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Enantioselective Total Synthesis of Desbromoarborescidines A–C and the Formal Synthesis of (*S*)-Deplancheine

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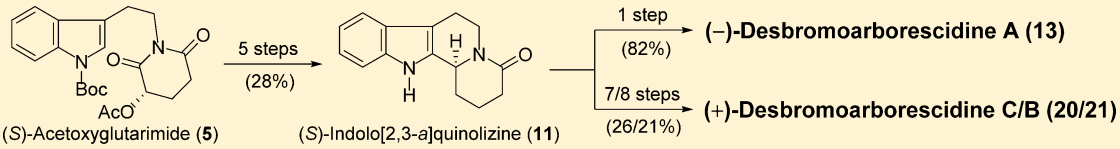
Supporting Information



ABSTRACT: Starting from Boc-protected tryptamine and (*S*)-tetrahydro-5-oxo-2-furancarboxylic acid, facile enantioselective total synthesis of desbromoarborescidines A–C and the formal synthesis of (*S*)-deplancheine have been accomplished via a common intermediate (*S*)-indolo[2,3-*a*]quinolizine. Synthesis of enantiomerically pure (*S*)-acetoxyglutarimide, stereoselective reductive intramolecular cyclization, hydroxyl group-assisted in situ *N*-Boc-deprotection, selective deoxygenation of the xanthate ester, and lactam hydrolysis followed by an appropriate exchange of nitrogen regioselectivity in intramolecular cyclization were the decisive steps.

The indole alkaloids have been imperative targets due to their novel structural architectures, wide range of promising biological activities and the current clinical applications.[1−6] More specifically, the indolo[2,3-*a*]quinolizine template is of great significance due to its presence in several exotic alkaloids such as ajmalicine, corynantheidine, magniflorine, reserpine, vellosimine and vincamine.[7−12] In 1966, Johns and Lamberton isolated the analogous (*S*)-desbromoarborescidine A from the leaves of *Dracontomelum mangiferum*.[13−16] In 1993, Païs and co-workers isolated another four new brominated alkaloids of the tetrahydro-*β*-carboline family, the arborescidines A–D from a marine tunicate *Pseudodistoma arborescens* (Figure 1).[17,18] Arborescidines, desbromoarborescidines and their analogs have been recently tested against human gastric adenocarcinoma (AGS), lung cancer (SK-MES-1), bladder carcinoma (J82) and leukemia (HL-60) cells, and they exhibited antiproliferative activity (IC_{50}, 9 to >100 μM).[19] A few racemic and some well-designed asymmetric synthesis of desbromoarborescidine A have been reported in the literature.[20−31] A straightforward racemic synthesis of arborescidines A–C have been known[32,33] and based on synthesis of proposed arborescidine D, a revision of structural assignment has been recommended.[32] Rawal and co-workers reported the enantioselective total synthesis of antipodes of arborescidines A–C and confirmed the assigned absolute stereochemistry of these natural products.[34] In continuance of our efforts to synthesize structurally interesting and biologically important natural and unnatural products from cyclic anhydrides and derivatives as the potential precursors,[35−38] we herein report the enantioselective convergent access to desbromoarborescidines A–C and (*S*)-deplancheine from (*S*)-acetoxyglutarimide (Schemes 1–3).

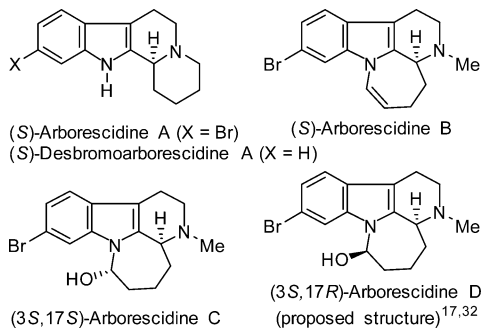


Figure 1. Bioactive arborescidine alkaloids.[13−18]

A careful scrutiny of desbromoarborescidines A–C structures and their retrosynthetic analysis revealed that they are the analogous indole alkaloids containing skeletonal 15-carbon and 2-nitrogen atoms (Scheme 1). We reasoned that (*S*)-acetoxyglutarimide has similar 15-carbon skeleton along with appropriately placed 2-nitrogens and it would be a suitable precursor for the synthesis of target compounds, namely, (i) the (*S*)-acetoxy function would serve as best detachable handle to embark the stereoselectivity, (ii) regioselective reduction of an imide carbonyl to the lactamol followed by an intramolecular stereoselective cyclization would provide an access to desbromoarborescidine A and (iii) hydrolytic cleavage of *δ*-lactam unit in the advanced intermediate (*S*)-indolo[2,3-*a*]quinolizine followed by an alternate intramolecular cyclization utilizing the indole nitrogen atom would constitute a path to desbromoarborescidines B and C.

The enantiomerically pure starting material (*S*)-tetrahydro-5-oxo-2-furancarboxylic acid (**2**) was prepared from (*S*)-glutamic acid by using known procedure.[39] EDCI induced dehydrative

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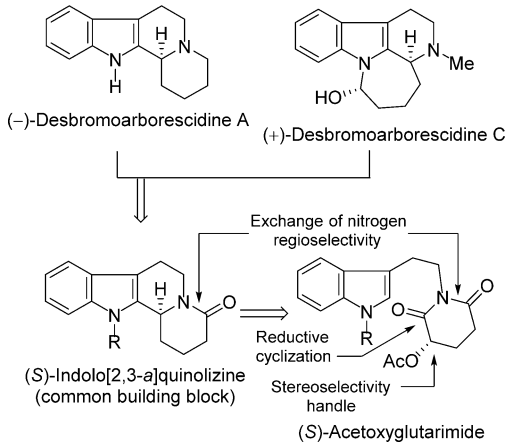
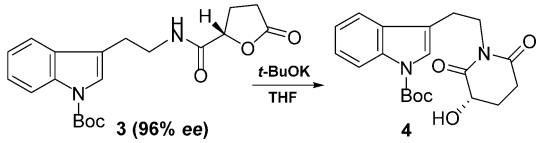
Scheme 1. Retrosynthetic Analysis of Desbromoarborescidines A and C



coupling reaction of Boc-protected tryptamine **1** with enantiomerically pure acid **2** furnished the desired product **3** in 86% yield with 96% *ee* (by HPLC) (Scheme 2). Control experiments on base-catalyzed rearrangement of amidolactone **3** to the desired (*S*)-hydroxyglutarimide **4** revealed that the starting material is very much prone to racemize. Hence, the yield and enantiomeric purity of formed ring expansion product are highly dependent on molar amount of base used, reaction temperature and time.[40,41] The results obtained on the basis of systematic studies on conversion of compound **3** to **4** have been summarized in Table 1. The use of 0.45 equivalents of *t*-BuOK at −78 to −50 °C in 1.50 h time furnished the product **4** in 65% yield with 96% enantiomeric purity (Table 1, entry 5). The (*S*)-hydroxyl group in compound **4** was transformed to the corresponding acetate **5** in 98% yield by using acetic anhydride and triethylamine. The regioselective sodium borohydride reduction of more reactive imide carbonyl group in compound **5** provided product **6** in 84% yield with ∼2:1 diastereomeric ratio (by ^{1}H NMR). Such type of lactamol units is known to display the ring−chain tautomerism[42] and hence to keep the complete control on diastereoselectivity is a difficult task. However, under controlled reaction conditions, the chemoselective trifluoroacetic acid induced intramolecular cyclization of a masked aldehyde in compound **6** at −10 to 0 °C furnished

