3$ (28.0 g, 333 mmol) and Dess–Martin periodinane (25.5 g, 60.2 mmol) at 0 °C. After stirring for 1 h at r.t., H_2O was added at the same temperature. The resulting solution was extracted with CH_2Cl_2 (3 ×). The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 10:1) to give **22** (22.2 g, 97%) as a colorless oil; $[\alpha]_D^{26}$ –44.3 (*c* = 1.00, $CHCl_3$).

IR (film): 2951, 2928, 2856, 1724, 1508, 1231, 1106, 1040, 835, 775 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.78 (dd, *J* = 2.3, 1.4 Hz, 1 H), 6.82 (s, 4 H), 5.48–5.36 (m, 1 H), 3.96–3.82 (m, 3 H), 3.76 (s, 3 H), 2.90–2.75 (m, 1 H), 2.63 (ddd, *J* = 17.0, 4.1, 1.4 Hz, 1 H), 2.52 (ddd, *J* = 17.0, 8.7, 2.3 Hz, 1 H), 2.23 (ddd, *J* = 18.3, 5.6, 5.6 Hz, 1 H), 2.12 (t, *J* = 7.6 Hz, 2 H), 2.06–1.94 (m, 2 H), 1.93–1.85 (m, 1 H), 1.84–1.73 (m, 1 H), 1.47 (ddd, *J* = 12.4, 10.1, 9.6 Hz, 1 H), 0.88 (s, 9 H), 0.06 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.4 (CH), 153.7 (C), 153.0 (C), 137.2 (C), 121.3 (CH), 115.4 (CH), 114.6 (CH), 67.9 (CH_2), 67.4 (CH), 55.6 (CH_3), 47.24 (CH_2), 38.6 (CH_2), 35.2 (CH_2), 32.4 (CH), 30.6 (CH_2), 27.5 (CH_2), 25.8 (CH_3), 18.1 (C), –4.7 (CH_3), –4.7 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{24}H_{38}O_4SiNa$: 441.2437; found: 441.2431.

Ethyl 4-{(1*S*,5*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-2-[3-(4-methoxyphenoxy)propyl]cyclohex-2-en-1-yl}-3-oxobutanoate (23)

To a solution of **22** (22.2 g, 53.0 mmol) in CH_2Cl_2 (750 mL) were added $SnCl_2$ (1.12 g, 5.91 mmol) and ethyl diazoacetate (15% solution in toluene, 61.0 mL, 80.2 mmol) at 0 °C. After stirring for 1 h at r.t., aq NH_4Cl was added at 0 °C. The resulting solution was extracted with CH_2Cl_2 (3 ×). The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 10:1 → 5:1) to give **23** (26.1 g, 98%) as a pale yellow oil; $[\alpha]_D^{26}$ –39.8 (*c* = 1.00, $CHCl_3$).

IR (film): 2951, 2928, 2856, 1724, 1508, 1231, 1106, 1040, 835, 775 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 12.13 (s, 0.13 H), 6.81 (s, 4 H), 5.42–5.30 (m, 1 H), 5.00 (s, 0.14 H), 4.19 (q, *J* = 7.1 Hz, 0.28 H), 4.18 (q, *J* = 7.1 Hz, 2.72 H), 3.95–3.80 (m, 3 H), 3.76 (s, 3 H), 3.42 (s, 1.66 H), 2.85–2.55 (m, 1.67 H), 2.54–2.51 (m, 1.12 H), 2.30–1.70 (m, 7 H), 1.45–1.30 (m, 1 H), 1.26 (t, *J* = 7.1 Hz, 3 H), 0.88 (s, 9 H), 0.05 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.1 (C), 177.2 (C), 172.5 (C), 167.0 (C), 153.7 (CH), 153.1 (CH), 138.2 (C), 137.6 (C), 120.9 (CH), 115.4 (CH), 114.6 (CH), 90.7 (CH), 68.0 (CH), 68.0 (CH_2), 67.4 (CH), 61.3 (CH_2), 59.9 (CH_2), 55.7 (CH_3), 50.0 (CH_2), 46.9 (CH_2), 39.1 (CH_2), 38.2 (CH_2), 37.9 (CH_2), 35.4 (CH_2), 35.2 (CH_2), 34.9 (CH), 33.0 (CH), 30.6 (CH_2), 27.5 (CH_2), 25.9 (CH_3), 18.2 (C), 14.2 (CH_2), 14.1 (CH_3), –4.7 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{28}H_{44}O_6SiNa$: 527.2804; found: 527.2789.

Ethyl 4-{(1*S*,5*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-2-[3-(4-methoxyphenoxy)propyl]cyclohex-2-en-1-yl}-2-diazo-3-oxobutanoate (25)

To a solution of **23** (26.0 g, 51.5 mmol) and Et_3N (14.9 mL, 107 mmol) in MeCN (93.0 mL) and THF (370 mL) was added 2-azido-1,3-dimethylimidazolium hexafluorophosphate (**24**; 17.6 g, 61.8 mmol) at 0 °C. After stirring for 1 h at the same temperature, EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 10:1) to give **25** (26.68 g, 98%) as a pale yellow oil; $[\alpha]_D^{26}$ –27.3 (*c* = 1.00, $CHCl_3$).

IR (film): 2952, 2929, 2856, 2132, 1718, 1654, 1508, 1470, 1306, 1231, 1106, 1070, 835, 775 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.81 (s, 4 H), 5.46–5.32 (m, 1 H), 4.28 (q, *J* = 7.3 Hz, 2 H), 3.94–3.78 (m, 3 H), 3.75 (s, 3 H), 3.10 (dd, *J* = 16.0, 3.2 Hz, 1 H), 2.93 (dd, *J* = 16.0, 9.6 Hz, 1 H), 2.92–2.80 (m, 1 H), 2.20 (ddd, *J* = 17.0, 5.0, 5.0 Hz, 1 H), 2.12 (t, *J* = 7.6 Hz, 2 H), 2.22–1.94 (m, 2 H), 1.93–1.84 (m, 1 H), 1.84–1.72 (m, 1 H), 1.42 (ddd, *J* = 12.4, 10.1, 10.1 Hz, 1 H), 1.32 (t, *J* = 7.3 Hz, 3 H), 0.87 (s, 9 H), 0.05 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.0 (C), 161.2 (C), 153.6 (C), 153.1 (C), 138.1 (C), 120.8 (CH), 115.4 (CH), 114.5 (CH), 76.3 (C), 68.1 (CH_2), 67.9 (CH), 61.3 (CH_2), 55.7 (CH_3), 43.6 (CH_2), 38.6 (CH_2), 35.4 (CH_2), 33.8 (CH), 30.5 (CH_2), 27.6 (CH_2), 25.9 (CH_3), 18.1 (C), 14.3 (CH_3), –4.6 (CH_3), –4.7 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{28}H_{42}N_2O_6SiNa$: 553.2710; found: 553.2693.

Ethyl (4*S*,5a*S*)-4-[(*tert*-Butyldimethylsilyl)oxy)-2a^1-[3-(4-methoxyphenoxy)propyl]-2-oxooctahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxylate (26)

To a solution of **25** (7.00 g, 9.42 mmol) in toluene (940 mL) was added bis(*N*-*tert*-butylsalicylaldiminato)copper(II) (**A**; 1.80 g, 61.8 mmol) at r.t., and the resulting solution was heated at 110 °C for 1 h. After cooling to r.t., the solvent was evaporated. The residual oil was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 20:1 → 7:1) to afford **26** (3.65 g, 55%) as a white solid; mp 72.1–73.0 °C; $[\alpha]_D^{27}$ +10.3 (*c* = 1.00, $CHCl_3$).

IR (film): 2951, 2931, 2856, 1732, 1508, 1231, 1106, 1033, 835, 775 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.80 (s, 4 H), 4.15 (q, *J* = 7.3 Hz, 2 H), 4.05–3.95 (m, 2 H), 3.87 (t, *J* = 6.0 Hz, 2 H), 3.74 (s, 3 H), 2.78 (dd, *J* = 17.8, 11.9 Hz, 1 H), 2.70–2.60 (m, 1 H), 2.40–2.22 (m, 3 H), 1.96–1.70 (m, 5 H), 1.56–1.45 (m, 2 H), 1.23 (t, *J* = 7.3 Hz, 3 H), 0.85 (s, 9 H), 0.02 (s, 3 H), 0.01 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.7 (C), 168.0 (C), 153.8 (C), 152.9 (C), 115.3 (CH), 114.6 (CH), 68.0 (CH_2), 64.5 (CH), 61.3 (CH_2), 55.6 (CH_3), 49.5 (C), 49.1 (CH_2), 46.7 (C), 34.2 (CH_2), 32.3 (CH), 30.0 (CH), 28.3 (CH_2), 28.2 (CH_2), 26.7 (CH_2), 25.7 (CH_3), 17.9 (C), 14.1 (CH_3), –4.9 (CH_3), –5.0 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{28}H_{42}O_6SiNa$: 525.2648; found: 525.2623.

(4*S*,5a*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2a^1-[3-(4-methoxyphenoxy)propyl]-2-oxooctahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxylic Acid (27)

To a solution of **26** (13.1 g, 26.1 mmol) in EtOH (250 mL) was added 1 M aq NaOH (125 mL) at 0 °C. After stirring for 1 h at r.t., EtOAc and aq NH_4Cl were added. The mixture was partitioned between EtOAc and H_2O. The aqueous phase was extracted with EtOAc and the combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 7:1) to afford **27** (11.2 g, 91%, >99.5% ee) as a pale yellow oil. The enantiomeric excess was determined by HPLC analysis with a chiral HPLC column (DAICEL CHIRALCEL AD-H, 10% *i*-PrOH in *n*-hexane, 1.0 mL/min at 25 °C, λ = 210 nm). The retention times corresponding to **27** and its enantiomer are 17.1 and 14.0 min, respectively; $[\alpha]_D^{27}$ –0.868 (*c* = 1.00, $CHCl_3$).

IR (film): 2951, 2930, 2856, 1751, 1685, 1508, 1231, 1089, 1040, 835, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.85–6.75 (m, 4 H), 4.07 (dddd, *J* = 6.1, 6.1, 6.1, 3.6 Hz, 1 H), 3.96–3.82 (m, 2 H), 3.75 (s, 3 H), 2.78 (dd, *J* = 17.4, 11.5 Hz, 1 H), 2.76–2.68 (m, 1 H), 2.63 (dd, *J* = 7.6, 3.6 Hz, 1 H), 2.57 (d, *J* = 17.4 Hz, 1 H), 2.37 (ddd, *J* = 16.0, 7.6, 7.6 Hz, 1 H), 2.18 (ddd, *J* = 14.2, 10.5, 5.0 Hz, 1 H), 2.06 (ddd, *J* = 14.2, 10.5, 5.5 Hz, 1 H), 1.95–1.75 (m, 3 H), 1.67–1.55 (m, 2 H), 0.86 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 216.1 (C), 169.2 (C), 153.8 (C), 152.9 (C), 115.3 (CH), 114.6 (CH), 68.2 (CH_2), 64.4 (CH), 55.6 (CH_3), 52.4 (C), 48.4 (C), 46.1 (CH_2), 41.5 (CH), 33.6 (CH_2), 29.9 (CH), 29.2 (CH_2), 27.5 (CH_2), 27.3 (CH_2), 25.7 (CH_3), 17.9 (C), –4.9 (CH_3), –5.0 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{26}H_{37}O_6SiNa_2$: 519.2154; found: 519.2164.

(4*S*,5a*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2a^1-[3-(4-methoxyphenoxy)propyl]-2-oxo-*N*-tosyloctahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxamide (53a)

To a solution of **27** (930 mg, 1.96 mmol) in THF (14.0 mL) was added 1,1′-carbonyldiimidazole (980 mg, 6.08 mmol) at r.t. and the solution was stirred at r.t. for 2 h. In another flask *p*-toluenesulfonamide (503 mg, 2.94 mmol) and DBU (410 μL, 2.74 mmol) were dissolved in THF (28 mL). To this solution was added the above solution containing the acyl imidazole reagent. After stirring for 3 h at the same temperature, EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 4:1) to give **53a** (1.10 g, 90%) as a white amorphous solid; $[\alpha]_D^{27}$ –32.1 (*c* = 1.00, $CHCl_3$).

IR (film): 3185, 2951, 2930, 2856, 1709, 1508, 1437, 1350, 1231, 1173, 1088, 835, 775 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.83 (s, 1 H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2 H), 6.82 (dd, *J* = 6.9, 2.7 Hz, 2 H), 6.75 (dd, *J* = 6.9, 2.7 Hz, 2 H), 4.01 (dddd, *J* = 6.6, 6.6, 6.6, 3.2 Hz, 1 H), 3.77 (s, 3 H), 3.73 (t, *J* = 6.2 Hz, 2 H), 2.71 (dd, *J* = 18.0, 11.5 Hz, 1 H), 2.66–2.60 (m, 1 H), 2.51 (dd, *J* = 8.0, 4.1 Hz, 1 H), 2.46 (dd, *J* = 18.0, 1.4 Hz, 1 H), 2.36 (s, 3 H), 2.31 (ddd, *J* = 15.6, 8.0, 6.6 Hz, 1 H), 2.06 (ddd, *J* = 13.8, 10.5, 5.0 Hz, 1 H), 1.96–1.82 (m, 2 H), 1.81–1.70 (m, 1 H), 1.60–1.43 (m, 3 H), 0.85 (s, 9 H), 0.010 (s, 3 H), 0.001 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.8 (C), 165.6 (C), 153.8 (C), 152.8 (C), 144.6 (C), 136.0 (C), 129.3 (CH), 128.4 (CH), 115.2 (CH), 114.6 (CH), 67.9 (CH_2), 64.4 (CH), 55.7 (CH_3), 53.1 (C), 49.2 (C), 46.6 (CH_2), 40.0 (CH), 33.6 (CH_2), 29.7 (CH), 29.1 (CH_2), 26.9 (CH_2), 26.7 (CH_2), 25.7 (CH_3), 17.9 (C), –4.9 (CH_3), –5.0 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{33}H_{44}NO_7SSiNa_2$: 672.2403; found: 672.2419.

