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N-Cbz sulfilimines as valuable intramolecular nucleophiles for the stereoselective synthesis of (−)-deoxocassine and (+)-desoxoprosophylline

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ABSTRACT

N-Cbz sulfilimine, prepared from the corresponding sulfoxide using the Burgess reagent, has been employed as an intramolecular nucleophile for the regio- and stereoselective preparation of a bromo-carbamate from an alkene. The bromo-carbamate has been utilized as an advanced common synthon for the synthesis of deoxocassine and desoxoprosophylline employing the ene and amidomercuration as key reactions.

1. Introduction

Piperidine alkaloids possessing a 2,3- or 2,3,6-substitution, particularly a hydroxy group at 3-position occur widely in nature.[1] The hydroxylated piperidines display a wide range of biological activities since they mimic carbohydrates in enzymatic processes.[2] They have been useful in the understanding of biochemical pathways by virtue of their ability to selectively inhibit enzymes involved in the processing of glycoproteins.[3] Numerous compounds possessing either the 2,6-cis or 2,6-trans substitution pattern have been discovered, in addition to ones with 3α- and 3β-configurations. Typical representatives of this class of compounds include (−)-cassine **1**, (+)-azimic acid **2**, (+)-julifloridine **3**, (−)-prosophylline **4**, and (−)-prosopinine **5**, Figure 1. Members of this class occur among the alkaloids of various species of the plant genera *Cassia* and *Prosopis*.[4]

Not surprisingly, because of their medical potential, interesting structural features and to showcase the potential of new synthetic methodologies, which are more efficient than those currently in existence, the piperidine alkaloids have been popular synthetic targets.

As a part of our investigations into the chemistry of sulfilimines,[5] we wish to describe herein (a) a facile method for the preparation of *N*-Cbz sulfilimines from the corresponding sulfoxide using the Burgess reagent, (b) its function as an intramolecular nucleophile for the regio- and stereoselective preparation of bromo-carbamates from an alkene, and (c) the utilization of the former as a common advanced intermediate in the synthesis of (−)-deoxocassine **6** and (+)-desoxoprosophylline **7**, Scheme 1.[6]

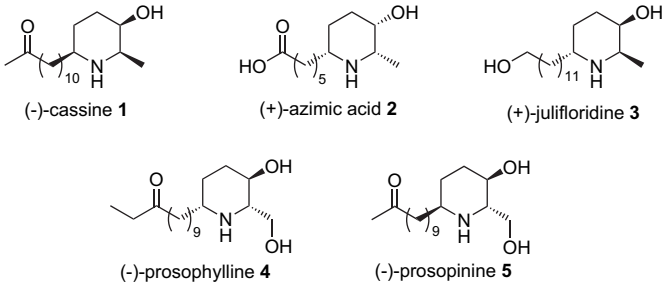

Figure 1.

2. Results and discussion

2.1. Synthesis of (−)-deoxocassine

(−)-Deoxocassine[7] **6**, a simple analog of the natural alkaloid (−)-cassine[8] **1**, was selected as the target for application of our methodology. By a retrosynthetic analysis, **6** was envisioned to be obtained from unsaturated carbamate **7** by a stereoselective

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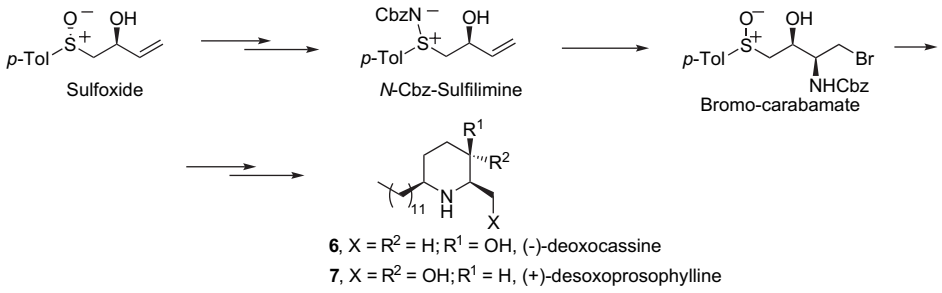
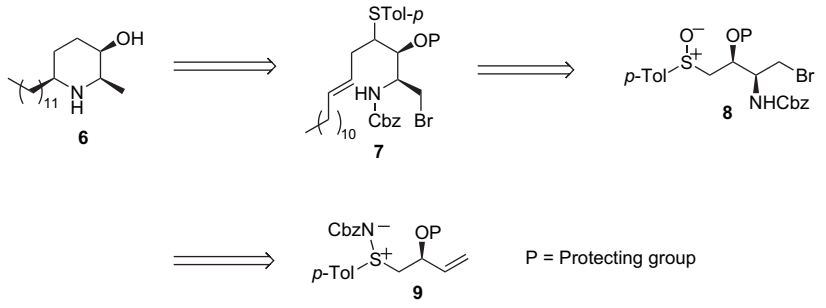


Scheme 1.