Table 1. Base Catalyzed Rearrangement of (*S*)-Amidolactone to (*S*)-Hydroxyglutarimide

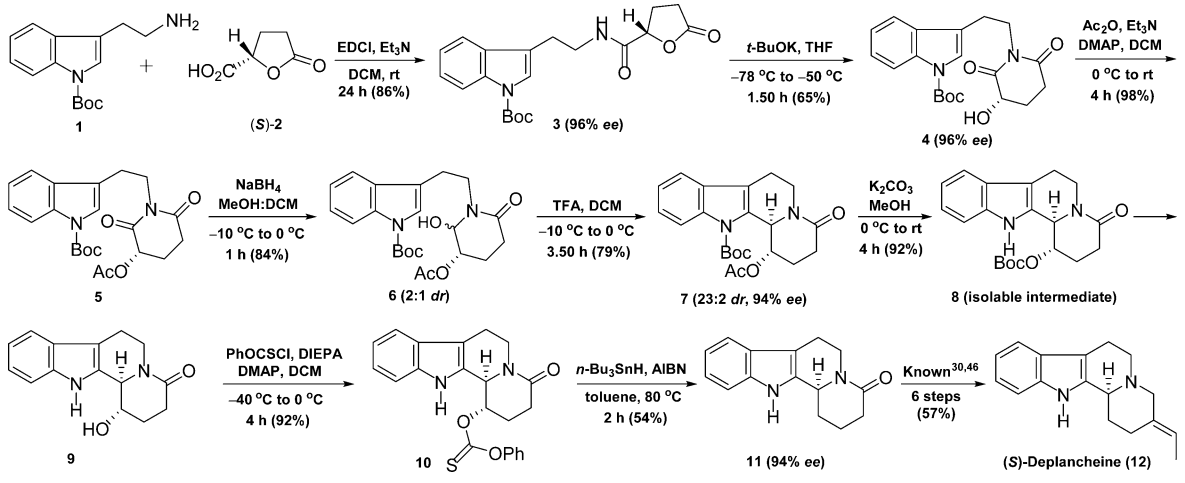


entry	*t*-BuOK (equiv)	temp. °C	time (h)	% yield[a]	% ee[b]
1	0.60	−78 to −40	3.00	82	68
2	0.50	−78 to −40	3.00	72	80
3	0.50	−78 to −40	2.00	68	89
4	0.45	−78 to −50	2.00	66	91
5	0.45	−78 to −50	1.50	65	96
6	0.40	−78 to −50	2.00	56	92

[a]Isolated yields. [b]Determined by chiral HPLC.

the desired cyclized product **7** in very good yield with high stereoselectivity (79%, 23:2 *dr*), via the *N*-acyliminium ion intermediate.[43] The present reaction was chemoselective as the Boc-protection remained intact with the use of two equivalents of TFA at lower temperature. In the transformation of **6** to **7**, the distinct enhancement in diastereoselectivity is attributed to the formation of flat iminium ion intermediate followed by the stereoselective intramolecular nucleophilic attack from the less hindered *β*-side. However, the repetition of the above experiment at −78 to 0 °C did not show any further refinement in diastereoselectivity and/or yield. The mixture of diastereoisomers **7** was quantitatively separated by using flash column chromatography and the required major isomer retained 94% enantiopurity (by HPLC). The major isomer **7** on treatment with K_2CO_3/MeOH underwent both one-pot deacylation and *N*-Boc-deprotection[44] in four hours to exclusively provide the product **9** in 92% yield. In the conversion of **7** to **9**, tlc-monitoring of the reaction progress indicated that one of the intermediate formed has a sufficient life span and its isolation would be feasible. Hence, the above-mentioned reaction was arrested after one hour time and immediate silica gel column chromatography of the reaction mass was performed. We could successfully isolate the intermediate **8** in almost 26% yield along with some amounts of both starting material and final product. Thus, mechanistically the deacylation followed by an in situ

Scheme 2. Stereoselective Synthesis of Pivotal Intermediate (*S*)-Indolo[2,3-*a*]quinolizine: Formal Synthesis of (*S*)-Deplancheine



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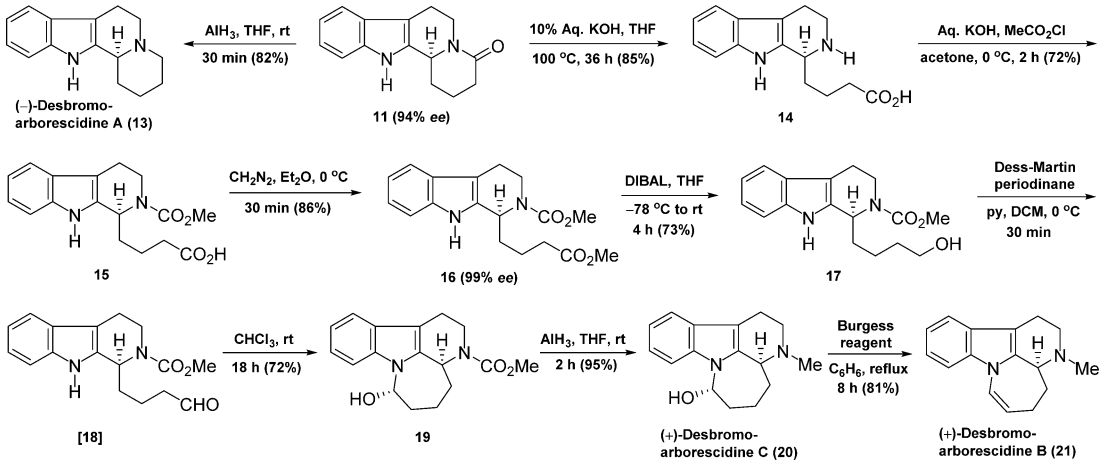
Scheme 3. Synthesis of Enantiomerically Pure Desbromoarborescidines A–C from (*S*)-Indolo[2,3-*a*]quinolizine