(4*S*,5a*S*)-4-Hydroxy-2a^1-[3-(4-methoxyphenoxy)propyl]-2-oxo-*N*-tosyloctahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxamide (28a)

To a solution of **53a** (1050 mg, 1.67 mmol) in THF (30.0 mL) was added TBAF (30.0 mL, 30.0 mmol, 1.0 M in THF) at 0 °C. After stirring for 3 h at r.t., EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 0:1) to give **28a** (820 mg, 96%) as a pale yellow amorphous solid; $[\alpha]_D^{27}$ –31.2 (*c* = 1.00, $CHCl_3$).

IR (film): 3531, 3109, 2937, 1707, 1508, 1438, 1347, 1230, 1172, 1087, 866, 825 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.81 (s, 1 H), 7.92 (d, *J* = 8.2 Hz, 2 H), 7.28 (d, *J* = 7.8 Hz, 2 H), 6.82 (dd, *J* = 6.9, 2.7 Hz, 2 H), 6.75 (dd, *J* = 6.9, 2.7 Hz, 2 H), 4.07 (dddd, *J* = 7.7, 7.7, 7.7, 4.1 Hz, 1 H), 3.76 (s, 3 H), 3.72 (t, *J* = 6.4 Hz, 1 H), 2.78 (dd, *J* = 19.2, 11.9 Hz, 1 H), 2.72–2.64 (m, 1 H), 2.54 (dd, *J* = 8.7, 4.6 Hz, 1 H), 2.42–2.37 (m, 1 H), 2.36 (s, 3 H), 2.35 (dd, *J* = 19.2, 2.3 Hz, 1 H), 2.20–1.95 (m, 3 H), 1.89 (ddd, *J* = 14.4, 10.3, 5.5 Hz, 1 H), 1.80–1.70 (m, 1 H), 1.57–1.45 (m, 2 H), 1.40 (ddd, *J* = 15.6, 7.7, 4.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.9 (C), 165.4 (C), 153.7 (C), 152.8 (C), 144.7 (C), 135.8 (C), 129.3 (CH), 128.3 (CH), 115.2 (CH), 114.6 (CH), 67.8 (CH_2), 64.1 (CH), 55.6 (CH_3), 52.8 (C), 49.1 (C), 46.9 (CH_2), 39.7 (CH), 33.0 (CH_2), 29.8 (CH), 28.3 (CH_2), 26.8 (CH_2), 26.5 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{30}NO_7SNa_2$: 558.1538; found: 558.1558.

(2a*S*,2a^1*S*,4a*S*,7a*S*)-2a^1-[3-(4-Methoxyphenoxy)propyl]-1-tosyltetrahydro-1*H*-cyclopenta[*cd*]indole-2,3,6(2a*H*,2a^1*H*,4*H*)-trione (32a)

To a solution of **28a** (660 mg, 1.29 mmol) and pyridine (1.00 mL) in CH_2Cl_2 (30.0 mL) was added Dess–Martin periodinane (572 mg, 1.35 mmol) at 0 °C and the solution was stirred for 1 h at r.t. After checking the reaction by TLC, the reaction mixture was stirred at 40 °C for 30 min. After cooling to 0 °C, EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1 → 1:3) to give **32a** (520 mg, 80%) as a pale yellow amorphous solid; $[\alpha]_D^{27}$ +29.6 (*c* = 1.00, $CHCl_3$).

IR (film): 2931, 1765, 1719, 1508, 1361, 1231, 1170, 1086, 826 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.2 Hz, 2 H), 7.28 (d, *J* = 8.2 Hz, 2 H), 6.90–6.72 (m, 4 H), 4.60 (dd, *J* = 6.4, 3.7 Hz, 1 H), 3.93 (t, *J* = 5.5 Hz, 2 H), 3.76 (s, 3 H), 3.30 (s, 1 H), 3.13 (dd, *J* = 18.3, 6.4 Hz, 1 H), 2.86 (dd, *J* = 18.3, 3.7 Hz, 1 H), 2.78 (dd, *J* = 19.0, 9.2 Hz, 1 H), 2.71–2.60 (m, 1 H), 2.45–2.34 (m, 4 H), 2.12 (dd, *J* = 19.0, 3.2 Hz, 1 H), 2.05–1.89 (m, 3 H), 1.88–1.75 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.9 (C), 205.5 (C), 165.8 (C), 154.0 (C), 152.5 (C), 145.8 (C), 134.8 (C), 129.7 (CH), 128.3 (CH), 115.3 (CH), 114.7 (CH), 67.6 (CH_2), 59.9 (CH), 59.6 (CH), 55.7 (CH_3), 46.4 (C), 44.2 (CH_2), 41.6 (CH_2), 41.1 (CH_2), 36.4 (CH), 34.4 (CH_2), 24.6 (CH_2), 21.6 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{29}NO_7SNa$: 534.1562; found: 534.1560.

(2*R*,2a*S*,2a^1*S*,3*R*,4a*S*,6*S*,7a*S*)-2a^1-[3-(4-Methoxyphenoxy)propyl]-1-tosyldecahydro-1*H*-cyclopenta[*cd*]indole-2,3,6-triol (33a)

To a solution of **32a** (460 mg, 0.900 mmol) in THF (100 mL) was added DIBAL-H (8.1 mL, 8.1mmol, 1 M in *n*-hexane) at –78 °C. After stirring for 10 min at the same temperature, the mixture was stirred for 1 h at –10 °C. Then aq 1 M NaOH (2.00 mL) was added at –40 °C. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered through a pad of Celite. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:3 → 0:1) to afford an 2:1 diastereomeric mixture of **33a** (150 mg, 32%) as a white amorphous solid; $[\alpha]_D^{27}$ –7.42 (*c* = 1.00, $CHCl_3$).

IR (film): 3473, 2935, 1508, 1468, 1325, 1231, 1156, 1038, 823 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.2 Hz, 1 H), 7.74 (dd, *J* = 8.2, 2.3 Hz, 1 H), 7.32–7.26 (m, 2 H), 6.82–6.71 (m, 4 H), 5.96 (d, *J* = 4.6 Hz, 2/3 1 H), 5.80 (d, *J* = 10.6 Hz, 1/3 1 H), 5.59 (dd, *J* = 7.3, 4.1 Hz, 1/3 1 H), 5.45–5.30 (m, 2/3 1 H), 5.28 (dd, *J* = 6.9, 6.9 Hz, 1/3 1 H), 4.35–4.20 (m, 2/3 3 H), 4.10–4.00 (m, 1/3 1 H), 3.86–3.76 (m, 2/3 2 H), 3.76–3.72 (m, 3 H), 3.63 (dd, *J* = 6.0, 6.0 Hz, 2/3 1 H), 3.52 (dd, *J* = 6.0, 6.0 Hz, 1/3 1 H), 3.46–3.34 (m, 2/3 1 H + 2/3 1 H), 2.53 (d, *J* = 8.0 Hz 2/3 1 H), 2.41–2.37 (m, 2/3 3 H + 1/3 3 H), 2.36–2.33 (br s, 1/3 2 H), 2.33–2.10 (m, 2/3 4 H), 2.10–1.40 (m, 2/3 6 H + 1/3 4 H), 1.25–1.07 (m, 1/4 2 H), 0.98–0.95 (m, 1/3 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 153.8 (C), 153.1 (C), 153.0 (C), 144.1 (C), 143.4 (C), 137.0 (C), 135.4 (C), 132.6 (CH), 130.0 (CH), 129.8 (CH), 128.2 (CH), 127.2 (CH), 127.0 (CH), 115.5 (CH), 115.4 (CH), 115.3 (CH), 114.7 (CH), 86.6 (CH), 85.2 (CH), 73.3 (CH), 72.3 (CH), 72.0 (CH), 68.8 (CH_2), 68.7 (CH_2), 68.4 (CH_2), 66.3 (CH), 64.3 (CH), 63.8 (CH), 60.0 (CH), 58.8 (CH), 58.3 (CH), 55.8 (CH_3), 53.5 (CH), 51.9 (C), 51.2 (C), 45.6 (CH), 44.6 (CH), 41.3 (CH_2), 40.0 (CH_2), 39.1 (CH), 38.6 (CH_2), 36.8 (CH), 36.4 (CH_2), 35.0 (CH_2), 31.0 (CH_2), 30.2 (CH_2), 25.6 (CH_2), 25.2 (CH_2), 25.1 (CH_2), 21.6 (CH).

HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{35}NO_7SNa$: 540.2032; found: 540.2006.

(3a*R*,3a^1*S*,4a*S*,4a^1*S*,6*S*,7a*S*,8a*R*)-4a^1-[3-(4-Methoxyphenoxy)propyl]-2,2-dimethyl-4-tosyldecahydro-3a*H*-1,3-dioxa-4-azacyclopenta[*def*]fluoren-6-ol (34a)

To a solution of **33a** (100 mg, 0.193 mmol) in acetone (14.0 mL) was added anhyd $CuSO_4$ (230 mg, 1.44 mmol) and PPTS (64 mg, 0.255 mnol) at 0 °C, and the solution was stirred for 2.5 h at r.t. After cooling to 0 °C, EtOAc and aq $NaHCO_3$ were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 3:1 → 1:2) to give **34a** (54 mg, 50%) as a white amorphous solid; $[\alpha]_D^{27}$ –34.7 (*c* = 1.00, $CHCl_3$).

IR (film): 3502, 2938, 1508, 1470, 1382, 1339, 1232, 1162, 1040, 947, 827 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.2 Hz, 2 H), 7.23 (d, *J* = 8.2 Hz, 2 H), 6.86–6.76 (m, 4 H), 5.86 (d, *J* = 6.9 Hz, 2 H), 4.40 (dd, *J* = 6.0, 4.6 Hz, 1 H), 3.93 (dd, *J* = 10.5, 8.2 Hz, 1 H), 3.82 (t, *J* = 6.0 Hz, 2 H), 3.39–3.30 (m, 1 H), 2.27 (dd, *J* = 6.9, 6.0 Hz, 1 H), 2.18 (ddd, *J* = 13.3, 7.8, 4.6 Hz, 1 H), 2.10–2.02 (m, 1 H), 2.00–1.60 (m, 8 H), 1.50–1.42 (m, 5 H), 1.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (C), 153.0 (C), 143.2 (C), 138.7 (C), 129.2 (CH), 127.7 (CH), 115.4 (CH), 114.6 (CH), 97.5 (C), 82.2 (CH), 72.4 (CH), 68.5 (CH_2), 67.1 (CH), 62.3 (CH), 55.8 (C), 55.7 (CH_3), 51.9 (CH), 42.1 (CH_2), 41.5 (CH), 40.6 (CH_2), 39.0 (CH_2), 38.7 (CH_2), 29.3 (CH_3), 25.6 (CH_2), 21.5 (CH_3), 20.7 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{30}H_{39}NO_7SNa$: 580.2345; found: 580.2364.

(4*S*,5a*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2a^1-[3-(4-methoxyphenoxy)propyl]-*N*-[(2-nitrophenyl)sulfonyl]-2-oxooctahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxamide (53b)

To a solution of **27** (930 mg, 1.96 mmol) in THF (14.0 mL) was added 1,1′-carbonyldiimidazole (980 mg, 6.08 mmol) at r.t. and the solution was stirred at r.t. for 2 h. In another flask *o*-nitrobenzenesulfonamide (594 mg, 2.94 mmol) and DBU (410 µL, 2.74 mmol) were dissolved in THF (28 mL). To this solution was added the above solution containing the acyl imidazole reagent. After stirring for 3 h at the same temperature, EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 4:1) to give inseparable products containing **53b** and *o*-nitrobenzenesulfonamide as a yellow oil, which was used in the next step without further purification. The spectroscopic data for **53b** were collected after purification by PTLC (SiO_2; *n*-hexane–EtOAc, 3:1); $[\alpha]_D^{27}$ +10.6 (*c* = 1.00, $CHCl_3$).

IR (film): 3100, 2951, 2931, 1712, 1542, 1508, 1423, 1362, 1231, 1182, 1036, 835, 779 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 11.32 (br s, 1 H), 8.34 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.75 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.68 (ddd, *J* = 7.5, 1.6, 1.6 Hz, 1 H), 7.65 (ddd, *J* = 7.5, 1.6, 1.6 Hz, 1 H), 6.81 (dd, *J* = 6.9, 2.7 Hz, 2H), 6.73 (dd, *J* = 6.9, 2.7 Hz, 2 H), 4.02 (dddd, *J* = 6.5, 6.5, 6.5, 3.2 Hz, 1 H), 3.74 (s, 3 H), 3.72–3.67 (m, 2 H), 2.78 (dd, *J* = 18.8, 11.4 Hz, 2 H), 2.70–2.62 (m, 1 H), 2.55–2.45 (m, 2 H), 2.32 (ddd, *J* = 15.8, 8.0, 6.5 Hz, 1 H), 2.03 (ddd, *J* = 12.6, 11.0, 4.6 Hz, 1 H), 1.95–1.72 (m, 3 H), 1.62–1.45 (m, 3 H), 0.84 (s, 9 H), 0.02 (s, 3 H), 0.01 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.0 (C), 166.1 (C), 153.8 (C), 152.8 (C), 148.2 (C), 134.6 (C), 133.3 (CH), 132.1 (CH), 131.8 (C), 124.7 (CH), 115.2 (CH), 114.6 (CH), 67.8 (CH_2), 64.4 (CH), 55.7 (CH_3), 53.5 (C), 49.2 (C), 46.6 (CH_2), 40.7 (CH), 33.7 (CH_2), 29.8 (CH), 29.1 (CH_2), 26.9 (CH_2), 26.7 (CH_2), 25.7 (CH_3), 17.9 (C), –4.9 (CH_3), –5.0 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{32}H_{41}N_2O_9SSiNa_2$: 703.2097; found: 703.2119.