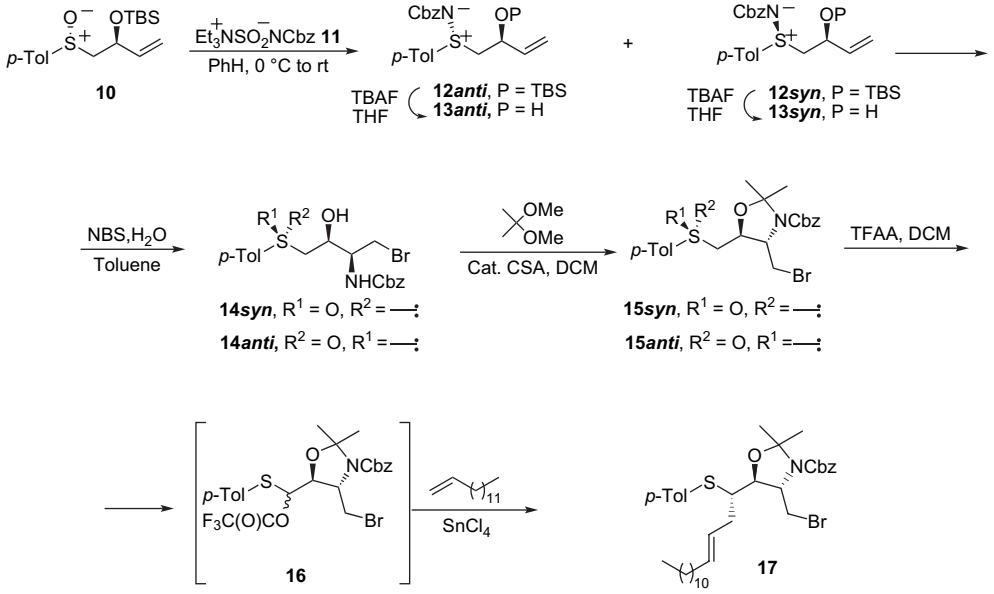


Scheme 2.

amidomercuration. Carbamate **7** can be derived from amino alcohol derivative **8**, which in turn can readily be obtained from sulfilimine **9**, Scheme 2.

The synthesis began with silyl ether[9] **10**, which on treatment with the Burgess reagent[10] **11** in anhydrous benzene furnished an equimolar mixture of readily separable sulfilimines **12**.[11] Deprotection of the silyl group yielded allyl alcohol **13**, which could also be separated as *syn* and *anti* isomers.[12] As we had earlier proven the stereoconvergency (at carbon) in the reactions of ***anti*-13** and ***syn*-13**,[9] we proceeded ahead with the mixture. Reaction of **13** with NBS yielded bromo-carbamate **14** regio- and stereoselectively.[13] Protection of **14** as its *N*,*O*-acetonide using 2,2-dimethoxypropane and cat. amounts of CSA yielded acetonide **15**. Subjecting **15** to an one-pot Pummerer followed by the ene reaction furnished homoallyl sulfide **17** cleanly as a single isomer. The Pummerer intermediate **16** without isolation was reacted with 1-tetradecene in the presence of stoichiometric amounts of $SnCl_4$ at 0 °C for 30 min to yield **17**, Scheme 3.

The configuration at the newly introduced stereogenic center in **17** was not assigned till after amidomercuration, vide infra. The entire carbon framework was introduced and it only remained to cyclize the unsaturated carbamate to form the piperidine ring. Toward this end, debromination of **17** was effected by treatment with *n*-tributyltin hydride in refluxing benzene in the presence of cat. amounts of AIBN to furnish acetonide **18**. Deprotection of the acetonide using cat. CSA in methanol proceeded cleanly to yield alcohol **19**, which was protected as its