intramolecular *N*-Boc-group migration to the proximal hydroxyl oxygen function takes place to form the intermediate **8**, which on methanolysis provides product **9**. The observed intramolecular 1,5-Boc migration is attributed to the geometrical features and the unusual carbamate to carbonate transformation is significant from a basic chemistry point of view. Finally, the absolute and relative stereochemistry of product (−)-**9** was confirmed by using single crystal X-ray crystallographic data. We feel that our present protocol will mirror to provide (+)-**9** from the corresponding (*R*)-glutamic acid. At this stage, the detachment of stereoselectivity handle, the (*S*)-hydroxyl group in compound **9** was decided to obtain the product (*S*)-**11**. In our hands, the preparation of mesylate derivative of compound **9** followed by its displacement by iodide resulted mostly in elimination product owing to the higher acidity of an adjacent methine proton. Alternatively, the chemoselective reaction of compound **9** with excess of phenyl chlorothionoformate in the presence of diisopropylethylamine exclusively provided the xanthate ester **10** in 92% yield. The xanthate ester **10** was not very stable and hence it was quickly filtered through the silica gel column and immediately used for the next step. The xanthate ester **10** on Barton–McCombie deoxygenation[45] using tributyltin hydride in the presence of AIBN gave the desired common chiral building block **11** in 54% yield (94% *ee*, by HPLC). The analytical and spectral data obtained for compound **11** were in complete agreement with the reported data.[30] Thus, the desired common intermediate **11** was obtained in 8-steps with 15% overall yield. A seven-step synthetic protocol to transform the compound **11** to (*S*)-deplancheine (**12**, antipode) in very good overall yield is known.[30,46,47]

In the next part of studies, syntheses of desbromoarborescidines A–C were planned from an advanced intermediate **11** (Scheme 3). Aluminum hydride reduction of δ-lactam carbonyl in compound **11** provided the natural product (*S*)-desbromoarborescidine A (**13**) in 82% yield. The exchange of nitrogen regioselectivity in intermediate **11** was then envisioned for synthesis of desbromoarborescidines B and C. The hydrolytic cleavage of δ-lactam unit in compound **11** was specifically intended under basic conditions to avoid racemization issues.[48] Compound **11** on hydrolysis with aqueous KOH followed by an acidification provided product **14** in 85% yield. At this stage, a selective carbomethoxy protection of piperidine nitrogen in compound **14** was undertaken, as initially it would serve as a protecting group and later on the source of essential methyl group. The regioselective reaction of more reactive piperidine nitrogen with methyl chloroformate in the presence of KOH gave the corresponding carbamate derivative **15** in 72% yield. Compound **15** on treatment with diazomethane formed the required ester **16** in 86% yield (99% ee, by HPLC).[49] DIBAL reduction of ester **16** furnished the corresponding alcohol **17** in 73% yield. The Dess–Martin periodinane oxidation of alcohol **17** formed aldehyde **18**. However, all our attempts to isolate aldehyde **18** in pure form were met with failure and it was always contaminated with the further cyclized product **19** (by ^{1}H NMR). The above mixture of products on stirring in chloroform at room temperature for 18 h underwent the smooth stereoselective intramolecular cyclization to exclusively yield the desired trans-aminol (+)-**19** in 72% yield. The catalytic amount of hydrochloric acid present in the chloroform was responsible for the above-mentioned intramolecular cyclization. On the basis of NMR data, all four products **15**–**19** were designated as the rotameric mixtures and are in accordance with literature precedent.[33] The conversion of (+)-aminol **19** to (+)-desbromoarborescidines C and B has been known in the literature.[19] Similarly, alane reduction of carbomethoxy group in compound (+)-**19** to the methyl group furnished the desired (3*S*,17*S*)-desbromoarborescidine C (**20**) in 95% yield. (3*S*,17*S*)-Desbromoarborescidine C (**20**) on treatment with Burgess reagent provided the corresponding dehydration product (*S*)-desbromoarborescidine B (**21**) in 81% yield. The analytical and spectral data obtained for desbromoarborescidines A–C were in complete agreement with reported data.[17,18,32,33] Starting from Boc-protected tryptamine **1**,[50] the desbromoarborescidines A/C/B (**13**/**20**/**21**) were respectively obtained in 9/15/16 steps with 13/4/3% overall yields.

In summary, we have demonstrated enantioselective convergent approach to deplancheine and desbromoarborescidines A–C from the corresponding (*S*)-acetoxyglutarimide. All three different oxygen functions present in (*S*)-acetoxyglutarimide were rationally utilized in a remarkable chemo-, regio- and stereoselective fashion to design these four desired tantamount targets in very good overall yields and high enantiomeric purities, using an appropriate protecting groups. The present practical approach to these products is general in nature and would be useful to synthesize their potential

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analogues and congeners for SAR studies. The witnessed in situ intramolecular Boc-group migration-deprotection is notable from mechanistic point of view. The chiral intermediate (1*S*,12*R*)-1-hydroxy-1,2,3,6,7,12*b*-hexahydroindolo[2,3-*a*]-quinolizin-4(12*H*)-one (**9**) is noteworthy and it will serve as an important synthon to design several other bioactive indole alkaloids.

EXPERIMENTAL SECTION

General Description. Melting points are uncorrected. Mass spectra were taken on MS-TOF mass spectrometer. HRMS (ESI) were taken on Orbitrap (quadrupole plus ion trap) and TOF mass analyzer. The IR spectra were recorded on an FT-IR spectrometer. Commercially available starting materials and reagents were used.

*tert-Butyl (S)-3-(2-(5-Oxotetrahydrofuran-2-carboxamido)ethyl)-1H-indole-1-carboxylate (**3**).* Solution of compound **1**[50] (5.50 g, 21.13 mmol) in CH_2Cl_2 (40 mL) was added to a stirred suspension of acid **2** (2.75 g, 21.13 mmol) and EDCI (8.10 g, 42.26 mmol) in CH_2Cl_2 (80 mL) at 0 °C. To the reaction mixture was added Et_3N (8.80 mL, 63.40 mmol) and stirred at rt for 24 h. The reaction was quenched with water (25 mL) and extracted with CH_2Cl_2 (100 mL × 3). The extract was washed with brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo and silica gel (60−120) column chromatographic purification of residue using ethyl acetate−petroleum ether (3:2) as an eluent gave product **3** (6.76 g, 86% yield; 96% *ee*). Mp 100−102 °C; $[\alpha]^{25}_D$ −13.6 (*c* 0.10 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.67 (s, 9H), 2.17−2.40 (m, 1H), 2.43−2.68 (m, 3H), 2.94 (t, *J* = 8 Hz, 2H), 3.63 (q, *J* = 8 Hz, 2H), 4.81 (t, *J* = 8 Hz, 1H), 6.59 (br t, *J* = 4 Hz, 1H), 7.24 (dt, *J* = 8 and 2 Hz, 1H), 7.33 (dt, *J* = 8 and 2 Hz, 1H), 7.41 (s, 1H), 7.53 (dd, *J* = 6 and 2 Hz, 1H), 8.13 (d, *J* = 8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.9, 25.6, 27.4, 28.1, 38.9, 77.3, 83.6, 115.3, 117.1, 118.7, 122.5, 123.1, 124.5, 130.2, 135.5, 149.5, 169.4, 175.6; ESIMS (*m*/*z*) 395 [M + Na]$^+$; HRMS (ESI) calcd for $C_{20}H_{24}N_2O_5Na$ 395.1577, found 395.1571; IR ($CHCl_3$) ν_{max} 3431, 3020, 1789, 1727, 1677 cm^{-1}.