(4*S*,5a*S*)-4-Hydroxy-2a^1-[3-(4-methoxyphenoxy)propyl]-*N*-[(2-nitrophenyl)sulfonyl]-2-oxooctahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxamide (28b)

To a solution of crude **53b** in THF (30.0 mL) was added TBAF (30.0 mL, 30.0 mmol, 1.0 M in THF) at 0 °C. After stirring for 3 h at r.t., EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 0:1) to give **28b** (950 mg, 89% for 2 steps) as a pale yellow amorphous solid; $[\alpha]_D^{27}$ +4.12 (*c* = 1.00, $CHCl_3$).

IR (film): 3546, 3100, 2937, 1711, 1541, 1508, 1426, 1362, 1230, 1182, 1056, 827 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 11.27 (br s, 1 H), 8.34 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.75 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.68 (ddd, *J* = 7.5, 1.6, 1.6 Hz, 1 H), 7.65 (ddd, *J* = 7.5, 1.6, 1.6 Hz, 1 H), 6.81 (d, *J* = 8.7 Hz, 2 H), 6.73 (d, *J* = 9.2 Hz, 2 H), 4.20–4.11 (m, 1 H), 3.75 (s, 3 H), 3.74–3.65 (m, 2 H), 2.85 (dd, *J* = 19.5, 11.7 Hz, 1 H), 2.56 (dd, *J* = 8.3, 4.6 Hz, 1 H), 2.55–2.53 (m, 1 H), 2.50–2.46 (m, 2 H), 2.25–1.95 (m, 3 H), 1.90 (ddd, *J* = 14.1, 10.5, 5.2 Hz, 1 H), 1.85–1.75 (m, 1 H), 1.66–1.45 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.4 (C), 165.8 (C), 153.7 (C), 152.7 (C), 148.1 (C), 134.7 (CH), 132.2 (CH), 132.1 (CH), 131.7 (C), 124.8 (CH), 115.2 (CH), 114.6 (CH), 67.8 (CH_2), 64.1 (CH), 55.7 (CH_3), 53.3 (C), 49.3 (C), 47.1 (CH_2), 40.3 (CH), 33.0 (CH_2), 29.9 (CH), 28.4 (CH_2), 26.8 (CH_2), 26.6 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{26}H_{27}N_2O_9SiNa_2$: 589.1233; found: 589.1219.

(2a*S*,2a^1*S*,4a*S*,7a*S*)-2a^1-[3-(4-Methoxyphenoxy)propyl]-1-[(2-nitrophenyl)sulfonyl]tetrahydro-1*H*-cyclopenta[*cd*]indole-2,3,6(2a*H*,2a^1*H*,4*H*)-trione (32b)

To a solution of **28b** (810 mg, 1.49 mmol) and pyridine (1.10 mL) in CH_2Cl_2 (30.0 mL) was added Dess–Martin periodinane reagent (662 mg, 1.56 mmol) at 0 °C and the solution was stirred for 1 h at r.t. After checking the reaction by TLC, the reaction mixture was stirred at 40 °C for 30 min. After cooling to 0 °C, EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1 → 1:3) to give **32b** (580 mg, 72%) as a pale yellow amorphous solid; $[\alpha]_D^{27}$ +263 (*c* = 1.00, $CHCl_3$).

IR (film): 2934, 1766, 1722, 1541, 1508, 1368, 1231, 1177, 1037, 827 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.40–8.36 (m, 1 H), 7.85–7.75 (m, 3 H), 6.86–6.76 (m, 4 H), 4.75 (dd, *J* = 4.6, 3.2 Hz, 1 H), 4.05–3.95 (m, 1 H), 3.77 (s, 3 H), 3.30 (s, 1 H), 3.26 (dd, *J* = 18.3, 4.6 Hz, 1 H), 2.84 (dd, *J* = 18.3, 3.2 Hz, 1 H), 2.83 (dd, *J* = 19.0, 9.2 Hz, 1 H), 2.76–2.66 (m, 1 H), 2.55 (dd, *J* = 18.3, 4.6 Hz, 1 H), 2.26 (dd, *J* = 19.0, 1.4 Hz, 1 H), 2.22 (dd, *J* = 18.3, 12.8 Hz, 1 H), 2.20–1.96 (m, 3 H), 1.95–1.82 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.0 (C), 165.8 (C), 154.1 (C), 152.6 (C), 147.9 (C), 135.8 (CH), 135.6 (CH), 132.3 (CH), 130.7 (C), 124.6 (CH), 115.4 (CH), 114.7 (CH), 67.8 (CH_2), 60.4 (CH), 58.6 (CH), 55.7 (CH_3), 46.9 (C), 44.2 (CH_2), 41.9 (CH_2), 41.4 (CH_2), 37.0 (CH), 33.5 (CH_2), 24.5 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{26}H_{26}N_2O_9SNa$: 565.1257; found: 565.1237.

(2*R*,2a*S*,2a^1*S*,3*R*,4a*S*,6*S*,7a*S*)-2a^1-[3-(4-Methoxyphenoxy)propyl]-1-[(2-nitrophenyl)sulfonyl]decahydro-1*H*-cyclopenta[*cd*]indole-2,3,6-triol (33b)

To a solution of **32b** (500 mg, 0.922 mmol) in THF (26 mL) was added DIBAL-H (8.3 mL, 8.3mmol, 1 M in *n*-hexane) at –78 °C. After stirring for 10 min at the same temperature, the mixture was stirred for 1 h at –10 °C. Then aq 1 M NaOH (2.00 mL) was added at –40 °C. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered through a pad of Celite. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:3 → 0:1) to afford a 1:1 diastereomeric mixture of **33b** (360 mg, 71%) as a white amorphous solid; $[\alpha]_D^{27}$ +46.2 (*c* = 1.00, $CHCl_3$).

IR (film): 3395, 2935, 2360, 1717, 1541, 1508, 1468, 1371, 1230, 1169, 1036, 826, 761 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20–8.02 (m, 1 H), 7.82–7.55 (m, 3 H), 6.85–6.70 (m, 4 H), 5.96 (d, *J* = 4.1 Hz, 1/2 1 H), 5.76 (d, *J* = 6.6 Hz, 1/2 1 H), 5.50–5.38 (m, 1/2 1 H), 4.35–4.11 (m, 1/2 3 H), 3.98–3.83 (m, 1/2 5 H), 3.83–3.76 (m, 1/2 2 H), 3.75 (s, 1/2 3 H), 3.74 (s, 1/2 3 H), 3.72–3.65 (m, 1/2 2 H), 2.87–2.61 (m, 1/2 2 H), 2.54 (dd, *J* = 7.6, 7.6 Hz, 1/2 1 H), 2.46–2.28 (m, 1/2 4 H), 2.21 (ddd, *J* = 12.4, 6.4, 6.4 Hz, 1/2 1 H), 2.51–1.61 (m, 1/2 20 H), 1.58–1.47 (m, 1/2 2 H), 1.46–1.11 (m, 1/2 4 H), 0.97–0.85 (m, 1/2 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 153.8 (C), 153.0 (C), 152.9 (C), 148.1 (C), 135.2 (CH), 134.2 (C), 134.0 (CH), 133.9 (CH), 133.3 (C), 132.3 (C), 132.1 (CH), 132.0 (CH), 131.1 (CH), 130.7 (CH), 129.5 (CH), 124.6 (CH), 124.5 (CH), 124.2 (CH), 115.5 (CH), 115.4 (CH), 114.7 (CH), 86.7 (CH), 86.1 (CH), 77.2 (CH), 73.1 (CH), 71.9 (CH), 68.7 (CH_2), 68.4 (CH_2), 67.8(CH_2), 66.2 (CH), 65.0 (CH), 64.5 (CH), 63.1 (CH), 62.2 (CH), 61.2 (CH), 58.5 (CH), 58.2 (CH), 55.7 (CH_3), 52.2 (C), 51.8 (C), 45.4 (CH_2), 42.6 (CH_2), 41.7 (CH_2), 40.6 (CH_2), 39.3 (CH_2), 38.9 (CH_2), 38.1 (CH_2), 37.1 (CH), 37.0 (CH), 35.7 (CH_2), 35.4 (CH_2), 34.2 (CH_2), 31.5 (CH_2), 30.9 (CH_2), 30.6 (CH_2), 29.0 (CH_2), 25.5 (CH_2), 25.1 (CH_2), 23.9 (CH_2), 22.9 (CH_2), 14.0 (CH), 11.1 (CH).

HRMS (ESI+): *m*/*z* calcd for $C_{26}H_{32}N_2O_9SNa$: 571.1726; found: 571.1710.

(3a*R*,3a^1*S*,4a*S*,4a^1*S*,6*S*,7a*S*,8a*R*)-4a^1-[3-(4-Methoxyphenoxy)propyl]-2,2-dimethyl-4-[(2-nitrophenyl)sulfonyl]decahydro-3a*H*-1,3-dioxa-4-azacyclopenta[*def*]fluoren-6-ol (34b)

To a solution of **33b** (220 mg, 0.401 mmol) in acetone (33.0 mL) was added anhyd $CuSO_4$ (530 mg, 3.32 mmol) and PPTS (150 mg, 0.598 mmol) at 40 °C and the solution was stirred for 12 h at the same temperature. After cooling to 0 °C, EtOAc and aq $NaHCO_3$ was added. The

resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1 → 1:2) to give **34b** (160 mg, 68%) as a white amorphous solid; $[\alpha]_D^{27}$ –32.2 (*c* = 1.00, $CHCl_3$).

IR (film): 3420, 2938, 1717, 1542, 1508, 1470, 1372, 1232, 1164, 1078, 1039, 947, 827, 781 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.26–8.22 (m, 1 H), 7.80–7.75 (m, 3 H), 6.81 (d, *J* = 9.2 Hz, 2 H), 6.73 (d, *J* = 9.2 Hz, 2 H), 5.85 (d, *J* = 6.9 Hz, 1 H), 4.44 (dd, *J* = 5.5, 4.5 Hz, 1 H), 3.92 (dd, *J* = 10.3, 8.5 Hz, 1 H), 3.76 (s, 3 H), 3.69 (t, *J* = 6.2 Hz, 2 H), 3.50–3.30 (m, 1 H), 2.36 (dd, *J* = 6.9, 5.5 Hz, 1 H), 2.29–2.15 (m, 2 H), 2.15–2.07 (m, 1 H), 2.07–1.85 (m, 4 H), 1.75–1.50 (m, 3 H), 1.46 (s, 3 H), 1.39 (s, 6 H), 1.40–1.30 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (C), 152.9 (C), 148.1 (C), 133.6 (C), 133.5 (CH), 131.5 (CH), 131.0 (CH), 123.9 (CH), 115.4 (CH), 114.6 (CH), 97.8 (C), 82.6 (CH), 72.3 (CH), 68.4 (CH_2), 67.0 (CH), 62.7 (CH), 56.2 (C), 55.7 (CH_3), 52.0 (CH), 42.2 (CH_2), 41.2 (CH), 40.3 (CH_2), 39.4 (CH_2), 38.7 (CH_2), 29.4 (CH_3), 25.5 (CH_2), 20.5 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{29}H_{36}N_2O_9SNa$: 611.2039; found: 611.2047

(4*S*,5a*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2a^1-[3-(4-methoxyphenoxy)propyl]-2-oxo-*N*-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxamide (53c)

To a solution of **27** (9.00 g, 19.0 mmol) in THF (130 mL) was added 1,1′-carbonyldiimidazole (6.15 g, 38.0 mmol) at r.t. and the solution was stirred at r.t. for 2 h. In another flask 4-(trifluoromethyl)benzenesulfonamide (6.40 g, 28.5 mmol) and DBU (4.00 mL, 26.6 mmol) were dissolved in THF (260 mL). To this solution was added the above solution containing the acyl imidazole reagent. After stirring for 4 h at the same temperature, EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified roughly by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 4:1) to give a mixture of **53c** and 4-(trifluoromethyl)benzenesulfonamide as a yellow oil, which was used in the next step without further purification. The spectroscopic data for **53c** were collected after purification by PTLC (SiO_2; *n*-hexane–EtOAc, 3:1); $[\alpha]_D^{27}$ –13.1 (*c* = 1.00, $CHCl_3$).

IR (film): 3105, 2952, 2931, 2857, 1710, 1508, 1322, 1231, 1175, 1062, 835, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 11.02 (s, 1 H), 8.19 (d, *J* = 8.3 Hz, 1 H), 7.76 (d, *J* = 8.3 Hz, 1 H), 6.82 (dd, *J* = 6.8, 2.8 Hz, 2 H), 6.74 (dd, *J* = 6.8, 2.8 Hz, 2 H), 4.02 (dddd, *J* = 6.5, 6.5, 6.5, 3.2 Hz, 1 H), 3.80–3.70 (m, 5 H), 2.73 (dd, *J* = 18.1, 10.9 Hz, 1 H), 2.68–2.63 (m, 1 H), 2.55–2.45 (m, 2 H), 2.32 (ddd, *J* = 15.8, 8.0, 8.0 Hz, 1 H), 2.10 (ddd, *J* = 14.2, 10.1, 4.6 Hz, 1 H), 2.00–1.81 (m, 2 H), 1.80–1.70 (m, 1 H), 1.62–1.45 (m, 3 H), 0.85 (s, 9 H), 0.02 (s, 3 H), 0.00 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.9 (C), 165.9 (C), 153.8 (C), 152.8 (C), 142.7 (C), 135.5 (C, q, *J* = 32.4 Hz), 129.0 (CH), 125.9 (CH, q, *J* = 3.8 Hz), 122.8 (CF_3, q, *J* = 271.7 Hz), 115.2 (CH), 114.7 (CH), 67.8 (CH_2), 64.3 (CH), 55.7 (CH_3), 53.5 (C), 49.3 (C), 46.6 (CH_2), 40.7 (CH), 33.6 (CH_2), 29.7 (CH), 29.2 (CH_2), 26.9 (CH_2), 26.8 (CH_2), 25.7 (CH_3), 17.9 (C), –4.9 (CH_3), –5.0 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{33}H_{41}F_3NO_7SSiNa_2$: 726.2121; found: 726.2147.