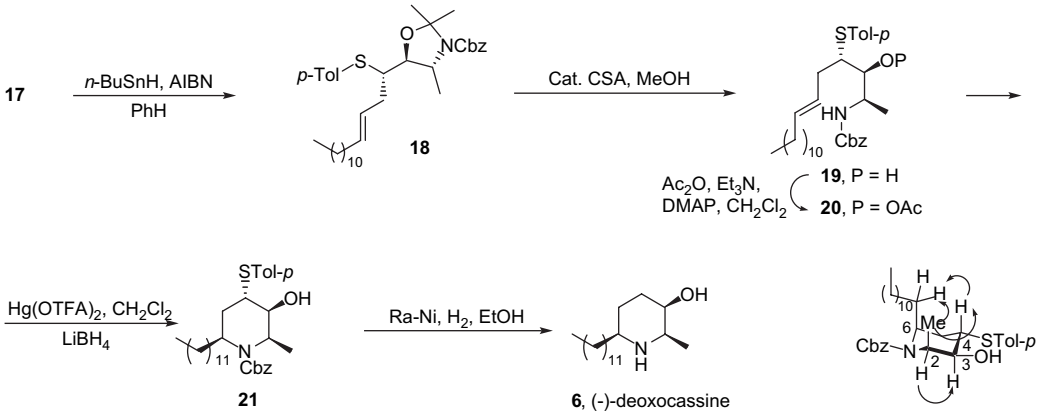


Scheme 3.

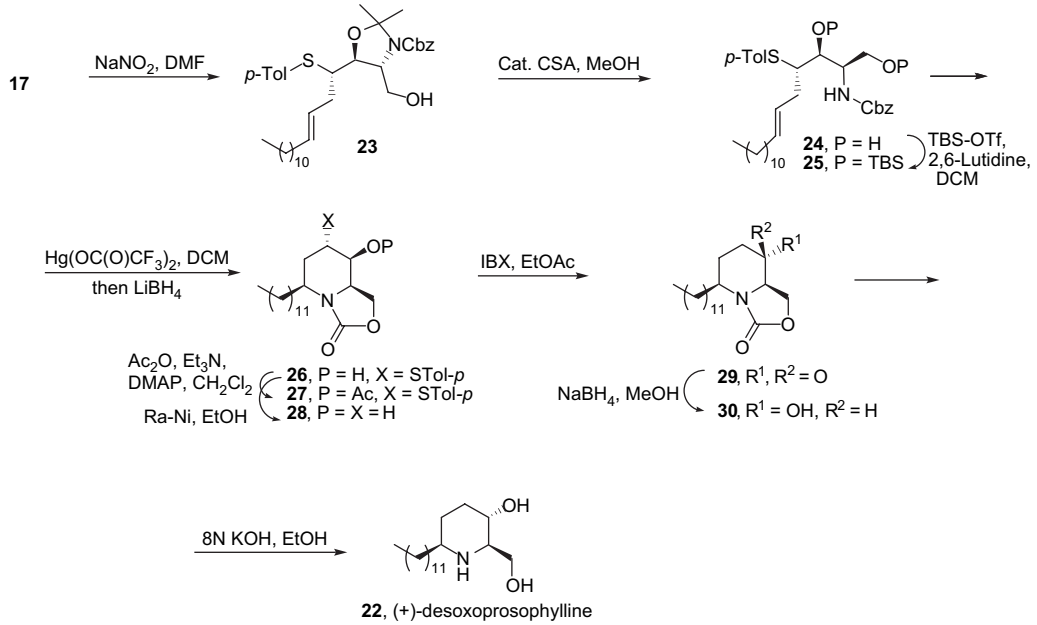
acetate **20** to chemoselectively involve the carbamate in the amidomercuration reaction. Studies into intramolecular amidomercuration of carbamates have revealed that the stereoselectivity of these cyclizations are dependant on the reaction conditions resulting in kinetic or thermodynamic control of the products. The stereoselective cyclization of ε-alkenyl carbamates proceeds under equilibrating conditions.[14] Thus treatment of **20** with mercuric trifluoroacetate in DCM at rt overnight followed by reductive demercuration using $LiBH_4$[15] at low temperature and gradual warming furnished 2,6-cis di-substituted piperidine derivative **21** by concomitant deacetylation. The structure of **21** was proven unambiguously by NOE experiments. NOE were observed between (a) the methyl and alkyl chain indicating their axial disposition, (b) methyl and C4 H, (c) C2 and C3 H, and (d) C4 H and alkyl chain proton, Scheme 4. Thus the structure of **21** also helps to assign the configuration of the newly established stereogenic center in **17** as depicted. The synthesis of deoxocassine was completed by subjecting **21** to hydrogenolysis using Ra-Ni in ethanol, Scheme 4. Synthetic deoxocassine had physical properties in excellent agreement to those reported in the literature.[7f]