*tert-Butyl (S)-3-(2-(3-Hydroxy-2,6-dioxopiperidin-1-yl)ethyl)-1H-indole-1-carboxylate (**4**).* Suspension of *t*-BuOK in THF (0.45 M, 5.35 mL) was added to a stirred solution of lactone **3** (2.00 g, 5.36 mmol) in THF (30 mL) at −78 °C over 10 min under argon atmosphere. The reaction mixture was stirred at −50 °C for 30 min. The reaction was quenched with saturated aq. NH_4Cl (5 mL) and concentrated in vacuo. To the residue was added ethyl acetate (150 mL) and the organic layer was washed with water, brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo and silica gel (230−400 mesh) column chromatographic purification of the residue using petroleum ether−ethyl acetate (1:1) as an eluent yielded (*S*)-hydroxyglutarimide **4** (1.30 g, 65% yield; 96% *ee*). Mp 136−138 °C; $[\alpha]^{25}_D$ −47.9 (*c* 0.108 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.67 (s, 9H), 1.89 (dq, *J* = 12 and 6 Hz, 1H), 2.28−2.43 (m, 1H), 2.55−2.75 (m, 1H), 2.83−3.00 (m, 1H), 2.93 (t, *J* = 6 Hz, 2H), 3.58 (br s, 1H), 3.93−4.28 (m, 3H), 7.28 (dt, *J* = 8 and 2 Hz, 1H), 7.34 (dt, *J* = 8 and 2 Hz, 1H), 7.45 (s, 1H), 7.70 (dd, *J* = 8 and 2 Hz, 1H), 8.13 (d, *J* = 8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 23.4, 25.2, 28.1, 30.7, 40.2, 68.2, 83.5, 115.2, 116.9, 119.0, 122.5, 123.3, 124.4, 130.3, 135.4, 149.6, 171.1, 175.1; ESIMS (*m*/*z*) 395 [M + Na]$^+$; HRMS (ESI) calcd for $C_{20}H_{24}N_2O_5Na$ 395.1577, found 395.1571; IR ($CHCl_3$) ν_{max} 3517, 1730, 1679 cm^{-1}.

*tert-Butyl (S)-3-(2-(3-Acetoxy-2,6-dioxopiperidin-1-yl)ethyl)-1H-indole-1-carboxylate (**5**).* To a stirred solution of hydroxyimide **4** (4.20 g, 11.28 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added Et_3N (1.88 mL, 13.54 mmol), Ac_2O (1.60 mL, 16.92 mmol) and DMAP (20 mg). The reaction mixture was stirred at rt for 4 h and quenched with water (10 mL). It was extracted with CH_2Cl_2 (50 mL × 3) and the combined organic layer was washed with saturated aq. $NaHCO_3$, brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo and silica gel (60−120 mesh) column chromatographic purification of the residue using petroleum ether−ethyl acetate (6:4) as an eluent afforded acetoxyimide **5** (4.60 g, 98%). Mp 104−106 °C; $[\alpha]^{25}_D$ −30.5 (*c* 0.106 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.64 (s, 9H), 1.97−2.25 (m, 2H), 2.20 (s, 3H), 2.58−2.78 (m, 1H), 2.78−2.98 (m, 3H), 3.89−4.13 (m, 2H), 5.45 (dd, *J* = 10 and 6 Hz, 1H), 7.18 (dt, *J* = 8 and 2 Hz, 1H), 7.24 (dt, *J* = 8 and 2 Hz, 1H), 7.36 (s, 1H), 7.63 (dd, *J* = 6 and 2 Hz, 1H), 8.04 (d, *J* = 8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.7, 23.1, 23.4, 28.1, 30.4, 40.3, 68.6, 83.4, 115.1, 117.0, 119.1, 122.5, 123.4, 124.4, 130.3, 135.4, 149.6, 169.1, 169.8, 170.6; ESIMS (*m*/*z*) 437 [M + Na]$^+$; HRMS (ESI) calcd for $C_{22}H_{26}N_2O_6Na$ 437.1683, found 437.1675; IR ($CHCl_3$) ν_{max} 1734, 1686 cm^{-1}.

*tert-Butyl 3-(2-((3S)-3-Acetoxy-2-hydroxy-6-oxopiperidin-1-yl)-ethyl)-1H-indole-1-carboxylate (**6**).* To a stirred solution of (*S*)-acetoxyglutarimide **5** (2.00 g, 4.83 mmol) in MeOH/CH_2Cl_2 (2:1, 30 mL) was added $NaBH_4$ (550 mg, 14.5 mmol) at −10 °C over 5 min. The reaction mixture was stirred at 0 °C for 1 h and quenched with saturated aq. $NaHCO_3$ (5 mL). It was extracted with CH_2Cl_2 (75 mL × 3) and the combined organic layer was washed with water, brine and dried over Na_2SO_4. Concentration of organic layer in vacuo and silica gel (60−120 mesh) column chromatographic purification of residue using ethyl acetate−petroleum ether (8:2) as an eluent afforded lactamol **6** (2:1 *dr*) as a thick oil (1.69 g, 84%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.66 (s, 9H), 2.01 (s, 1H), 2.08 (s, 2H), 2.10−2.35 (m, 2H), 2.40−2.64 (m, 2H), 2.93−3.08 (m, 2H), 3.50−3.63 (m, 1H), 3.75−3.94 (m, 1H), 4.83−5.00 (m, 2H), 7.20−7.27 (m, 1H), 7.27−7.35 (m, 1H), 7.41 (s, 1H), 7.58−7.65 (m, 1H), 8.10 (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.4, 20.5, 20.9, 21.0, 23.7, 23.8, 27.4, 28.2, 29.3, 29.7, 45.9, 46.4, 69.5, 70.0, 79.8, 81.4, 83.5, 115.3, 117.8, 119.0, 119.1, 122.49, 122.53, 123.07, 123.11, 124.4, 130.3, 135.4, 149.7, 169.4, 169.9, 170.4; ESIMS (*m*/*z*) 439 [M + Na]$^+$; HRMS (ESI) calcd for $C_{22}H_{28}N_2O_6Na$ 439.1840, found 439.1836; IR ($CHCl_3$) ν_{max} 3384, 1734, 1635 cm^{-1}.