(4*S*,5a*S*)-4-Hydroxy-2a^1-[3-(4-methoxyphenoxy)propyl]-2-oxo-*N*-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxamide (28c)

To a solution of a mixture containing **53c** and 4-(trifluoromethyl)benzenesulfonamide in THF (250 mL) was added TBAF (190 mL, 190 mmol, 1.0 M in THF) at 0 °C. After stirring for 1 h at r.t., EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 0:1) to give **28c** (9.25 g, 86% for 2 steps) as a pale yellow amorphous solid; $[\alpha]_D^{27}$ –32.1 (*c* = 1.00, $CHCl_3$).

IR (film): 3538, 2938, 1709, 1508, 1433, 1356, 1322, 1230, 1133, 1062, 826 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 10.98 (s, 1 H), 8.18 (d, *J* = 8.2 Hz, 2 H), 7.76 (d, *J* = 8.2 Hz, 2 H), 6.84–6.80 (m, 2 H), 6.78–6.70 (m, 2 H), 4.15–4.05 (m, 1 H), 3.80–3.70 (m, 4 H), 2.81 (dd, *J* = 19.3, 11.7 Hz, 1 H), 2.74–2.62 (m, 1 H), 2.54 (dd, *J* = 8.3, 4.6 Hz, 1 H), 2.44–2.34 (m, 2 H), 2.10 (ddd, *J* = 14.2, 9.6, 4.6 Hz, 1 H), 2.04–1.90 (m, 2 H), 1.88–1.69 (m, 2 H), 1.65–1.50 (m, 2 H), 1.44 (ddd, *J* = 15.6, 7.8, 4.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.9 (C), 165.7 (C), 153.8 (C), 152.7 (C), 142.3 (C), 135.0 (C, q, *J* = 32.4 Hz), 125.9 (CH, q, *J* = 3.8 Hz), 123.0 (CF_3, q, *J* = 271.7 Hz), 115.2 (CH), 114.7 (CH), 67.8 (CH_2), 64.1 (CH), 55.7 (CH_3), 53.1 (C), 49.3 (C), 47.0 (CH_2), 40.3 (CH), 33.0 (CH_2), 29.8 (CH), 28.5 (CH_2), 26.8 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{27}F_3NO_7SNa_2$: 612.1258; found: 612.1231.

(2a*S*,2a^1*S*,4a*S*,7a*S*)-2a^1-[3-(4-Methoxyphenoxy)propyl)-1-{[4-(trifluoromethyl)phenyl]sulfonyl}tetrahydro-1*H*-cyclopenta[*cd*]indole-2,3,6(2a*H*,2a^1*H*,4*H*)-trione (32c)

To a solution of **28c** (2.20 g, 3.88 mmol) and pyridine (3.80 mL) in CH_2Cl_2 (130 mL) was added Dess–Martin periodinane (1.73 g, 4.07 mmol) at 0 °-C and the solution was stirred for 1 h at r.t. After checking the reaction by TLC, the reaction mixture was stirred at 40 °C for 30 min. After cooling to 0 °C, EtOAc and aq NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1) to give **32c** (1.75 g, 80%) as a pale orange amorphous solid, $[\alpha]_D^{27}$ +32.9 (*c* = 1.00, $CHCl_3$).

IR (film): 2934, 1768, 1720, 1508, 1405, 1370, 1322, 1231, 1174, 1133, 1062, 827 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.2 Hz, 2 H), 7.77 (d, *J* = 8.2 Hz, 2 H), 6.87–6.75 (m, 4 H), 4.65 (dd, *J* = 6.0, 3.6 Hz, 1 H), 3.95 (t, *J* = 5.5 Hz, 2 H), 3.77 (s, 3 H), 3.35 (s, 1 H), 3.16 (dd, *J* = 18.3, 6.0 Hz, 1 H), 2.88 (dd, *J* = 18.3, 3.6 Hz, 1 H), 2.80 (dd, *J* = 19.0, 9.2 Hz, 1 H), 2.64–2.54 (m, 1 H), 2.42 (dd, *J* = 18.3, 4.8 Hz, 1 H), 2.15 (dd, *J* = 19.0, 3.0 Hz, 1 H), 2.10–1.95 (m, 2 H), 1.89 (dd, *J* = 18.3, 11.0 Hz, 1 H), 1.95–1.55 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.6 (C), 205.0 (C), 166.1 (C), 154.1 (C), 152.5 (C), 141.1 (C), 136.0 (C, q, *J* = 32.4 Hz), 129.1 (CH), 126.3 (CH, q, *J* = 3.8 Hz), 122.9 (CF_3, q, *J* = 271.7 Hz), 115.4 (CH), 114.7 (CH), 67.6 (CH_2), 60.1 (CH), 59.4 (CH), 55.7 (CH_3), 46.6 (C), 44.1 (CH_2), 41.6 (CH_2), 41.0 (CH_2), 36.4 (CH), 34.4 (CH_2), 24.6 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{26}F_3NO_7SNa$: 588.1280; found: 588.1253.

(2*R*,2a*S*,2a^1*S*,3*R*,4a*S*,6*S*,7a*S*)-2a^1-[3-(4-Methoxyphenoxy)propyl]-1-{[4-(trifluoromethyl)phenyl]sulfonyl}decahydro-1*H*-cyclopenta[*cd*]indole-2,3,6-triol (33c)

To a solution of **32c** (2.20 g, 4.01 mmol) in THF (100 mL) was added DIBAL-H (37 mL, 37 mmol, 1 M in *n*-hexane) at –78 °C. After stirring for 10 min at the same temperature, the mixture was stirred for 1 h at –10 °C. Then aq 1 M NaOH (2.00 mL) was added at –40 °C. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered through a pad of Celite. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:3 → 0:1) to afford a 3:1 diastereomeric mixture of **33c** (2.20 g, 88%) as a white amorphous solid; $[\alpha]_D^{27}$ +20.5 (*c* = 1.00, $CHCl_3$).

IR (film): 3389, 2945, 1508, 1469, 1403, 1355, 1323, 1231, 1164, 1132, 1062, 826 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.3 Hz, 3/4 2 H), 8.03 (d, *J* = 8.3 Hz, 1/4 2 H), 7.83–7.73 (m, 2 H), 6.87–6.71 (m, 4 H), 6.10–5.96 (m, 3/4 1 H), 5.85 (d, *J* = 5.5 Hz, 1/4 1 H), 5.76–5.65 (m, 1/4 1 H), 4.90–4.76 (m, 3/4 1 H), 4.32–4.15 (m, 1 H), 4.15–4.03 (m, 3/4 1 H), 4.02–3.89 (m, 1/4 1 H + 1/4 1 H), 3.89–3.80 (m, 3/4 2 H), 3.77 (s, 1/4 3 H), 3.74 (s, 3/4 3 H), 3.72–3.61 (m, 1/4 2 H + 1/4 1 H), 3.51 (br s, 3/4 1 H), 3.48–3.42 (m, 3/4 1 H), 3.33–3.21 (br s, 1/4 1 H), 2.61 (d, *J* = 17.0 Hz, 3/4 10.69 H), 2.42 (d, *J* = 8.2 Hz, 3/4 1 H), 2.40–2.28 (m, 3/4 3 H), 2.27–2.18 (m, 1/4 2 H), 2.14 (s, 1 H), 2.11–1.73 (m, 3/4 6 H + 1/4 4 H), 1.73–1.54 (m, 3/4 2 H + 1/4 1 H), 1.54–1.38 (m, 1/4 2 H), 1.38–1.20 (m, 1/4 2 H), 1.15–0.99 (m, 1/4 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 153.8 (C), 152.8 (C), 152.7 (C), 142.8 (C), 141.9 (C), 134.4 (C, q, *J* = 32.4 Hz), 134.5 (C, q, *J* = 32.4 Hz), 129.0 (CH), 127.7 (CH), 126.3 (CH, q, *J* = 3.8 Hz), 126.1 (CH, q, *J* = 3.8 Hz), 123.2 (CF_3, q, *J* = 271.7 Hz), 123.1 (CF_3, q, *J* = 271.7 Hz), 115.4 (CH), 115.3 (CH), 114.6 (CH), 114.6 (CH), 86.6 (CH), 85.3 (CH), 73.2 (CH), 71.9 (CH), 68.6 (CH_2), 68.2 (CH_2), 66.0 (CH), 64.3 (CH), 63.0 (CH), 60.1 (CH), 58.9 (CH), 58.4 (CH), 55.7 (2 × CH_3), 51.9 (C), 51.4 (C), 44.8 (CH_2), 41.2 (CH_2), 41.0 (CH_2), 37.8 (CH_2), 37.2 (CH), 36.4 (CH), 34.8 (CH_2), 34.5 (CH_2), 30.4 (CH_2), 30.0 (CH_2), 25.5 (CH_2), 25.1 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{32}F_3NO_7SNa$: 594.1745; found: 594.1746.

(3a*R*,3a^1*S*,4a*S*,4a^1*S*,6*S*,7a*S*,8a*R*)-4a^1-[3-(4-Methoxyphenoxy)propyl]-2,2-dimethyl-4-{[4-(trifluoromethyl)phenyl]sulfonyl}decahydro-3a*H*-1,3-dioxa-4-azacyclopenta[*def*]fluoren-6-ol (34c)

To a solution of **33c** (1.93 g, 3.38 mmol) in acetone (140 mL) was added anhyd $CuSO_4$ (1.8 g, 11.3 mmol) and PPTS (850 mg, 3.38 mmol) at r.t. and the solution was stirred for 16 h at the same temperature. The solution was evaporated and the residue was partitioned between EtOAc and aq $NaHCO_3$. The aqueous phase was extracted with EtOAc and the combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1) to give **34c** (1.65 g, 80%) as a white amorphous solid; $[\alpha]_D^{27}$ –43.4 (*c* = 1.00, $CHCl_3$).

IR (film): 3504, 2939, 1508, 1470, 1403, 1355, 1323, 1232, 1166, 1107, 1062, 948, 826 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.5 Hz, 2 H), 7.72 (d, *J* = 8.5 Hz, 2 H), 6.85–6.77 (m, 4 H), 5.89 (d, *J* = 6.4 Hz, 1 H), 4.42 (dd, *J* = 6.4, 4,4 Hz, 1 H), 4.03 (dd, *J* = 10.5, 8.2 Hz, 1 H), 3.87 (t, *J* = 6.0 Hz, 2 H), 3.77 (s, 3 H), 3.42–3.30 (m, 1 H), 2.33 (dd, *J* = 6.4, 6.4 Hz, 1 H), 2.20 (ddd, *J* = 14.0, 7.8, 4.4 Hz, 1 H), 2.13–2.07 (m, 1 H), 1.94 (d, *J* = 14.0 Hz, 1 H), 1.91–1.50 (m, 9 H), 1.45 (s, 3 H), 1.31 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (C), 153.0 (C), 145.5 (C), 134.1 (C, q, *J* = 32.4 Hz), 128.3 (CH), 125.6 (CH, q, *J* = 3.8 Hz), 123.3 (CF_3, q, *J* = 271.7 Hz), 115.4 (CH), 114.6 (CH), 97.6 (C), 82.3 (CH), 72.4 (CH), 68.4 (CH_2), 66.9 (CH), 62.8 (CH), 55.7 (C), 55.7 (CH_3), 51.7 (CH), 42.0 (CH_2), 41.7 (CH), 40.8 (CH_2), 38.8 (CH_2), 38.7 (CH_2), 29.2 (CH_3), 25.6 (CH_2), 20.6 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{30}H_{36}F_3NO_7SNa$: 634.2062; found: 634.2059.

(3a*R*,3a^1*S*,4a*S*,4a^1*S*,6*S*,7a*R*,8a*R*)-4a^1-[3-(4-Methoxyphenoxy)propyl]-2,2-dimethyl-4-{[4-(trifluoromethyl)phenyl]sulfonyl}decahydro-3a*H*-1,3-dioxa-4-azacyclopenta[*def*]fluoren-6-yl methanesulfonate (54c)

To a solution of **34c** (1.54 g, 2.52 mmol) and Et_3N (528 μL, 3.78 mmol) in CH_2Cl_2 (70 mL) was added methanesulfonyl chloride (216 μL, 2.77 mmol) at 0 °C. After stirring for 30 min at the same temperature, aq $NaHCO_3$ was added. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1) to afford **54c** (1.62 g, 93%) as a white amorphous solid; $[\alpha]_D^{27}$ –37.2 (*c* = 1.00, $CHCl_3$).