2.2. Synthesis of (+)-desoxoprosophylline

The interesting structural features and the varied biological activity of (+)-desoxoprosophylline **22** has attracted the attention of synthetic chemists and several reports detail its synthesis. Many among them rely on chiral pool starting materials[16] and there are only a handful reports on asymmetric syntheses.[17] The synthesis of **22** commenced from homoallyl sulfide **17**, which on treatment with excess sodium nitrite in DMF[18] yielded the alcohol **23**. Deprotection of the acetonide using cat. CSA and protection of the resulting diol **24** as its silyl ether using TBS-OTf in the presence of 2,6-lutidine furnished **25** cleanly. Amidomercuration of **25** using mercuric trifluoroacetate followed by demercuration using $LiBH_4$ furnished the oxazolidinone **26** via concomitant desilylation under the reaction conditions, Scheme 5. The structure of alcohol **26** was confirmed by NOE studies on the acetate derivative **27**. The *p*-tolyl thio group was removed by hydrogenolysis by treatment with Ra-Ni to furnish alcohol **28**. Attempted Mitsunobu reaction on **28** using chloroacetic acid[19] as the acid partner only returned unreacted starting material. We therefore resorted to an oxidation–reduction sequence to prepare the inverted alcohol. In the event, treatment of **28** with IBX in



Scheme 4.



Scheme 5.

refluxing ethyl acetate furnished the corresponding ketone **29**, which was not stable to column chromatography on silica gel. The crude product was reduced with $NaBH_4$[20] to yield alcohol **30** as the sole product. Deprotection of the oxazolidinone was achieved by base promoted hydrolysis[21] to afford (+)-desoxoprosophylline **22** with physical characteristics that were in excellent agreement with those reported in the literature.[16a]

3. Conclusion

In summary, we have described a novel asymmetric synthesis of (−)-deoxocassine and (+)-desoxoprosophylline using a sulfilimine as an intramolecular nucleophile. The sulfilimine was readily obtained from the corresponding sulfoxide using the Burgess reagent as the source of the carbamate moiety. The route disclosed is suitable for the synthesis of several related natural products by (a) varying the nucleophile used for bromide displacement (*C*-heteroatom and C–C bonds can be made), (b) varying the chain length of the alkene employed in the Pummerer ene reaction, and (c) the conditions of amidomercuration, using kinetic rather than thermodynamic conditions to prepare 2,6-trans di-substituted piperidine derivatives.[22]

4. Experimental

4.1. General remarks

All air or moisture sensitive reactions were carried out under nitrogen atmosphere. Solvents were distilled over Na/benzophenone ketyl for THF, over P_2O_5 followed by CaH_2 for DCM, and over P_2O_5 for toluene. Commercially available reagents were used without purification except NBS, which was freshly recrystallized from hot water before use. Thin layer chromatography was performed on precoated silica gel plates. Column chromatography was carried out using silica gel (60–120 mesh). NMR spectra were recorded on a 200, 300 or 400 MHz spectrometer. ^{1}H and ^{13}C NMR samples were internally referenced to TMS (0.00 ppm). Melting points are uncorrected.