*tert-Butyl (1S,12bR)-1-Acetoxy-4-oxo-1,3,4,6,7,12b-hexahydroindolo[2,3-a]quinolizine-12(2H)-carboxylate (**7**).* To a stirred solution of lactamol **6** (3.50 g, 8.40 mmol) in CH_2Cl_2 (50 mL) at −10 °C was added TFA (1.36 mL, 16.8 mmol) and it was stirred at −10 to 0 °C for 3.50 h. The reaction was quenched with saturated aq. $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (75 mL × 3). The combined organic layer was washed with brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo and silica gel (230−400 mesh) column chromatographic purification of the residue using ethyl acetate−petroleum ether (7:3) as an eluent afforded the minor diastereomer (200 mg, 6%) and the required major diastereomer **7** (2.44 g, 73% yield; 94% *ee*). Major isomer **7**: Mp 63−65 °C; $[\alpha]^{25}_D$ −136.1 (*c* 0.10 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.68 (s, 9H), 1.70−1.85 (m, 1H), 1.95−2.10 (m, 1H), 2.15 (s, 3H), 2.33−2.50 (m, 1H), 2.50−3.00 (m, 4H), 4.98−5.17 (m, 1H), 5.30−5.38 (m, 1H), 5.41−5.50 (m, 1H), 7.21−7.40 (m, 2H), 7.46 (dd, *J* = 8 and 2 Hz, 1H), 8.00 (dd, *J* = 8 and 2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.0, 21.4, 23.4, 27.3, 27.9, 40.6, 59.9, 70.6, 84.6, 115.2, 118.2, 120.7, 122.9, 124.8, 128.5, 131.8, 136.7, 150.2, 169.5, 169.6; ESIMS (*m*/*z*) 421 [M + Na]$^+$; HRMS (ESI) calcd for $C_{22}H_{26}N_2O_5Na$ 421.1739, found 421.1724; IR (Nujol) ν_{max} 1733, 1652 cm^{-1}.

*(1S,12bR)-1-Hydroxy-2,3,6,7,12,12b-hexahydroindolo[2,3-a]-quinolizin-4(1H)-one (**9**).* Anhydrous K_2CO_3 (666 mg, 4.82 mmol) was added to a stirred solution of acetate **7** (2.40 g, 6.02 mmol) in MeOH (30 mL) at 0 °C. The reaction mixture was stirred for 4 h at rt and concentrated in vacuo. The obtained residue on silica gel (230−400 mesh) column chromatographic purification using ethyl acetate−methanol (98:2) as an eluent afforded product **9** (1.42 g, 92%). Mp 247−249 °C; $[\alpha]^{25}_D$ −169.4 (*c* 0.10 MeOH); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 1.80−1.87 (m, 2H), 2.25−2.34 (m, 1H), 2.43 (td, *J* = 20 and 5 Hz, 1H), 2.57−2.70 (m, 2H), 2.79 (dt, *J* = 15 and 5 Hz, 1H), 3.90 (quintet, *J* = 5 Hz, 1H), 4.57 (d, *J* = 10 Hz, 1H), 4.80 (dd, *J* = 15 and 5 Hz, 1H), 5.90 (d, *J* = 5 Hz, 1H), 6.96 (t, *J* = 10 Hz, 1H), 7.04 (t, *J* = 10 Hz, 1H), 7.38 (d, *J* = 10 Hz, 1H), 7.42 (d, *J* = 10 Hz, 1H), 10.38 (s, 1H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 21.0, 28.2, 29.7, 40.6, 60.0, 68.6, 108.0, 112.2, 118.1, 119.1, 121.5, 126.4, 133.8, 136.4, 168.7; ESIMS (*m*/*z*) 279 [M + Na]$^+$; HRMS (ESI) calcd for $C_{15}H_{17}N_2O_2$ 257.1285, found 257.1281; IR (Nujol) ν_{max} 3292, 1715, 1612 cm^{-1}.

*tert-Butyl ((1S,12bR)-4-Oxo-1,2,3,4,6,7,12,12b-octahydroindolo-[2,3-a]quinolizin-1-yl) carbonate (**8**).* The above reaction was

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performed on a 100 mg scale and arrested after 1 h. Similar work up and column chromatographic purification afforded intermediate **8** (23 mg, 26%). Mp 74−76 °C; $[\alpha]^{25}_{D}$ −42.8 (*c* 0.50 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.57 (s, 9H), 2.00−2.10 (m, 1H), 2.15−2.24 (m, 1H), 2.50−2.58 (m, 1H), 2.67−2.94 (m, 4H), 4.87 (d, *J* = 5 Hz, 1H), 4.98−5.04 (m, 1H), 5.09−5.18 (m, 1H), 7.14 (t, *J* = 10 Hz, 1H), 7.22 (t, *J* = 10 Hz, 1H), 7.37 (d, *J* = 10 Hz, 1H), 7.52 (d, *J* = 10 Hz, 1H), 8.58 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.9, 24.8, 27.8, 28.8, 40.8, 58.1, 74.6, 83.9, 110.9, 111.1, 118.4, 119.8, 122.5, 126.5, 130.5, 136.1, 152.8, 168.8; ESIMS (*m*/*z*) 357 $[M + H]^+$; HRMS (ESI) calcd for $C_{20}H_{25}N_2O_4$ 357.1809, found 357.1806; IR ($CHCl_3$) ν_{max} 3473, 1746, 1635 cm^{-1}.