IR (film): 3449, 2940, 1508, 1350, 1232, 1172, 1062, 943, 827 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.2 Hz, 2 H), 7.74 (d, *J* = 8.2 Hz, 2 H), 6.86–6.75 (m, 4 H), 5.89 (d, *J* = 6.9 Hz, 1 H), 4.44 (dd, *J* = 6.0, 4,6 Hz, 1 H), 4.38–4.27 (m, 1 H), 4.06 (dd, *J* = 10.1, 8.2 Hz, 1 H), 3.86 (t, *J* = 5.9 Hz, 2 H), 3.77 (s, 3 H), 2.91 (s, 3 H), 2.35 (dd, *J* = 6.9, 6.0 Hz, 1 H), 2.25–2.06 (m, 5 H), 1.95 (d, *J* = 14.2 Hz, 1 H), 1.97–1.87 (m, 1 H), 1.85–1.64 (m, 2 H), 1.58–1.52 (m, 2 H), 1.45 (s, 3 H), 1.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 152.9 (C), 145.2 (C), 134.1 (C, q, *J* = 32.4 Hz), 128.3 (CH), 125.6 (CH, q, *J* = 3.8 Hz), 123.3 (CF_3, q, *J* = 271.7 Hz), 115.4 (CH), 114.6 (CH), 97.7 (C), 82.3 (CH), 72.4 (CH), 68.4 (CH_2), 66.9 (CH), 62.8 (CH), 55.7 (C), 55.7 (CH_3), 51.7 (CH), 42.0 (CH_2), 41.7 (CH), 40.8 (CH_2), 38.8 (CH_2), 38.7 (CH_2), 29.2 (CH_3), 25.5 (CH_2), 20.5 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{31}H_{38}F_3NO_9S_2Na$: 712.1838; found: 712.1848.

(3a*R*,3a^1*S*,4a*S*,4a^1*S*,6*R*,7a*S*,8a*R*)-4a^1-[3-(4-Methoxyphenoxy)propyl]-2,2-dimethyl-4-{[4-(trifluoromethyl)phenyl]sulfonyl}decahydro-3a*H*-1,3-dioxa-4-azacyclopenta[*def*]fluorene-6-carbonitrile (35c)

To a solution of **54c** (1.83 g, 2.52 mmol) in DMSO (30 mL) was added 18-crown-6 (4.36 g, 16.5 mmol) and KCN (4.36 g, 66.7 mmol) at r.t. and the solution was stirred for 5 h at 80 °C. After cooling to r.t., EtOAc and aq $NaHCO_3$ were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residual oil was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 3:1 → 2:1) to afford **35c** (1.69 g, 97%) as a white amorphous solid; $[\alpha]_D^{27}$ –79.4 (*c* = 1.00, $CHCl_3$).

IR (film): 3483, 2990, 2939, 1508, 1468, 1403, 1383, 1350, 1323, 1232, 1172, 1132, 1062, 943, 828 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.3 Hz, 2 H), 7.73 (d, *J* = 8.3 Hz, 2 H), 6.85–6.76 (m, 4 H), 5.89 (d, *J* = 6.4 Hz, 1 H), 4.45 (dd, *J* = 6.4, 5.0 Hz, 1 H), 4.10 (dd, *J* = 10.1, 8.2 Hz, 1 H), 3.90–3.83 (m, 2 H), 3.77 (s, 3 H), 2.82–2.75 (m, 1 H), 2.43 (dd, *J* = 6.4, 6.4 Hz, 1 H), 2.31–2.20 (m, 2 H), 2.09 (ddd, *J* = 13.3, 11.5, 3.2 Hz, 1 H), 2.00–1.65 (m, 8 H), 1.46 (s, 3 H), 1.29 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (C), 153.0 (C), 145.3 (C), 134.3 (C, q, *J* = 32.4 Hz), 128.3 (CH), 125.8 (CH, q, *J* = 3.8 Hz), 123.2 (CF_3, q, *J* = 271.7 Hz), 120.8 (C), 115.5 (CH), 114.6 (CH), 97.8 (C), 82.5 (CH), 72.6 (CH), 68.4 (CH_2), 60.0 (CH), 55.7 (CH_3), 55.6 (C), 55.4 (CH), 41.8 (CH_2), 41.3 (CH_2), 40.2 (CH), 31.5 (CH_2), 30.9 (CH_2), 29.3 (CH_3), 24.8 (CH_2), 24.0 (CH), 20.5 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{31}H_{35}F_3N_2O_6SNa$: 643.2066; found: 643.2058.

(2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-2-Allyl-3-hydroxy-2a^1-[3-(4-methoxyphenoxy)propyl]-1-{[4-(trifluoromethyl)phenyl]sulfonyl}decahydro-1*H*-cyclopenta[*cd*]indole-6-carbonitrile (36)

To a solution of **35c** (1.21 g, 4.01 mmol) in CH_2Cl_2 (60 mL) was added allyltrimethylsilane (6.30 mL, 39.6 mmol) and BF_3·OEt_2 (2.90 mL, 22.9 mmol) at –78 °C. After stirring for 10 min at –78 °C, the mixture was stirred for 30 min at 0 °C. The reaction was quenched with aq $NaHCO_3$. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residual oil was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1) to afford **36** (1.13 g, 96%) as a white amorphous solid; $[\alpha]_D^{27}$ –0.812 (*c* = 1.00, $CHCl_3$).

IR (film): 3504, 2947, 2388, 2241, 1508, 1366, 1402, 1323, 1231, 1161, 1134, 1062, 923, 827 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.2 Hz, 2 H), 7.84 (d, *J* = 8.2 Hz, 2 H), 6.90–6.76 (m, 4 H), 5.63 (dddd, *J* = 16.9, 11.5, 3.2, 1.8 Hz, 1 H), 5.10 (dd, *J* = 11.5, 0.9 Hz, 1 H), 5.06 (dd, *J* = 16.9, 0.9 Hz, 1 H), 4.68 (dd, *J* = 10.1, 3.2 Hz, 1 H), 4.24–4.10 (m, 1 H), 3.96–3.85 (m, 2 H), 3.77 (s, 3 H), 3.65–3.60 (m, 1 H), 2.78 (dd, *J* = 15.3, 2.1 Hz, 1 H), 2.70–2.63 (m, 1 H), 2.52–2.10 (m, 2 H), 2.28 (d, *J* = 7.8 Hz, 1 H), 2.04 (d, *J* = 4.1 Hz, 1 H), 2.02–2.00 (m, 1 H), 1.97–1.86 (m, 1 H), 1.82–1.57 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.0 (C), 152.7 (C), 145.2 (C), 134.7 (C, q, *J* = 33.4 Hz), 133.7 (CH), 127.6 (CH), 126.7 (CH, q, *J* = 2.9 Hz), 123.2 (CF_3, q, *J* = 271.7 Hz), 121.6 (C), 118.7 (CH_2), 115.3 (CH), 114.7 (CH), 71.9 (CH), 68.1 (CH_2), 61.7 (CH), 60.2 (CH), 55.7 (CH_3), 52.1 (CH), 51.7 (C), 38.4 (CH_2), 37.9 (CH_2), 36.4 (CH), 34.2 (CH_2), 28.8 (CH_2), 28.1 (CH_2), 25.8 (CH_2), 19.0 (CH).

HRMS (ESI+): *m*/*z* calcd for $C_{31}H_{35}F_3N_2O_5SNa$: 627.2117; found: 627.2091.

(2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-2-Allyl-3-[(*tert*-butyldimethylsilyl)oxy]-2a^1-[3-(4-methoxyphenoxy)propyl]-1-{[4-(trifluoromethyl)phenyl]sulfonyl}decahydro-1*H*-cyclopenta[*cd*]indole-6-carbonitrile (55)

To a solution of **36** (2.00 g, 3.30 mmol) in CH_2Cl_2 (60 mL) were added 2.6-lutidine (6.90 mL, 59.6 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.53 mL, 6.60 mmol) at 0 °C. After stirring for 1 h at the same temperature, aq $NaHCO_3$ was added. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residual oil was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 20:1 → 1:1) to afford **55** (2.20 g, 93%) as a white amorphous solid; $[\alpha]_D^{27}$ –5.20 (*c* = 1.00, $CHCl_3$).

IR (film): 2952, 2857, 2239, 1508, 1471, 1402, 1323, 1232, 1163, 1135, 1062, 835, 778 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.2 Hz, 2 H), 7.83 (d, *J* = 8.2 Hz, 2 H), 6.85–6.76 (m, 4 H), 5.60 (dddd, *J* = 16.5, 10.1, 3.2, 1.8 Hz, 1 H), 5.08 (d, *J* = 10.1 Hz, 1 H), 5.04 (d, *J* = 16.5 Hz, 1 H), 4.64 (dd, *J* = 10.8, 3.0 Hz, 1 H), 4.04 (ddd, *J* = 17.8, 8.2, 2.8 Hz, 1 H), 3.95–3.85 (m, 2 H), 3.77 (s, 3 H), 3.68–3.63 (m, 1 H), 2.82 (dd, *J* = 15.4, 2.1 Hz, 1 H), 2.74–2.66 (m, 1 H), 2.30–2.20 (m, 1 H), 2.22 (d, *J* = 8.2 Hz, 1 H), 2.05–1.92 (m, 2 H), 1.90–1.85 (m, 1 H), 1.85–1.46 (m, 8 H), 0.92 (s, 9 H), 0.07 (s, 3 H), 0.05 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.0 (C), 152.7 (C), 145.4 (C), 134.6 (C, q, *J* = 32.4 Hz), 134.0 (CH), 127.6 (CH), 126.5 (CH, q, *J* = 2.9 Hz), 124.4 (CH), 123.0 (CF_3, q, *J* = 271.7 Hz), 121.6 (C), 118.4 (CH_2), 115.3 (CH), 114.7 (CH), 72.3 (CH), 68.1 (CH_2), 61.7 (CH), 55.7 (CH_3), 52.5 (CH), 50.9 (C), 39.0 (CH_2), 38.2 (CH_2), 36.3 (CH), 34.2 (CH_2), 28.7 (CH_2), 28.1 (CH_2), 25.8 (CH_2), 25.7 (CH_3), 19.0 (CH), 18.0 (C), –4.6 (CH_3), –5.0 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{37}H_{49}F_3N_2O_5SSiNa$: 741.2981; found: 741.3003.

(2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-2-Allyl-3-[(*tert*-butyldimethylsilyl)oxy]-2a^1-[3-(4-methoxyphenoxy)propyl]decahydro-1*H*-cyclopenta[*cd*]indole-6-carbonitrile (37)

To a solution of **55** (1.84 g, 2.56 mmol) in MeOH (200 mL) was added Mg (6.00 g, 247 mmol) at r.t. and the solution was heated at 40 °C for 3 h. After cooling to r.t., EtOAc was added and then the solution was concentrated. The residue was partitioned between EtOAc and H_2O. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 2:1) to afford **37** (1.26 g, 96%) as a pale yellow oil; $[\alpha]_D^{27}$ +5.47 (*c* = 1.00, $CHCl_3$).

IR (film): 3464, 2929, 2856, 2237, 1639, 1508, 1470, 1413, 1359, 1231, 1143, 1044, 914, 835, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (s, 4 H), 5.70 (dddd, *J* = 17.0, 13.4, 8.2, 1.4 Hz, 1 H), 5.07 (dd, *J* = 8.2, 1.4 Hz, 1 H), 5.02 (dd, *J* = 17.0, 1.4 Hz, 1 H), 4.05 (ddd, *J* = 10.8, 8.0, 2.8 Hz, 1 H), 3.91 (t, *J* = 6.2 Hz, 2 H), 3.77 (s, 3 H), 3.66 (dd, *J* = 6.9, 6.9 Hz, 1 H), 3.36–3.32 (m, 1 H), 3.22 (dddd, *J* = 12.4, 12.4, 2.8, 2.8 Hz, 1 H), 2.14–2.05 (m, 2 H), 2.02–1.86 (m, 5 H), 1.85–1.68 (m, 4 H), 1.65–1.51 (m, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H), 0.03 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 152.9 (C), 136.2 (CH), 123.8 (C), 117.2 (CH_2), 115.4 (CH), 114.7 (CH), 72.9 (CH), 68.8 (CH_2), 59.0 (CH), 58.5 (CH), 55.7 (CH_3), 54.3 (CH), 48.6 (C), 41.0 (CH_2), 39.6 (CH_2), 36.3 (CH), 35.3 (CH_2), 31.7 (CH_2), 29.4 (CH_2), 26.3 (CH_2), 25.8 (CH_2), 18.2 (CH), 18.0 (C), –4.7 (CH_3), –4.9 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{30}H_{47}N_2O_3Si$: 511.3356; found: 511.3354.

***tert*-Butyl (2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-2-Allyl-3-[(*tert*-butyldimethylsilyl)oxy]-6-cyano-2a^1-[3-(4-methoxyphenoxy)propyl]decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (38)**

To a solution of **37** (1.74 g, 3.41 mmol) and Et_3N (1.43 mL, 10.2 mmol) in DMF (20.0 mL) was added *N*-(*tert*-butoxycarbonyloxy)succinimide (1.47 g, 6.82 mmol) at r.t. and the solution was heated at 40 °C for 3 h. After cooling to 0 °C, EtOAc and aq $NaHCO_3$ were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 5:1) to give **38** (1.91 g, 92%) as a white amorphous solid; $[\alpha]_D^{27}$ +17.9 (*c* = 1.00, $CHCl_3$).