4.1.1. Sulfilimine ***12***

To a solution of **10** (6.4 g, 20 mmol) in dry benzene (40 mL) cooled at 0 °C was added a solution of Burgess reagent **11** (12.5 g, 40 mmol) in dry benzene (60 mL) over a period of 30 min and the reaction mixture was stirred for 4 h at rt. The reaction was quenched by the addition of water (20 mL), diluted with EtOAc (100 mL), washed successfully with water (2×70 mL) and brine (100 mL). The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure to give a viscous oil, which was purified by column chromatography using 30% EtOAc/petroleum ether (v/v) to afford sulfilimine **12** (7.4 g, 16.4 mmol) as a 1:1 mixture of *syn* and *anti* isomers in a combined yield of 82%. Data for ***anti*-12**: gummy oil; TLC, R_f (30% EtOAc/hexane) 0.35; $[\alpha]_D^{25}$ +8.5 (*c* 0.35, $CHCl_3$); IR (neat) 3446, 2928, 1637, 1384, 1258, 1084, 777 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.6 (d, *J*=8.3 Hz, 2H), 7.4–7.2 (m, 7H), 5.8–5.7 (m, 1H), 5.3 (d, *J*=17.4 Hz, 1H), 5.2–5.0 (m, 3H), 4.7–4.6 (m, 1H), 3.2 (dd, *J*=12.1, 2.3 Hz, 1H), 2.8 (dd, *J*=12.1, 10.6 Hz, 1H), 2.4 (s, 3H), 0.9 (s, 9H), 0.1 (s, 3H), 0.0 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2, 142.9, 138.1, 137.4, 133.0, 130.5, 128.1, 128.0, 127.5, 126.4, 116.8, 67.9, 67.4, 59.5, 25.7, 21.4, 17.9, −4.5, −5.2; MS (FAB) 458 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{25}H_{36}NO_3SiS$ 458.2185; found 458.2190. Data for ***syn*-12**: gummy oil; TLC, R_f (30% EtOAc/hexane) 0.30; $[\alpha]_D^{25}$ −17.5 (*c* 1.0, $CHCl_3$); IR (neat) 3446, 2928, 1637, 1384, 1258, 1084, 777 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J*=8.2 Hz, 2H), 7.4–7.2 (m, 7H), 6.0–5.8 (m, 1H), 5.3–5.2 (m, 2H), 5.0 (ABq, *J*=12.7 Hz, 2H), 4.3 (m, 1H), 3.5 (dd, *J*=12.7, 6.0 Hz, 1H), 3.0 (dd, *J*=12.7, 6.0 Hz, 1H), 2.4 (s, 3H), 0.9 (s, 9H), 0.0 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 143.1, 137.8, 137.6, 132.2, 130.5, 128.1, 127.9, 127.4, 127.2, 117.5, 69.4, 67.4, 59.4, 25.7, 21.4, 18.0, −4.1, −5.0; MS (FAB) 458 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{25}H_{36}NO_3SiS$ 458.2185; found 458.2210.

4.1.2. Sulfilimine ***13***

To a solution of ***syn*-12** (3.35 g, 7.39 mmol) in anhydrous THF (15 mL) at rt was added tetra *n*-butyl ammonium fluoride (11.3 mL, 1 M in THF, 11.3 mmol) dropwise and stirred for 30 min. The solvent was evaporated under reduced pressure to yield a viscous oil, which was purified by column chromatography using 50% EtOAc/petroleum ether (v/v) to afford sulfilimine ***syn*-13** (2.36 g, 6.9 mmol) in 93% yield as a gummy liquid. TLC, R_f (50% EtOAc/hexane) 0.20; $[\alpha]_D^{25}$ −103 (*c* 2.25, $CHCl_3$); IR (neat) 3445, 2924, 1626, 1384, 1259 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.7 (d, *J*=7.6 Hz, 2H), 7.4–7.2 (m, 7H), 5.9–5.8 (m, 1H), 5.3 (d, *J*=16.6 Hz, 1H), 5.2 (d, *J*=10.6 Hz, 1H), 5.1 (ABq, *J*=12.8 Hz, 2H), 4.4–4.3 (m, 1H), 3.4 (dd, *J*=12.8, 9.1 Hz, 1H), 3.1 (dd, *J*=12.8, 3.8 Hz, 1H), 2.4 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 164.5, 143.5, 137.4, 137.2, 131.5, 130.7, 128.3, 128.0, 127.7, 127.0, 116.9, 68.3, 67.8, 57.1, 21.5; MS (FAB) 344 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{19}H_{21}NO_3NaS$ 366.1139; found 366.1146. Similarly ***anti*-12** (3.45 g, 7.61 mmol) was treated with tetra *n*-butyl ammonium fluoride (11.4 mL, 1 M in THF, 11.4 mmol) to furnish ***anti*-13** (2.44 g, 7.1 mmol) in 93% yield as a gummy liquid. TLC, R_f (50% EtOAc/hexane) 0.25; $[\alpha]_D^{25}$ +23 (*c* 0.35, $CHCl_3$); IR (neat) 3445, 2924, 1626, 1384, 1259 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.7 (d, *J*=8.3 Hz, 2H), 7.5–7.3 (m, 7H), 5.9–5.8 (m, 1H), 5.4 (d, *J*=17.4 Hz, 1H), 5.2 (d, *J*=10.6 Hz, 1H), 4.7–4.6 (m, 1H), 3.1–3.0 (m, 2H), 2.4 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 143.3, 136.8, 130.7, 130.3, 128.3, 128.0, 127.7, 126.8, 116.8, 68.0, 67.0, 58.8, 21.5; MS (FAB) 344 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{19}H_{21}NO_3S$ 344.1314; found 344.1324.