*(1S,12bR)-4-Oxo-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]-quinolizin-1-yl phenyl carbonate (**10**).* Anhydrous DIPEA (1.02 mL, 5.85 mmol) was added to a stirred solution of alcohol **9** (500 mg, 1.95 mmol) and DMAP (71.5 mg, 0.59 mmol) in CH_2Cl_2 (30 mL) at −40 °C under argon atmosphere and stirred for 10 min. To the reaction mixture was added *o*-phenyl chlorothionoformate (0.81 mL, 5.85 mmol) and stirred at −15 to 0 °C for 4 h. Concentration of reaction mixture in vacuo and silica gel (60−120 mesh) column chromatographic purification of residue using petroleum ether−ethyl acetate (6:4) as an eluent afforded xanthate **10** (704 mg, 92%). Mp 82−84 °C; $[\alpha]^{25}_{D}$ −48.1 (*c* 0.104 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.20−2.40 (m, 2H), 2.58−2.68 (m, 1H), 2.73−2.88 (m, 2H), 2.88−3.05 (m, 2H), 5.10−5.30 (m, 2H), 5.78 (s, 1H), 7.13−7.60 (m, 9H), 8.55 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.0, 23.7, 28.3, 41.3, 58.0, 80.2, 111.2, 111.6, 118.5, 120.0, 121.7, 122.7, 126.6, 127.0, 129.7, 129.8, 136.2, 153.0, 168.4, 193.9; ESIMS (*m*/*z*) 415 $[M + Na]^+$; HRMS (ESI) calcd for $C_{22}H_{20}N_2O_3SNa$ 415.1087, found 415.1082; IR ($CHCl_3$) ν_{max} 3361, 1714, 1652 cm^{-1}.

*(S)-2,3,6,7,12,12b-Hexahydroindolo[2,3-a]quinolizin-4(1H)-one (**11**).* To a stirred solution of ester **10** (500 mg, 1.27 mmol) and AIBN (21 mg, 0.13 mmol) in dry toluene (20 mL) was added *n*-Bu_3SnH (0.55 mL, 2.05 mmol) at rt for 15 min under argon atmosphere. The reaction mixture was heated at 80 °C for 2 h and toluene was distilled off in vacuo. The obtained residue was dissolved in acetonitrile (40 mL) and washed with hexane (15 mL × 3). Concentration of the acetonitrile layer in vacuo and silica gel (230−400 mesh) column chromatographic purification of the residue using ethyl acetate as an eluent afforded product **11** (165 mg, 54% yield; 94% *ee*). Mp 194−196 °C; $[\alpha]^{25}_{D}$ −220.2 (*c* 0.10 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.70−2.00 (m, 3H), 2.35−2.55 (m, 2H), 2.55−2.65 (m, 1H), 2.72−2.95 (m, 3H), 4.80 (dd, *J* = 10 and 5 Hz, 1H), 5.13−5.24 (m, 1H), 7.13 (t, *J* = 10 Hz, 1H), 7.19 (t, *J* = 10 Hz, 1H), 7.35 (d, *J* = 10 Hz, 1H), 7.52 (d, *J* = 10 Hz, 1H), 8.30 (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.4, 21.0, 29.0, 32.4, 40.2, 54.4, 109.5, 110.9, 118.4, 119.8, 122.1, 126.8, 133.3, 136.2, 169.3; ESIMS (*m*/*z*) 241 $[M + H]^+$; HRMS (ESI) calcd for $C_{15}H_{17}N_2O$ 241.1335, found 241.1332; IR ($CHCl_3$) ν_{max} 3283, 1733, 1623 cm^{-1}.

*(S)-1,2,3,4,6,7,12,12b-Octahydroindolo[2,3-a]quinolizine (Desbromoarborescidine A, **13**).* To a stirred slurry of $AlCl_3$ (22 mg, 0.16 mmol) in THF (4 mL) was added suspension of $LiAlH_4$ (21 mg, 0.55 mmol) in THF (2 mL) at 0 °C under argon atmosphere. After stirring for 10 min, a solution of lactam **11** (44 mg, 0.18 mmol) in THF (2 mL) was added to the reaction mixture. It was stirred for 30 min at rt and quenched with saturated aq. NH_4Cl (2 mL). The reaction mixture was filtered through Celite and the residue was washed with ethyl aceatate (10 mL × 3). The filtrate was dried over Na_2SO_4 and concentrated in vacuo. Silica gel (230−400 mesh) column chromatographic purification of the residue using chloroform−methanol (9:1) as an eluent afforded desbromoarborescidine A (**13**) (34 mg, 82%). Mp 148−150 °C; $[\alpha]^{25}_{D}$ −80.5 (*c* 0.10 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.42−1.57 (m, 1H), 1.60 (dq, *J* = 12 and 4 Hz, 1H), 1.70−1.85 (m, 2H), 1.91 (d, *J* = 12 Hz, 1H), 2.06 (dd, *J* = 12 and 4 Hz, 1H), 2.41 (dt, *J* = 12 and 4 Hz, 1H), 2.60−2.78 (m, 2H), 2.98−3.09 (m, 2H), 3.10 (t, *J* = 4 Hz, 1H), 3.24 (d, *J* = 8 Hz, 1H), 7.11 (t, *J* = 8 Hz, 1H), 7.15 (t, *J* = 8 Hz, 1H), 7.30 (d, *J* = 8 Hz, 1H), 7.50 (d, *J* = 8 Hz, 1H), 7.80 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 24.3, 25.7, 29.9, 53.5, 55.7, 60.2, 108.0, 110.7, 118.1, 119.3, 121.2, 127.4, 135.1, 135.9; ESIMS (*m*/*z*) 227 $[M + H]^+$; IR ($CHCl_3$) ν_{max} 3476, 1599 cm^{-1}.

*(S)-4-(2,3,4,9-Tetrahydro-1H-pyrido[3,4-b]indol-1-yl)butanoic Acid (**14**).* Aqueous KOH (10%, 20 mL) was added to a stirred solution of lactam **11** (300 mg, 1.25 mmol) in THF (4 mL) at rt. The reaction mixture was heated at 100 °C for 36 h. It was neutralized by addition of 2 N HCl at 0 °C. The product precipitated in between pH 8 to 7 was filtered and dried to obtain acid **14** (274 mg, 85%). Mp 198−200 °C; ^{1}H NMR (D_2O, 200 MHz) δ 1.69 (t, *J* = 6 Hz, 1H), 1.76 (t, *J* = 8 Hz, 1H), 1.91 (q, *J* = 8 Hz, 1H), 2.00−2.25 (m, 1H), 2.44 (t, *J* = 8 Hz, 2H), 2.90−3.04 (m, 2H), 3.20−3.38 (m, 1H), 3.65 (td, *J* = 12 and 6 Hz, 1H), 4.45−4.57 (m, 1H), 7.13 (dt, *J* = 8 and 2 Hz, 1H), 7.24 (dt, *J* = 8 and 2 Hz, 1H), 7.43 (d, *J* = 8 Hz, 1H), 7.54 (d, *J* = 8 Hz, 1H); ^{13}C NMR (D_2O, 50 MHz) δ 20.3, 22.3, 33.2, 35.7, 44.0, 55.5, 108.6, 114.1, 120.9, 122.3, 125.2, 128.1, 131.4, 138.8, 180.5; HRMS (ESI) calcd for $C_{15}H_{19}N_2O_2$ 259.1441, found 259.1439; IR (Nujol) ν_{max} 3350, 1791, 1623 cm^{-1}. NMR data of **14** was collected as monohydrochloride for solubility reasons.