IR (film): 2932, 2857, 2362, 2238, 1695, 1508, 1472, 1394, 1232, 1174, 1130, 1045, 884, 835, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.82 (s, 4 H), 5.67 (dddd, *J* = 18.4, 13.4, 7.3, 2.3 Hz, 1 H), 5.05 (d, *J* = 15.6 Hz, 1 H), 5.04 (d, *J* = 12.4 Hz, 1 H), 4.43 (ddd, *J* = 8.2, 4.1, 2.3 Hz, 1 H), 4.04 (ddd, *J* = 13.2, 8.2, 7.3 Hz, 2 H), 3.91 (t, *J* = 6.0 Hz, 2 H), 3.76 (s, 3 H), 3.58 (dd, *J* = 3.2, 2.7 Hz, 1 H), 2.68

(dddd, *J* = 12.4, 12,4, 3.0, 3.0 Hz, 1 H), 2.36–2.20 (m, 2 H), 2.07 (dd, *J* = 7.3, 2.3 Hz, 1 H), 2.02–1.90 (m, 2 H), 1.85–1.70 (m, 3 H), 1.69–1.54 (m, 6 H), 1.47 (s, 9 H), 0.89 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 153.5 (C), 152.8 (C), 134.7 (CH), 123.0 (C), 117.2 (CH_2), 115.4 (CH), 114.6 (CH), 79.7 (C), 72.6 (CH), 68.5 (CH_2), 60.5 (CH), 57.0 (CH), 55.7 (CH_3), 53.6 (CH), 50.2 (C), 39.2 (CH_2), 38.6 (CH_2), 36.7 (CH), 34.8 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 28.4 (CH_3), 25.8 (CH_2), 25.8 (CH_3), 19.1 (CH), 18.0 (C), –4.6 (CH_3), –4.9 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{35}H_{54}N_2O_5SiNa$: 633.3700; found: 633.3719.

tert-Butyl (2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-6-cyano-2a^1-[3-(4-methoxyphenoxy)propyl]-2-(2-oxoethyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (56)

To a solution of **38** (820 mg, 1.34 mmol) in 1.4-dioxane (70.0 mL) and H_2O (23.0 mL) was added 2.6-lutidine (1.37 mL, 11.8 mmol), $NaIO_4$ (5.73 g, 26.8 mmol), and OsO_4 (33.6 mL, 1.34 mmol, 0.04 M in *t*-BuOH) at 0 °C. The mixture was stirred for 3 h at r.t. After cooling to 0 °C, CH_2Cl_2 and aq $NaHCO_3$ were added. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 2:1) to give **56** (730 mg, 89%) as a white amorphous solid; $[\alpha]_D^{27}$ +30.6 (*c* = 1.00, $CHCl_3$).

IR (film): 2932, 2857, 2238, 1725, 1697, 1508, 1471, 1393, 1366, 1231, 1172, 1127, 1043, 836, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.70 (t, *J* = 2.5 Hz, 1 H), 6.83 (s, 4 H), 4.80 (m, 1 H), 4.09 (ddd, *J* = 10.5, 6.9, 6.9 Hz, 1 H), 3.92 (t, *J* = 5.7 Hz, 2 H), 3.77 (s, 3 H), 3.69 (m, 1 H), 2.74–2.64 (m, 2 H), 2.54 (ddd, *J* = 14.6, 5.5, 2.5 Hz, 1 H), 2.04–1.93 (m, 3 H), 1.88–1.58 (m, 9 H), 1.47 (s, 9 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.2 (CH), 154.0 (C), 153.1 (C), 152.8 (C), 122.7 (C), 115.5 (CH), 114.7 (CH), 80.8 (C), 72.6 (CH), 68.4 (CH_2), 60.4 (CH), 56.1 (CH), 55.7 (CH_3), 53.3 (CH), 50.2 (C), 49.0 (CH_2), 39.1 (CH_2), 36.9 (CH), 35.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 28.4 (CH_3), 25.7 (CH_2), 25.7 (CH_3), 19.2 (CH), 17.9 (C), –4.6 (CH_3), –5.0 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{34}H_{52}N_2O_6SiNa$: 635.3492; found: 635.3509.

tert-Butyl (2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-6-cyano-2-(2-hydroxyethyl)-2a^1-[3-(4-methoxyphenoxy)propyl]decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (39)

To a solution of **56** (685 mg, 1.12 mmol) in MeOH (20.0 mL) was added $NaBH_4$ (96.0 mg, 2.46 mmol) at 0 °C. The solution was stirred for 30 min at the same temperature. To this solution was added CH_2Cl_2 and aq $NaHCO_3$. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1) to give **39** (510 mg, 74%) as a white amorphous solid; $[\alpha]_D^{26}$ +7.71 (*c* = 1.00, $CHCl_3$).

IR (film): 3481, 2932, 2857, 2238, 1692, 1508, 1472, 1393, 1366, 1313, 1231, 1173, 1128, 1044, 836, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (s, 4 H), 4.61 (br s, 1 H), 4.07 (ddd, *J* = 6.4, 6.4, 10.6 Hz, 1 H), 3.92 (t, *J* = 6.0 Hz, 2 H), 3.77 (s, 3 H), 3.68–3.45 (m, 4 H), 2.70 (dddd, *J* = 12.4, 12.4, 2.5, 2.5 Hz, 1 H), 2.10–1.91 (m, 3 H), 1.89–1.49 (m, 11 H), 1.46 (s, 9 H), 0.91 (s, 9 H), 0.07 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 153.6 (C), 152.8 (C), 122.7 (C), 115.4 (CH), 114.7 (CH), 80.9 (C), 72.9 (CH), 68.4 (CH_2), 59.6 (CH), 59.5 (CH), 55.7 (CH), 55.3 (CH_3), 54.6 (C), 50.6 (CH_2), 38.9 (CH_2), 38.0 (CH_2), 36.8 (CH), 34.3 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 28.4 (CH_3), 25.8 (CH_2), 25.8 (CH_3), 19.5 (CH), 18.0 (C), –4.5 (CH_3), –4.8 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{34}H_{54}N_2O_6SiNa$: 637.3649; found: 637.3658.

tert-Butyl (2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-6-cyano-2a^1-[3-(4-methoxyphenoxy)propyl]-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (40)

To a solution of **39** (470 mg, 0.764 mmol) in toluene (11.0 mL) was added *N*-methyl-2-nitrobenzenesulfonamide (181 mg, 0.840 mmol), PPh_3 (260 mg, 0.993 mmol) and diethyl azadicarboxylate (451 µL, 0.993 mmol, 2.2 M in toluene) at 0 °C. The solution was stirred for 1 h at r.t. To this solution was added CH_2Cl_2 and aq $NaHCO_3$. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 5:1 → 2:1) to give **40** (600 mg, 97%) as a white amorphous solid; $[\alpha]_D^{26}$ +13.5 (*c* = 1.00, $CHCl_3$).

IR (film): 2932, 2857, 2238, 1692, 1545, 1508, 1471, 1367, 1231, 1169, 1126, 1042, 835, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (m, 1 H), 7.68–7.59 (m, 2 H), 7.58 (m, 1 H), 6.84 (s, 4 H), 4.30 (m, 1 H), 4.07 (ddd, *J* = 10.5, 6.4, 6.4 Hz, 1 H), 3.94 (t, *J* = 5.7 Hz, 2H), 3.76 (s, 3 H), 3.58 (m, 1 H), 3.23 (ddd, *J* = 13.1, 13.1, 4.1 Hz, 1 H), 3.07 (ddd, *J* = 13.1, 12.8, 5.3 Hz, 1 H), 2.89 (s, 3 H), 2.68 (dddd, *J* = 13.0, 13.0, 2.8, 2.8 Hz, 1 H), 2.03–1.92 (m, 4 H), 1.87–1.61 (m, 7 H), 1.61–1.51 (m, 3 H), 1.46 (s, 9 H), 0.85 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 153.3 (C), 152.9 (C), 148.1 (C), 133.5 (CH), 132.6 (C), 131.6 (CH), 130.7 (CH), 124.1 (CH), 122.9 (C), 115.5 (CH), 114.7 (CH), 80.1 (C), 72.6 (CH), 68.5 (CH_2), 60.1 (CH), 55.7 (CH_3), 55.3 (CH), 54.9 (CH), 50.5 (C), 47.3 (CH_2), 39.1 (CH_2), 36.9 (CH), 34.6 (CH_3), 34.6 (CH_2), 34.6 (CH_2), 32.9 (CH_2), 29.1 (CH_2), 28.4 (CH_3), 25.8 (CH_3), 25.7 (CH_2), 19.3 (CH), 17.9 (C), –4.5 (CH_3), –4.9 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{41}H_{60}N_4O_9SSiNa$: 835.3748; found: 835.3735.

tert-Butyl (2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-6-formyl-2a^1-[3-(4-methoxyphenoxy)propyl]-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (57)

To a solution of **40** (544 mg, 0.669 mmol) in toluene (14.0 mL) was added DIBAL-H (1.0 M in toluene, 1.34 mL, 1.34 mmol) at –78 °C. The solution was stirred for 1 h at the same temperature. To this solution was added H_2O carefully. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 2:1 → 5:1) to give **57** (510 mg, 93%) as a pale yellow amorphous solid; $[\alpha]_D^{26}$ +13.9 (*c* = 0.600, $CHCl_3$).

IR (film): 2930, 2857, 2390, 1722, 1693, 1546, 1508, 1470, 1366, 1231, 1169, 1126, 1043, 835, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.69 (s, 1 H), 7.97 (m, 1 H), 7.70–7.60 (m, 2 H), 7.59 (m, 1 H), 6.83 (s, 4 H), 4.33 (m, 1 H), 4.08 (ddd, *J* = 10.5, 6.4, 6.4 Hz, 1 H), 3.93 (t, *J* = 5.7 Hz, 2 H), 3.77 (s, 3 H), 3.64 (m, 1 H), 3.24 (ddd, *J* = 13.1, 13.1, 4.1 Hz, 1 H), 3.09 (ddd, *J* = 13.1, 12.7, 4.6 Hz, 1

H), 2.90 (s, 3 H), 2.50 (m, 1 H), 2.05–1.70 (m, 7 H), 1.70–1.50 (m, 6 H), 1.44 (s, 9 H), 1.32 (ddd, *J* = 13.3, 13.3, 2.7 Hz, 1 H), 0.86 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.7 (CH), 153.9 (C), 153.3 (C), 153.0 (C), 148.1 (C), 133.4 (CH), 132.7 (C), 131.5 (CH), 130.7 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 79.6 (C), 72.8 (CH), 68.7 (CH_2), 60.9 (CH), 55.7 (CH_3), 55.5 (CH), 55.2 (CH), 51.3 (C), 47.3 (CH_2), 40.2 (CH), 39.5 (CH_2), 37.2 (CH), 34.9 (CH_2), 34.6 (CH_3), 33.7 (CH_2), 28.4 (CH_2), 28.4 (CH_3), 25.8 (CH_3), 25.8 (CH_2), 25.0 (CH_2), 17.9 (C), –4.5 (CH_3), –4.9 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{41}H_{61}N_3O_{10}SSiNa$: 838.3745; found: 838.3752.

tert-Butyl (2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-6-(hydroxymethyl)-2a^1-[3-(4-methoxyphenoxy)propyl]-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (41)

To a solution of **57** (1.41 g, 1.73 mmol) in THF (10.0 mL) and MeOH (10.0 mL) was added $NaBH_4$ (130 mg, 3.46 mmol) at 0 °C. The solution was stirred for 1 h at the same temperature. To this solution were added CH_2Cl_2 and aq NH_4Cl. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1) to give **41** (1.37 g, 97%) as a pale yellow amorphous solid; $[\alpha]_D^{27}$ +20.9 (*c* = 1.70, $CHCl_3$).

IR (film): 3464, 2930, 2857, 1681, 1545, 1508, 1471, 1366, 1231, 1169, 1125, 1042, 971, 898, 835, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (m, 1 H), 7.70–7.60 (m, 2 H), 7.58 (m, 1 H), 6.84 (s, 4 H), 4.32 (m, 1 H), 4.07 (ddd, *J* = 9.6, 7.3, 7.3 Hz, 1 H), 3.93 (t, *J* = 6.2 Hz, 2 H), 3.76 (s, 3 H), 3.57 (m, 1 H), 3.53–3.40 (m, 2 H), 3.22 (ddd, *J* = 12.8, 12.8, 4.3 Hz, 1 H), 3.18–3.00 (m, 2 H), 2.90 (s, 3 H), 2.00–1.84 (m, 3 H), 1.84–1.51 (m, 10 H), 1.44 (s, 9 H), 1.27 (ddd, *J* = 13.3, 13.3, 6.4 Hz, 1 H), 1.08 (ddd, *J* = 14.2, 11.9, 2.7 Hz, 1 H), 0.86 (s, 9 H), 0.04 (s, 3 H), 0.01 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 153.3 (C), 153.1 (C), 148.1 (C), 133.4 (CH), 132.8 (C), 131.5 (CH), 130.7 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 79.3 (C), 73.0 (CH), 68.9 (CH_2), 68.1 (CH_2), 61.8 (CH), 55.7 (CH_3), 55.4 (CH), 55.4 (CH), 51.2 (C), 47.5 (CH_2), 39.7 (CH_2), 37.9 (CH), 35.1 (CH_2), 34.6 (CH_3), 33.5 (CH_2), 29.4 (CH), 28.8 (2 × CH_2), 28.5 (CH_3), 26.0 (CH_2), 25.8 (CH_3), 18.0 (C), –4.4 (CH_3), –4.8 (CH_3).

HRMS (ESI+): *m*/*z* calcd for $C_{41}H_{63}N_3O_{10}SSiNa$: 840.3901; found: 840.3923.

tert-Butyl (2*S*,2a*R*,2a^1*S*,3*R*,4a*S*,6*R*,7a*S*)-3-Hydroxy-6-(hydroxymethyl)-2a^1-[3-(4-methoxyphenoxy)propyl]-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (42)

To a solution of **41** (650 mg, 0.795 mmol) in DMF (4.50 mL) was added tris(dimethylamino)sulfonium difluorotrimethylsilicate (1.20 g, 4.36 mmol) in DMF (3.00 mL) at r.t. The solution was stirred for 3 h at the same temperature. To this solution was added CH_2Cl_2 and H_2O. The resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 0:1) to afford **42** (540 mg, 97%) as a pale yellow amorphous solid, $[\alpha]_D^{27}$ +13.6 (*c* = 1.00, $CHCl_3$).