4.1.3. Bromo-carbamate ***14***

To a solution of ***syn*-13** (1.7 g, 5 mmol) in toluene (20 mL) was added water (0.14 mL, 7.5 mmol) followed by freshly recrystallized NBS (0.47 g, 6 mmol) and the mixture stirred at rt for 30 min. The reaction mixture was then diluted with EtOAc (25 mL), washed with saturated aq $NaHCO_3$ (15 mL), water (15 mL), brine (15 mL), and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product, which was purified by column chromatography using 50% EtOAc/petroleum ether (v/v) to afford ***anti*-14** (1.85 g, 4.25 mmol) in 85% yield as a white solid. Mp 102–104 °C; TLC, R_f (50% EtOAc/hexane) 0.30; $[\alpha]_D^{25}$ +11.5 (*c* 0.2, $CHCl_3$); IR (KBr) 3332, 2925, 1698, 1530, 1240, 1030, 641 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.5 (d, *J*=8.3 Hz, 2H), 7.4–7.2 (m, 7H), 5.4 (d, *J*=9.0 Hz, 1H), 5.1 (s, 2H), 4.6 (br s, 1H), 4.5 (d, *J*=9.7 Hz, 1H), 3.7 (q, *J*=8.3 Hz, 1H), 3.5–3.2 (m, 3H), 2.5 (d, *J*=14.6 Hz, 1H), 2.4 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 156.5, 142.3, 141.2, 137.4, 130.3, 128.8, 128.2, 128.0, 124.2, 65.9, 65.6, 62.0, 58.0, 33.6, 21.3; MS (FAB) 440 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{19}H_{22}NO_4NaSBr$ 462.0350; found 462.0368. Likewise ***anti*-13** was reacted with NBS to afford ***syn*-14** as a white solid. Mp 98–100 °C; TLC, R_f (50% EtOAc/hexane) 0.30; IR (KBr) 3332, 2925, 1698, 1530, 1240, 1030, 641 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.5 (d, *J*=7.8 Hz, 2H), 7.4–7.3 (m, 7H), 5.4 (d, *J*=9.4 Hz, 1H), 5.1 (s, 2H), 4.9–4.7 (m, 1H), 4.5 (d, *J*=10.9 Hz, 1H), 3.7 (q, *J*=9.4 Hz, 1H), 3.5–3.3 (m, 2H), 3.2 (dd, *J*=14.1, 10.2 Hz, 1H), 2.5 (dd, *J*=13.3, 1.6 Hz, 1H), 2.4 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4, 142.1, 136.1, 135.3, 130.2, 128.6, 128.3, 128.1, 124. 1, 67.2, 65.4, 57.4, 56.1, 31.5, 21.4; MS (FAB) 440 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{19}H_{23}NO_4SBr$ 440.0525; found 440.0518.

4.1.4. N,O-Acetonide ***15***

To a solution of ***anti*-14** (1.85 g, 4.3 mmol) in toluene (9 mL) were added 2,2-dimethoxypropane (2.2 g, 22 mmol) and catalytic amounts of (+/−)-camphor-10-sulfonic acid (10 mol %). The mixture was stirred for 3 h at 90 °C. Few drops of Et_3N were added and