*(S)-4-(2-(Methoxycarbonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]-indol-1-yl)butanoic Acid (**15**).* Solution of KOH (117 mg, 2.09 mmol) in water (2 mL) was added at 0 °C to a stirred suspension of amine **14** (270 mg, 1.05 mmol) in acetone:water (1:1, 8 mL). Reaction mixture was stirred for 10 min and methyl chloroformate (0.09 mL, 1.15 mmol) was added. It was stirred for 2 h at 0 °C and neutralized with 2 N HCl. Acetone was removed in vacuo and residue was extracted with ethyl acetate (20 mL × 3). Combined organic layer was washed with brine and dried over Na_2SO_4. Concentration of organic layer in vacuo and silica gel (60−120 mesh) column chromatographic purification of residue using petroleum ether−ethyl acetate (1:9) as an eluent provided carbamate **15** (238 mg, 72%). Mp 56−58 °C; $[\alpha]^{25}_{D}$ +77.0 (*c* 0.48 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.80 (br s, 3H), 1.90 (br s, 1H), 2.41 (br s, 2H), 2.64 (s, 0.35H), 2.68 (s, 0.65H), 2.79 (br s, 1H), 3.16 (br d, *J* = 12 Hz, 1H), 3.71 (s, 1.05H), 3.75 (s, 1.95H), 4.30 (d, *J* = 12 Hz, 0.65H), 4.48 (d, *J* = 8 Hz, 0.35H), 5.16 (s, 0.35H), 5.34 (s, 0.65H), 6.95−7.15 (m, 2H), 7.25 (d, *J* = 8 Hz, 1H), 7.43 (d, *J* = 8 Hz, 1H), 8.32 (s, 0.35H), 8.57 (s, 0.65H), 8.50−9.50 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.0, 21.1, 21.4, 33.4, 33.7, 34.0, 38.3, 38.5, 51.1, 52.9, 53.0, 107.8, 108.5, 111.0, 117.9, 118.1, 119.3, 121.7, 126.6, 133.6, 134.0, 136.0, 156.4, 156.9, 178.4; ESIMS (*m*/*z*) 339 $[M + Na]^+$; HRMS (ESI) calcd for $C_{17}H_{21}N_2O_4$ 317.1496, found 317.1494; IR ($CHCl_3$) ν_{max} 3333, 2700−2500, 1700, 1685 cm^{-1}.

*Methyl (S)-1-(4-Methoxy-4-oxobutyl)-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate (**16**).* Diazomethane in ether was added at 0 °C to a stirred solution of acid **15** (230 mg, 0.73 mmol) in ether and THF (1:1, 6 mL) until persistence of a yellow color. Reaction mixture was stirred at 0 °C for 30 min and concentrated in vacuo. Silica gel (60−120 mesh) column chromatographic purification of the residue using petroleum ether−ethyl acetate (6:4) as an eluent afforded ester **16** as a gum (206 mg, 86% yield; 99% ee). $[\alpha]^{25}_{D}$ +91.0 (*c* 0.14 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.85 (quintet, *J* = 6 Hz, 4H), 2.43 (t, *J* = 8 Hz, 2H), 2.60−3.00 (m, 2H), 3.05−3.30 (m, 1H), 3.69 (s, 3H), 3.75 (s, 3H), 4.25−4.60 (br m, 1H), 5.19 (br s, 0.35H), 5.33 (br s, 0.65H), 7.09 (t, *J* = 8 Hz, 1H), 7.16 (t, *J* = 8 Hz, 1H), 7.32 (d, *J* = 8 Hz, 1H), 7.47 (d, *J* = 8 Hz, 1H), 8.08 (br s, 0.35H), 8.18 (br s, 0.65H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.0, 21.3, 33.5, 33.9, 34.2, 38.3, 38.5, 51.0, 51.6, 52.8, 107.9, 108.6, 110.9, 117.9, 119.3, 121.6, 126.7, 133.7, 134.1, 136.0, 156.3, 156.6, 174.1; ESIMS (*m*/*z*) 353 $[M + Na]^+$; HRMS (ESI) calcd for $C_{18}H_{23}N_2O_4$ 331.1652, found 331.1648; IR ($CHCl_3$) ν_{max} 3331, 1735, 1685, 1623 cm^{-1}.

*Methyl (S)-1-(4-Hydroxybutyl)-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate (**17**).* DIBAL solution (1 M in cyclohexane, 0.60 mL) was added at −78 °C to a stirred solution of ester **16** (200 mg, 0.60 mmol) in THF (8 mL) under argon atmosphere. The reaction mixture was stirred for 4 h to reach rt. It was quenched with saturated aq. potassium sodium tartrate (4 mL), stirred for 1 h and concentrated in vacuo. The obtained residue was extracted with CH_2Cl_2 (25 mL × 3) and the combined organic layer was washed with brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo and silica gel (230−400 mesh) column chromatographic

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purification of residue using ethyl acetate−petroleum ether (8:2) as an eluent afforded alcohol **17** (134 mg, 73%). Mp 56−58 °C; $[\alpha]^{25}_{D}$ +89.9 (*c* 0.50 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.40−1.75 (m, 4H), 1.75−2.07 (m, 2H), 2.60−3.00 (m, 2H), 3.05−3.35 (m, 1.30H), 3.35−3.55 (m, 0.70H), 3.55−3.75 (m, 2H), 3.83 (s, 3H), 4.38 (dd, *J* = 10 and 2 Hz, 0.70H), 4.54 (d, *J* = 10 Hz, 0.30H), 5.21 (br s, 0.30H), 5.40 (br s, 0.70H), 7.05−7.24 (m, 2H), 7.32 (dd, *J* = 8 and 2 Hz, 1H), 7.51 (dd, *J* = 8 and 2 Hz, 1H), 8.81 (br s, 0.30H), 9.26 (br s, 0.70H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.0, 21.4, 22.3, 22.5, 32.1, 34.1, 34.4, 38.3, 38.4, 51.4, 51.7, 52.6, 52.9, 62.2, 107.3, 108.0, 110.9, 117.8, 118.0, 119.0, 119.1, 121.3, 121.5, 126.5, 134.0, 134.5, 136.0, 156.4, 156.8; ESIMS (*m*/*z*) 325 $[M + Na]^+$; IR ($CHCl_3$) ν_{max} 3405, 3468, 1684, 1623 cm^{-1}.