IR (film): 3444, 2932, 1671, 1543, 1508, 1456, 1405, 1367, 1347, 1231, 1165, 1137, 1041, 826, 758 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (m, 1 H), 7.70–7.65 (m, 2 H), 7.59 (m, 1 H), 6.83 (s, 4 H), 4.38 (m, 1 H), 4.21 (ddd, *J* = 8.0, 8.0, 8.0 Hz, 1 H), 3.92 (t, *J* = 6.2 Hz, 2 H), 3.77 (s, 3 H), 3.60 (m, 1 H), 3.52–3.42 (m, 2 H), 3.36 (ddd, *J* = 13.3, 8.2, 8.2 Hz, 1 H), 3.19 (ddd, *J* = 13.3, 8.2, 4.1 Hz, 1 H), 2.92 (s, 3 H), 2.49 (br s, 1 H), 2.10 (dd, *J* = 7.3, 1.8 Hz, 1 H), 2.05–1.93 (m, 2 H), 1.85–1.51 (m, 11 H), 1.46 (s, 9 H), 1.28 (m, 1 H), 1.10 (ddd, *J* = 14.2, 11.9, 2.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (C), 153.5 (C), 153.0 (C), 148.2 (C), 133.6 (CH), 131.8 (C), 131.6 (CH), 130.8 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 79.6 (C), 72.3 (CH), 68.9 (CH_2), 68.1 (CH_2), 61.7 (CH), 55.7 (CH_3), 54.9 (CH), 54.1 (CH), 52.4 (C), 47.1 (CH_2), 38.8 (CH_2), 37.9 (CH), 35.3 (CH_2), 34.4 (CH_3), 31.8 (CH_2), 29.2 (CH), 28.9 (2 × CH_2), 28.6 (CH_3), 26.0 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{35}H_{49}N_3O_{10}SNa$: 726.3036; found: 726.3032.

tert-Butyl (2*S*,2a*R*,2a^1*S*,4a*S*,6*R*,7a*S*)-6-Formyl-2a^1-[3-(4-methoxyphenoxy)propyl]-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]-3-oxodecahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (43)

To a solution of **42** (510 mg, 0.725 mmol) in CH_2Cl_2 (25.0 mL) was added $NaHCO_3$ (1.90 g, 22.6 mmol) and Dess–Martin periodinane (677 mg, 1.56 mmol) at 0 °C, and the solution was stirred for 3 h at the same temperature. To this solution was added CH_2Cl_2 and H_2O and then the resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:2) to afford **43** (497 mg, 98%) as a white amorphous solid; $[\alpha]_D^{27}$ +16.3 (*c* = 1.00, $CHCl_3$).

IR (film): 2933, 2360, 1737, 1687, 1545, 1508, 1468, 1368, 1232, 1166, 1125, 1038, 982, 826, 760 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.70 (s, 1 H), 7.96 (m, 1 H), 7.70–7.64 (m, 2 H), 7.58 (m, 1 H), 6.82 (s, 4 H), 4.00–3.91 (m, 2 H), 3.86 (m, 1 H), 3.76 (s, 3 H), 3.60 (br s, 1 H), 3.38 (m, 1 H), 3.14 (ddd, *J* = 15.6, 10.1, 5.5 Hz, 1 H), 2.94 (s, 3 H), 2.77–2.61 (m, 2 H), 2.60–2.20 (m, 3 H), 2.13 (dd, *J* = 18.5, 6.0 Hz, 1 H), 2.18–1.53 (m, 9 H), 1.46 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 217.1 (C), 202.3 (CH), 153.9 (C), 153.5 (C), 152.9 (C), 148.2 (C), 133.5 (CH), 132.1 (C), 131.6 (CH), 130.7 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 80.4 (C), 68.3 (CH_2), 60.2 (CH), 58.3 (CH), 58.2 (CH), 55.7 (CH_3), 52.1 (C), 47.1 (CH_2), 44.0 (CH_2), 41.1 (CH), 35.1 (CH_3), 34.6 (CH_2), 33.6 (CH_2), 32.3 (CH_2), 28.4 (CH_3), 24.8 (CH_2), 22.6 (CH). One sp^3 carbon signal missing, possibly due to broadening.

HRMS (ESI+): *m*/*z* calcd for $C_{35}H_{45}N_3O_{10}SNa$: 722.2723; found: 722.2705.

tert-Butyl (2*S*,2a*R*,2a^1*S*,4*S*,4a*S*,6*S*,7a*S*,8*S*)-8-Hydroxy-2a^1-[3-(4-methoxyphenoxy)propyl]-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (44)

To a solution of **43** (497 mg, 0.710 mmol) in MeOH (27.0 mL) was added KOH (8.70 mL, 15.5 mmol, 10% w/w in MeOH) at 0 °C and the solution was stirred for 1.5 h at r.t. To this solution was added CH_2Cl_2 and aq NH_4Cl at 0 °C and then the resulting solution was extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:3) to afford **44** (490 mg, 98%) as a white amorphous solid; $[\alpha]_D^{27}$ +40.1 (*c* = 1.00, $CHCl_3$).

IR (film): 3466, 2946, 2391, 1731, 1683, 1544, 1508, 1455, 1370, 1348, 1231, 1164, 1132, 1033, 826, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (3:2 mixture of rotamers) = 8.00–7.91 (m, 1 H), 7.68–7.60 (m, 2 H), 7.58–7.52 (m, 1 H), 6.84 (s, 4 H), 4.05–3.94 (m, 3 H), 3.85 (m, 3/5 1 H), 3.80–3.73 (m, 3 H + 2/5 1 H), 3.63 (t, *J* = 9.1 Hz, 2/5 1 H), 3.47 (t, *J* = 9.1 Hz, 3/5 1 H), 3.41–3.25 (m, 1 H), 3.22–3.08 (m, 1 H), 2.94 (s, 3/5 3 H), 2.92 (s, 2/5 3 H), 2.84–2.72 (m, 3 H), 2.69–2.36 (m, 3 H), 2.17–2.10 (m, 1 H + 3/5 1 H), 2.6–1.84 (m, 4 H + 3/5 1 H), 1.78–1.43 (m, 1 H), 1.70 (br s, 3/5 1 H), 1.67 (br s, 2/5 1 H), 1.44 (s, 2/5 9 H), 1.42 (s, 3/5 9 H), 0.38 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 218.0 (C), 217.6 (C), 154.5 (C), 154.1 (C), 153.9 (2 C), 153.0 (2 C), 148.3 (C), 148.1 (C), 133.6 (CH), 133.4 (CH), 132.2 (C), 131.6 (CH), 130.7 (CH), 130.6 (CH), 124.2 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 84.5 (CH), 84.4 (CH), 80.3 (C), 79.9 (C), 68.5 (2 × CH_2), 60.9 (CH), 60.8 (CH), 60.5 (CH), 59.2 (CH), 58.2 (CH), 58.1 (CH), 57.4 (CH), 57.0 (CH), 55.8 (CH_3), 54.0 (C), 53.0 (C). 47.8 (2 × CH_2), 39.3 (CH), 39.2 (CH), 38.9 (CH), 38.7 (CH), 35.0 (2 × CH_3), 34.0 (2 × CH_2), 32.9 (CH_2), 31.8 (CH_2), 30.4 (CH_2), 29.6 (CH_2), 28.5 (2 × CH_3), 27.8 (CH_2), 27.7 (CH_2), 24.6 (CH_2), 24.4 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{35}H_{45}N_3O_{10}SNa$: 722.2723; found: 722.2701.

tert-Butyl (2*S*,2a*R*,2a^1*S*,4*S*,4a*S*,6*S*,7a*S*,8*R*)-8-Hydroxy-2a^1-[3-(4-methoxyphenoxy)propyl]-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (45)

To a solution of **43** (30.0 mg, 0.0429 mmol) in THF (3.0 mL) was added DBU (30.0 µL, 0.201 mmol) at 0 °C and the solution was stirred for 15 min at r.t. To this solution were added CH_2Cl_2 and aq NH_4Cl at 0 °C and then the resulting solution was extracted with CH_2Cl_2 (3 ×). The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by PTLC (SiO_2; *n*-hexane–EtOAc, 1:3) to afford **44** (8.1 mg, 27%) as a pale yellow gum and **45** (20.2 mg, 67%) as a white amorphous solid; $[\alpha]_D^{27}$ +27.6 (*c* = 1.25, $CHCl_3$).

IR (film): 3479, 2938, 1730, 1682, 1544, 1508, 1456, 1369, 1231, 1167, 1127, 1102, 1036, 826, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.92 (m, 1 H), 7.71–7.62 (m, 2 H), 7.60–7.52 (m, 1 H), 6.83 (s, 4 H), 4.18 (d, *J* = 10.5 Hz, 1 H), 4.10–3.92 (m, 2 H), 3.90–3.60 (m, 4.6 H), 3.51 (t, *J* = 8.7 Hz, 0.7 H), 3.45–3.25 (m, 1.7 H), 3.25–3.10 (m, 1.4 H), 3.00–2.85 (m, 3 H), 2.80 (dd, *J* = 10.5, 8.3 Hz, 1 H), 2.70 (dd, *J* = 8.2, 5.5, 1.6 Hz, 1.6 H), 2.60–2.50 (m, 1.7 H), 2.44–2.30 (m, 0.7 H), 2.25–2.15 (m, 1 H), 2.00–1.70 (m, 4.5 H), 1.55–1.50 (m, 3 H), 1.50–1.35 (m, 10 H), 1.15–1.10 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 220.4 (C), 154.7 (C), 153.9 (C), 153.0 (C), 148.2 (C), 133.5 (CH), 133.4 (CH), 132.1 (C), 131.6 (CH), 130.7 (CH), 130.6 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 80.3 (C), 79.9 (C), 77.3 (CH), 77.2 (CH), 68.4 (CH_2), 59.0 (CH), 57.8 (CH), 56.3 (CH), 55.7 (CH_3), 55.0 (C), 50.3 (CH), 50.2 (CH), 47.8 (CH_2), 40.7 (CH), 40.6 (CH), 35.2 (CH), 35.1 (CH), 33.8 (CH_2), 32.9 (CH_2), 31.8 (CH_2), 29.7 (CH_2), 28.5 (CH_3), 25.9 (CH_2), 25.8 (CH_2), 25.4 (CH_2), 24.5 (CH_2), 24.4 (CH_2), 24.3 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{35}H_{45}N_3O_{10}SNa$: 722.2723; found: 722.2742.

tert-Butyl (2*S*,2a*R*,2a^1*S*,4*S*,4a*S*,6*S*,7a*S*,8*S*)-8-(Benzoyloxy)-2a^1-[3-(4-methoxyphenoxy)propyl]-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (58)

To a solution of **44** (460 mg, 0.657 mmol) in pyridine (8.0 mL) was added benzoyl chloride (152 µL, 1.31 mmol) at 0 °C and the solution was stirred for 1 h at r.t. To this solution was added CH_2Cl_2 and aq $NaHCO_3$ at 0 °C and then the resulting solution was extracted with CH_2Cl_2 (3 ×). The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc = 4:1 → 1:2) to afford **58** (486 mg, 92%) as a white amorphous solid; $[\alpha]_D^{26}$ +88.1 (*c* = 1.50, $CHCl_3$).

IR (film): 3471, 2952, 1736, 1716, 1687, 1545, 1508, 1453, 1369, 1273, 1231, 1168, 1110, 1069, 1026, 953, 826, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (3:2 mixture of rotamers) = 8.10–7.92 (m, 3 H), 7.70–7.52 (m, 4 H), 7.50–7.27 (m, 2 H), 6.92–6.80 (m, 4 H), 5.10–5.00 (m, 1 H), 4.20–3.70 (m, 3 H), 3.75 (s, 3 H), 3.67 (t, *J* = 9.2 Hz, 2/5 1 H), 3.50 (t, *J* = 9.2 Hz, 3/5 1 H), 3.45–3.25 (m, 1 H), 3.22–2.84 (m, 3 H), 2.94 (s, 3/5 3 H), 2.92 (s, 2/5 3 H), 2.78–2.55 (m, 1 + 3/5 2 H), 2.55–2.40 (m, 1 + 2/5 1 H), 2.15–1.35 (m, 7 + 2/5 1 H), 1.45 (s, 3.8 H), 1.43 (s, 5.2 H), 0.60 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 216.5 (C), 216.2 (C), 165.5 (2 C), 154.3 (C), 154.0 (C), 153.8 (2 C), 153.0 (2 C), 148.3 (2 C), 133.5 (CH), 133.4 (CH), 133.1 (2 × CH), 132.1 (2 C), 131.6 (2 × CH), 130.6 (CH), 130.5 (CH), 130.1 (2 C), 130.0 (2 × CH), 128.4 (2 × CH), 124.1 (CH), 124.0 (CH), 115.5 (2 × CH), 114.7 (2 × CH), 85.8 (2 × CH), 80.3 (C), 80.0 (C), 68.4 (2 × CH_2), 60.4 (CH), 59.2 (CH), 57.9 (CH), 57.8 (CH), 57.6 (2 × CH), 57.3 (CH), 57.1 (CH), 55.7 (2 × CH_3), 54.2 (C), 53.1 (C), 47.9 (2 × CH_2), 39.4 (CH), 39.3 (CH), 36.7 (CH), 36.5 (CH), 35.2 (CH_3), 35.1 (CH_3), 33.9 (2 × CH_2), 33.1 (CH_2), 32.1 (CH_2), 30.3 (CH_2), 29.4 (CH_2), 28.4 (2 × CH_3), 28.3 (CH_2), 28.0 (CH_2), 24.5 (CH_2), 24.3 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{42}H_{49}N_3O_{11}SNa$: 826.2986; found: 826.2996.

tert-Butyl (2*S*,2a*R*,2a^1*S*,4*S*,4a*S*,6*S*,7a*S*,8*S*)-8-(Benzoyloxy)-2a^1-(3-hydroxypropyl)-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (46)

To a solution of **58** (760 mg, 0.946 mmol) in MeCN (20.0 mL) and H_2O (5.0 mL) was added cerium(IV) ammonium nitrate (570 mg, 1.04 mmol) at 0 °C and the solution was stirred for 2.5 h at the same temperature. To this solution was added CH_2Cl_2 and aq $NaHCO_3$ at 0 °C and then the resulting solution was extracted with CH_2Cl_2 (3 ×). The organic phase was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:1 → 1:3) to afford **46** (590 mg, 89%) as a white amorphous solid; $[\alpha]_D^{27}$ +67.7 (*c* = 1.00, $CHCl_3$).