the solvent was removed under reduced pressure. The crude compound was purified by column chromatography using 20% EtOAc/petroleum ether (v/v) as the eluent to furnish acetonide ***anti*-15** (1.73 g, 3.6 mmol) in 85% yield as rotameric mixture. Gummy liquid; TLC, R_f (30% EtOAc/hexane) 0.25; $[\alpha]_D^{25}$ +64 (*c* 0.5, $CHCl_3$); IR (neat) 3780, 2926, 1701, 1591, 1383, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, *J*=7.6 Hz, 2H), 7.4–7.5 (m, 7H), 5.1 (ABq, *J*=12.1 Hz, 2H), 4.7–4.6 (m, 1H), 4.1–3.9 (m, 1H), 3.8–3.6 (m, 1H), 3.6–3.4 (m, 1H), 3.2–3.0 (m, 1H), 2.9 (dd, *J*=12.8, 9.1 Hz, 1H), 2.5 (s, 3H), 1.7–1.5 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) 162.9, 141.9, 140.9, 135.8, 130.1, 128.7, 128.3, 128.1, 123.9, 96.2, 95.9, 74.1, 73.3, 67.5, 67.3, 63.5, 62.4, 62.0, 31.7, 30.9, 28.6, 27.7, 27.1, 27.0, 21.4; MS (FAB) 480 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{22}H_{27}NO_4SBr$ 480.0838; found 480.0841. Data for ***syn*-15**: gummy liquid; TLC, R_f (30% EtOAc/hexane) 0.20; $[\alpha]_D^{25}$ −5.0 (*c* 1.0, $CHCl_3$); IR (neat) 3780, 2926, 1701, 1591, 1383, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.6 (d, *J*=7.7 Hz, 2H), 7.4–7.3 (m, 7H), 5.3–5.0 (m, 2H), 4.3–4.2 (m, 2H), 3.8–3.6 (m, 1H), 3.6–3.5 (m, 1H), 3.3–3.1 (m, 1H), 3.1 (dd, *J*=13.6, 5.3 Hz, 1H), 2.5 (s, 3H), 1.8–1.5 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 142.1, 139.7, 135.8, 130.1, 128.7, 128.4, 128.1, 124.4, 95.4, 74.2, 73.7, 67.5, 67.3, 62.0, 61.1, 60.8, 32.0, 31.2, 29.6, 28.5, 27.3, 26.6, 21.5; MS (FAB) 480 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{22}H_{26}NO_4NaSBr$ 502.0663; found 502.0663.

4.1.5. Homoallyl sulfide *17*

To a solution of the mixture of 1-tetradecene (1.96 g, 10 mmol) and acetonide **15** (2.4 g, 5 mmol) in dry DCM (25 mL) under an atmosphere of nitrogen was added TFAA (2.8 mL, 20 mmol) dropwise at 0 °C and stirred for 15 min. Then $SnCl_4$ (0.65 mL, 5.5 mmol) was added to the reaction mixture at 0 °C and stirred for another 30 min at the same temperature. The reaction mixture was cooled to −10 °C and then quenched by the addition of saturated aq Na_2CO_3 solution (10 mL). The layers were separated and aqueous layer extracted with DCM (3×15 mL). The combined organic layers were washed successively with water (2×20 mL), brine (30 mL) and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography using 5% ethyl acetate/petroleum ether (v/v) as the eluent to afford the product **17** (2.1 g, 3.25 mmol) in 65% yield as viscous oil. TLC, R_f (10% EtOAc/hexane) 0.40; $[\alpha]_D^{25}$ +2.5 (*c* 1.85, $CHCl_3$); IR (neat) 3320, 1582, 1523, 1404, 1384, 1354, 1080 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.4–7.2 (m, 7H), 7.1 (d, *J*=6.7 Hz, 2H), 5.6–5.3 (m, 2H), 5.2 (ABq, *J*=13.5 Hz, 2H), 4.4–4.2 (m, 2H), 3.8–3.4 (m, 2H), 3.1 (t, *J*=6.7 Hz, 1H), 2.5–2.2 (m, 4H), 2.1–1.8 (m, 2H), 1.8–1.0 (m, 25H), 0.9 (t, *J*=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 137.1, 136.1, 134.2, 133.3, 132.6, 129.9, 128.6, 128.2, 128.0, 126.3, 95.7, 94.9, 79.6, 78.8, 67.2, 67.1, 59.5, 58.9, 53.1, 53.0, 36.3, 32.6, 31.9, 29.65, 29.6, 29.4, 29.2, 27.8, 27.4, 26.6, 26.2, 22.7, 21.1, 14.1; MS (FAB) 659 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{36}H_{53}NO_3SBr$ 658.2929; found 658.2915. *Note*. In the ^{13}C spectrum, the peak for carbonyl carbon could not be picked up.