*Methyl (3aS,7S)-7-Hydroxy-1,3a,4,5,6,7-hexahydro-3,7a-diazacyclohepta[jk]fluorene-3(2H)-carboxylate (**19**).* To a stirred solution of alcohol **17** (130 mg, 0.43 mmol) in CH_2Cl_2 (6 mL) at 0 °C was added Dess−Martin periodinane (274 mg, 0.65 mmol) and pyridine (0.05 mL, 0.65 mmol). It was stirred for 30 min and quenched with a mixture of aq. sodium thiosulphate (40%, 2 mL) plus saturated aq. $NaHCO_3$ (2 mL). It was extracted with CH_2Cl_2 (20 mL × 3) and the combined organic layer was washed with brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo and silica gel (60−120 mesh) column chromatographic purification of the residue using ethyl acetate−petroleum ether (1:1) as an eluent resulted in the mixture of aldehyde **18** and further cyclized product **19** as a thick oil (by ^{1}H NMR). The mixture of products was stirred in chloroform (8 mL) at rt for 18 h. Concentration of the chloroform solution in vacuo and silica gel (60−120 mesh) column chromatographic purification of the residue using petroleum ether−ethyl acetate (6:4) as an eluent afforded product **19** as a gum (93 mg, 72%). $[\alpha]^{25}_{D}$ +110.4 (*c* 0.25 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.62 (t, *J* = 12 Hz, 1H), 1.80 (d, *J* = 8 Hz, 2H), 2.00−2.14 (m, 1H), 2.25−2.50 (m, 2H), 2.60−2.82 (m, 2H), 3.04 (t, *J* = 12 Hz, 1.50H), 3.28 (br s, 0.50H), 3.72 (s, 1.50H), 3.74 (s, 1.50H), 4.31 (d, *J* = 12 Hz, 0.50H), 4.49 (d, *J* = 12 Hz, 0.50H), 5.31 (d, *J* = 12 Hz, 0.50H), 5.41 (d, *J* = 12 Hz, 0.50H), 6.23 (d, *J* = 4 Hz, 1H), 7.11 (t, *J* = 8 Hz, 1H), 7.19 (t, *J* = 8 Hz, 1H), 7.32 (d, *J* = 8 Hz, 1H), 7.45 (d, *J* = 8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.5, 21.3, 21.6, 33.3, 33.9, 38.8, 39.1, 52.4, 52.7, 52.8, 76.1, 108.4, 108.9, 109.6, 118.2, 118.3, 119.47, 119.53, 121.55, 121.64, 126.3, 135.7, 136.5, 155.7, 156.0; ESIMS (*m*/*z*) 323 $[M + Na]^+$; IR ($CHCl_3$) ν_{max} 3384, 1683, 1615 cm^{-1}.

*(3aS,7S)-3-Methyl-1,2,3,3a,4,5,6,7-octahydro-3,7a-diazacyclohepta[jk]fluoren-7-ol (Desbromoarborescidine C, **20**).* To a stirred solution of carbamate **19** (90 mg, 0.30 mmol) in THF (3 mL) at rt was added a solution of AlH_3 (1.55 M, 0.40 mL, 0.60 mmol) and the reaction mixture was stirred for 2 h under an argon atmosphere. It was quenched with aq. saturated Na_2SO_4 (2 mL) and filtered. The residue was washed with CH_2Cl_2 (30 mL) and the filtrate was dried over Na_2SO_4. Concentration of the filtrate in vacuo and silica gel (230−400 mesh) column chromatographic purification of the residue using chloroform−methanol (9:1) as an eluent afforded desbromoarborescidine C (**20**) (73 mg, 95%). Mp 140−142 °C; $[\alpha]^{25}_{D}$ +3.2 (*c* 0.25 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.51 (dq, *J* = 12 and 4 Hz, 1H), 1.66 (qt, *J* = 12 and 4 Hz, 1H), 1.80−1.90 (m, 1H), 2.20 (tq, *J* = 12 and 4 Hz, 1H), 2.30−2.41 (m, 2H), 2.56 (s, 3H), 2.73−2.88 (m, 1H), 2.81 (d, *J* = 4 Hz, 2H), 3.11 (quintet, *J* = 8 Hz, 1H), 3.80 (d, *J* = 8 Hz, 1H), 6.24 (dd, *J* = 8 and 4 Hz, 1H), 7.11 (dt, *J* = 8 and 4 Hz, 1H), 7.19 (dt, *J* = 8 and 4 Hz, 1H), 7.31 (d, *J* = 8 Hz, 1H), 7.48 (d, *J* = 8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.8, 20.1, 32.0, 34.2, 42.2, 50.4, 61.4, 76.4, 108.4, 108.6, 118.3, 119.4, 121.4, 126.5, 136.1, 136.7; ESIMS (*m*/*z*) 257 $[M + H]^+$; IR (Nujol) ν_{max} 3365, 1612 cm^{-1}.

*(S)-3-Methyl-1,2,3,3a,4,5-hexahydro-3,7a-diazacyclohepta[jk]-fluorene (Desbromoarborescidine B, **21**).* Burgess reagent (95 mg, 0.40 mmol) was added at rt to a stirred solution of aminol **20** (50 mg, 0.20 mmol) in benzene (10 mL) under an argon atmosphere. The reaction mixture was refluxed for 8 h and diluted with ethyl acetate (25 mL). The organic layer was washed three times with brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo and silica gel (230−400 mesh) column chromatographic purification of the residue using CH_2Cl_2−methanol (95:5) as an eluent afforded desbromoarborescidine B (**21**) (38 mg, 81%). Mp 98−100 °C; $[\alpha]^{25}_{D}$ +62.1 (*c* 0.36 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.91 (dq, *J* = 12 and 4 Hz, 1H), 2.34−2.50 (m, 2H), 2.50−2.63 (m, 1H), 2.57 (s, 3H), 2.70−2.80 (m, 2H), 2.90−3.02 (m, 1H), 3.18 (dd, *J* = 12 and 4 Hz, 1H), 3.45 (d, *J* = 12 Hz, 1H), 5.07 (td, *J* = 8 and 4 Hz, 1H), 6.95 (d, *J* = 12 Hz, 1H), 7.15 (t, *J* = 8 Hz, 1H), 7.22 (t, *J* = 8 Hz, 1H), 7.35 (d, *J* = 8 Hz, 1H), 7.49 (d, *J* = 8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.6, 28.0, 29.9, 42.4, 52.8, 62.5, 109.1, 109.2, 110.0, 118.2, 120.2, 121.8, 122.0, 126.9, 136.1, 137.1; ESIMS (*m*/*z*) 239 $[M + H]^+$; IR (Nujol) ν_{max} 1674 cm^{-1}.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR, ^{13}C NMR and DEPT spectra of compounds **3**−**11**, **13**−**17** and **19**−**21**. HPLC data for the enantiomeric purity of the compounds **3**, **4**, **7**, **11** and **16**. X-ray crystallographic data (CIF), and the ORTEP diagram for compound **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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