IR (film): 3503, 2944, 1735, 1716, 1683, 1543, 1454, 1369, 1274, 1166, 1112, 1068, 985, 852, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (2:1 mixture of rotamers) = 8.00–7.91 (m, 3 H), 7.74–7.52 (m, 4 H), 7.47–7.40 (m, 2 H), 5.08–5.02 (m, 1 H), 3.92 (d, *J* = 9.2 Hz, 2/3 1 H), 3.84–3.75 (m, 1 H + 1/3 1 H), 3.73–3.60 (m, 1 H + 1/3 1 H), 3.50–3.30 (m, 1 H + 2/3 1 H), 3.15–2.84 (m, 3 H),

2.95 (s, 2/3 3 H), 2.94 (s, 1/3 3 H), 2.75–2.62 (m, 2 H + 2/3 1 H), 2.55–2.38 (m, 1 H + 1/3 1 H), 1.98–1.55 (m, 7 H), 1.46 (s, 1/3 9 H), 1.43 (s, 2/3 9 H), 0.66–0.53 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 216.7 (C), 216.4 (C), 165.5 (2 C), 154.2 (C), 153.9 (C), 148.2 (2 C), 133.7 (CH), 133.6 (CH), 133.1 (2 × CH), 131.9 (C), 131.8 (C), 131.7 (2 × CH), 130.6 (CH), 130.4 (CH), 130.1 (C), 129.5 (2 × CH), 128.4 (2 × CH), 124.1 (CH), 124.1 (CH), 85.8 (CH), 85.7 (CH), 80.2 (C), 80.0 (C), 62.6 (2 × CH_2), 59.4 (CH), 58.4 (CH), 58.2 (CH), 58.0 (CH), 57.5 (CH), 57.5 (CH), 57.3 (CH), 57.0 (CH), 54.4 (C), 53.3 (C), 48.0 (2 × CH_2), 39.2 (CH), 39.0 (CH), 36.7 (CH), 36.5 (CH), 35.5 (CH_3), 35.3 (CH_3), 33.1 (CH_2), 33.0 (CH_2), 32.9 (CH_2), 31.9 (CH_2), 30.5 (CH_2), 29.6 (CH_2), 28.4 (2 × CH_3), 28.1 (CH_2), 27.8 (CH_2), 27.5 (CH_2), 27.3 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{35}H_{43}N_3O_{10}SNa$: 720.2567; found: 720.2587.

tert-Butyl (2*S*,2a*R*,2a^1*S*,4*S*,4a*S*,6*S*,7a*S*,8*S*)-8-(Benzoyloxy)-2-[2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl]-3-oxo-2a^1-(3-oxopropyl)decahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (47)

To a solution of **46** (550 mg, 0.788 mmol) in CH_2Cl_2 (600 mL) was added $NaHCO_3$ (1.10 g, 13.1 mmol), Dess–Martin periodinane (401 mg, 0.946 mmol) at 0 °C. After stirring for 1 h at r.t., H_2O was added at the same temperature. The resulting solution was extracted with CH_2Cl_2 (3 ×). The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; *n*-hexane–EtOAc, 1:2) to give **47** (540 mg, 98%) as a colorless oil; $[\alpha]_D^{27}$ +76.7 (*c* = 1.75, $CHCl_3$).

IR (film): 3854, 2968, 1718, 1685, 1544, 1453, 1369, 1273, 1167, 1111, 1069, 985, 852, 759 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (2:1 mixture of rotamers) = 9.90 (s, 2/3 1 H), 9.88 (s, 1/3 1 H), 8.00–7.88 (m, 3 H), 7.75–7.65 (m, 2 H), 7.65–7.52 (m, 2 H), 7.47–7.40 (m, 2 H), 5.04 (s, 1 H), 3.91 (d, *J* = 10.0 Hz, 2/3 1 H), 3.81 (d, *J* = 10.0 Hz, 1/3 1 H), 3.67 (dd, *J* = 8.6, 8.6 Hz, 1/3 1 H), 3.50 (dd, *J* = 9.2, 9.2 Hz, 2/3 1 H), 3.46–3.30 (m, 1 H), 3.15–3.00 (m, 2 H), 2.95 (s, 2/3 3 H), 2.94 (s, 1/3 3 H), 2.90–2.58 (m, 5 H + 2/3 1 H), 2.55–2.41 (m, 1 H + 1/3 1 H), 2.22–2.17 (m, 1 H), 2.02–1.92 (m, 2 H), 1.75–1.49 (m, 3 H), 1.45 (s, 1/3 9 H), 1.43 (s, 2/3 9 H), 0.65–0.50 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 216.1 (C), 215.7 (C), 201.2 (CH), 200.9 (CH), 165.5 (2 C), 154.2 (C), 153.9 (C), 148.3 (C), 148.2 (C), 133.7 (CH), 133.6 (CH), 133.2 (2 × CH), 132.0 (2 C), 131.7 (2 × CH), 130.6 (CH), 130.4 (CH), 130.0 (2 C), 129.6 (2 × CH), 128.4 (2 × CH), 124.2 (CH), 124.1 (CH), 85.7 (CH), 85.6 (CH), 80.5 (C), 80.2 (C), 60.3 (CH), 58.6 (CH), 58.3 (CH), 57.9 (CH), 57.7 (CH), 57.5 (CH), 57.3 (CH), 57.1 (CH), 53.7 (C), 52.7 (C), 47.9 (2 × CH_2), 39.4 (CH), 39.2 (CH), 39.0 (CH_2), 38.8 (CH_2), 36.7 (CH), 36.5 (CH), 35.6 (CH_3), 35.4 (CH_3), 33.3 (CH_2), 32.3 (CH_2), 30.1 (CH_2), 29.3 (CH_2), 28.7 (CH_2), 28.5 (2 × CH_3), 28.3 (CH_2), 28.2 (CH_2), 27.8 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{35}H_{41}N_3O_{10}SNa$: 718.2410; found: 718.2388.

(2*S*,2a*S*,2a^1*S*,4*S*,5a*S*,6*S*,7*S*,10a*S*,10b*R*,13*S*)-8-Methyl-1-oxododecahydro-1*H*-2a^1,7-ethano-2,4-methanocyclopenta[*cd*]pyrimido[1,6-*a*]indol-13-yl Benzoate (49)

To a solution of **47** (67.0 mg, 0.144 mmol) in CH_2Cl_2 (3.0 mL) was added TFA (2.0 mL) at –78 °C. After stirring for 15 min at r.t., CH_2Cl_2 and aq $NaHCO_3$ were added at 0 °C. The resulting solution was extracted with CH_2Cl_2 (2 ×). The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo*. The residual oil containing **48** was dissolved in MeCN (40.0 mL) and treated with K_3PO_4 (200 mg, 0.941 mmol) and thiophenol (230 µL, 2.26 mmol) at room temperature. After stirring for 2 h at r.t., AcOH (320 µL) was added and then the reaction mixture was heated at 50 °C for 18 h. After cooling to r.t., the solution was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2; $CHCl_3$–MeOH, 5:1) to give **49** (49.0 mg, 89% for 2 steps) as a white solid; mp 212.2–213.0 °C; $[\alpha]_D^{27}$ +156 (*c* = 1.75, $CHCl_3$).

IR (film): 3421, 2943, 1722, 1451, 1274, 1177, 1110, 1068, 984, 855 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (dd, *J* = 7.6, 1.4 Hz, 2 H), 7.55 (dd, *J* = 7.6, 7.6 Hz, 1 H), 7.42 (dd, *J* = 7.6, 7.6 Hz, 2 H), 5.02 (s, 1 H), 3.70 (t, *J* = 8.2 Hz, 1 H), 3.51–3.43 (m, 1 H), 3.00–2.90 (m, 2 H), 2.71–2.57 (m, 2 H), 2.56–2.46 (m, 2 H), 2.45 (s, 3 H), 2.41 (d, *J* = 6.4 Hz, 1 H), 2.38–2.30 (m, 1 H), 2.22 (ddd, *J* = 15.6, 9.9, 9.9 Hz, 1 H), 2.10–1.93 (m, 2 H), 1.80–1.70 (m, 3 H), 0.99 (dd, *J* = 15.6, 10.1 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 219.9 (C), 165.5 (C), 133.0 (CH), 130.2 (C), 129.6 (CH), 128.4 (CH), 86.4 (CH), 76.5 (CH), 65.1 (CH), 63.2 (CH), 61.2 (CH), 60.8 (CH), 54.4 (C), 42.7 (CH_3), 42.6 (CH_2), 42.0 (CH), 38.5 (CH), 35.8 (CH_2), 28.1 (CH_2), 26.6 (CH_2), 24.5 (CH_2), 23.4 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{24}H_{29}N_2O_3$ 393.2178; found: 393.2180.

Lycopalhine A (2)

To a solution of **49** (20.0 mg, 0.0509 mmol) in MeOH (1.0 mL) was added K_2CO_3 (20 mg 0.145 mmol) at 0 °C. After stirring for 3 h at r.t., the solution was concentrated *in vacuo* and the residue was purified by PTLC (NH_2 silica gel; $CHCl_3$–MeOH, 10:1) to give lycopalhine A (**2**) and *epi*-lycopalhine A (**50**) (13.0 mg, 89%) as a colorless gum; $[\alpha]_D^{25}$ +105 (*c* = 0.200, MeOH) {Lit.[6] $[\alpha]_D^{15}$ +89.1 (*c* = 0.17, MeOH)}.

IR (film): 3411, 2940, 1714, 1659, 1454, 1367, 1300, 1177, 1048, 1026, 854 cm^{-1}.

^{1}H NMR (400 MHz, pyridine-d_5): δ = 4.46 (dd, *J* = 11.0, 5.5 Hz, 0.2 H, minor isomer), 4.29 (s, 1 H), 3.95–3.89 (m, 0.2 H, minor isomer), 3.81 (dd, *J* = 10.1, 7.4 Hz, 0.2 H, minor isomer), 3.65 (dd, *J* = 10.1, 6.4 Hz, 1 H), 3.59–3.54 (m, 1 H), 3.05 (d, *J* = 8.2 Hz, 1 H), 2.98 (ddd, *J* = 12.8, 9.2, 3.2 Hz, 1 H), 2.84 (ddd, *J* = 10.6, 7.8, 2.5 Hz, 0.2 H, minor isomer), 2.63–2.55 (m, 0.2 H, minor isomer), 2.57 (dd, *J* = 9.9, 9.9 Hz, 1 H), 2.47–2.22 (m, 6 H), 2.45 (s, 3 H), 2.16 (ddd, *J* = 11.5, 4.6, 4.6 Hz, 1 H), 2.07 (ddd, *J* = 15.6, 9.6, 9.6 Hz, 1 H), 1.87 (ddd, *J* = 11.9, 11.9, 7.4 Hz, 1 H), 1.75–1.60 (m, 4 H), 1.55 (dd, *J* = 12.5, 7.8 Hz, 1 H), 1.35–1.25 (m, 0.2 H, minor isomer), 0.93 (dd, *J* = 15.1, 10.3 Hz, 1 H).

^{13}C NMR (100 MHz, pyridine-d_5): δ (major isomer) = 221.6 (C), 85.6 (CH), 77.0 (CH), 65.6 (CH), 65.3 (CH), 63.4 (CH), 61.1 (CH), 54.3 (C), 43.0 (CH_2), 42.8 (CH_3), 42.3 (CH), 41.4 (CH), 36.0 (CH_2), 27.9 (CH_2), 27.3 (CH_2), 25.4 (CH_2), 24.2 (CH_2); δ (minor isomer) = 219.1 (C), 76.3 (CH), 75.5 (CH), 64.3 (CH), 62.1 (CH), 58.7 (CH), 58.2 (CH), 55.6 (C), 43.8 (CH), 42.1 (CH_3), 41.0 (CH_2), 37.6 (CH), 36.7 (CH_2), 27.0 (CH_2), 23.5 (CH_2), 23.0 (CH_2), 22.8 (CH_2).

HRMS (ESI+): *m*/*z* calcd for $C_{17}H_{25}N_2O_2$: 289.1916; found: 289.1902.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588878.

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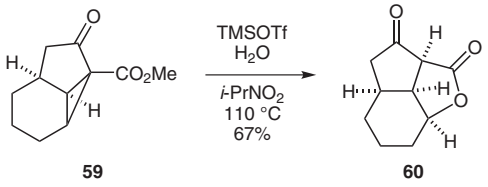

Scheme 7 Formation of tricyclic lactone **60**

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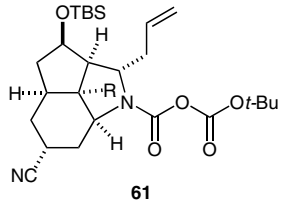

Figure 2 Structure of product **61**

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