4.1.6. Debromination of homoallyl sulfide *18*

To a solution of the bromoacetonide **17** (3.2 g, 4.5 mmol) and *n*-Bu_3SnH (1.44 g, 5.0 mmol) in dry benzene (18.0 mL) was added AIBN (38 mg, 0.23 mmol) and the mixture was refluxed under an atmosphere of nitrogen for 3 h. The solvent was evaporated under reduced pressure and the residue was chromatographed using 5% EtOAc/petroleum ether (v/v) to afford acetonide **18** (2.1 g, 3.6 mmol) in 80% yield as a gummy oil. TLC, R_f (10% EtOAc/hexane) 0.35; $[\alpha]_D^{25}$ +2.0 (*c* 0.85, $CHCl_3$); IR (neat) 3235, 1680, 1589, 1219, 1184 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4–7.2 (m, 7H), 7.05 (d, *J*=8.3 Hz, 2H), 5.5–5.3 (m, 2H), 5.1 (ABq *J*=12.8 Hz, 2H), 4.2–3.9 (m, 1H), 3.9 (dd, *J*=6.8, 3.8 Hz, 1H), 3.1–3.0 (m, 1H), 2.5–2.2 (m, 5H), 2.1–1.8 (m, 2H), 1.8–1.0 (m, 25H), 0.9 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 138.0, 136.9, 134.0, 132.4, 132.3, 129.73, 129.7, 128.5, 128.0, 126.4, 95.1, 95.0, 82.2, 66.8, 66.7, 54.9, 52.0, 51.9, 34.7, 32.5, 31.9, 29.7, 29.6, 29.55, 29.52, 29.4, 29.33, 29.3, 29.2, 22.7, 21.0, 14.1; MS (FAB) 580 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{36}H_{54}NO_3S$ 580.3824; found 580.3839. *Note*. The doubling of peaks in ^{13}C is because of rotamers of Cbz group.

4.1.7. Acetonide cleavage *19*

To a solution of acetonide **18** (1.85 g, 3.0 mmol) in methanol (9 mL) was added catalytic amount of (+/−)-camphor-10-sulfonic acid (10 mol %) and the reaction mixture was stirred for 24 h at rt. Few drops of Et_3N were added and the solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography using 10% EtOAc/petroleum ether (v/v) as eluent to afford amino alcohol **19** (1.5 g, 2.8 mmol) in 93% yield as a gummy liquid. TLC, R_f (20% EtOAc/hexane) 0.30; $[\alpha]_D^{25}$ +5.0 (*c* 0.45, $CHCl_3$); IR (neat) 3416, 2979, 2932, 1456, 1373, 1216 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4–7.2 (m, 7H), 7.1 (d, *J*=7.9 Hz, 2H), 5.5–5.4 (m, 2H), 5.1–5.0 (m, 3H), 4.0 (q, *J*=7.0 Hz, 1H), 3.3–3.2 (m, 2H), 2.9 (ddd, *J*=11.3, 8.1, 3.0 Hz, 1H), 2.5–2.4 (m, 1H), 2.3 (s, 3H), 2.2–1.9 (m, 3H), 1.5–1.1 (m, 21H), 0.9 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 138.0, 136.6, 134.0, 133.8, 132.5, 129.8, 128.4, 128.0, 127.9, 125.7, 74.4, 66.6, 55.9, 47.2, 33.9, 32.6, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 28.4, 27.6, 22.6, 21.1, 19.5, 14.1; MS (FAB) 562 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{33}H_{50}NO_3S$ 540.3511; found 540.3513.

4.1.8. Amino alcohol derivative *20*

To a solution of the alcohol **19** (950 mg, 1.77 mmol) in dry DCM (9 mL), cooled at 0 °C were added successively Et_3N (0.45 mL, 5.3 mmol), catalytic DMAP (20 mg), and acetic anhydride (0.24 mL, 2.7 mmol) dropwise and the mixture stirred under nitrogen atmosphere for 1 h. It was then diluted with DCM (15 mL). The reaction mixture was washed with aq saturated $NaHCO_3$ (15 mL), water (2×10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure to yield viscous oil, which was purified by column chromatography using 10% EtOAc/petroleum ether to afford the acetate (990 mg, 1.7 mmol) as a gummy oil in quantitative yield. TLC, R_f (20% EtOAc/hexane) 0.30; $[\alpha]_D^{25}$ +11.0 (*c* 0.5, $CHCl_3$); IR (neat) 3453, 2925, 1742, 1539, 1461, 1239, 1112 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4–7.2 (m, 7H), 7.0 (d, *J*=8.3 Hz, 2H), 5.5–5.4 (m, 2H), 5.1 (ABq, *J*=12.1 Hz, 2H), 4.9 (t, *J*=6.0 Hz, 1H), 4.8 (d, *J*=9.8 Hz, 1H), 4.3–4.2 (m, 1H), 3.1 (q, *J*=6.8 Hz, 1H), 2.4–2.2 (m, 5H), 2.0–1.9 (m, 5H), 1.4–1.2 (m, 18H), 1.1 (d, *J*=6.0 Hz, 3H), 0.9 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 155.7, 137.0, 136.5, 134.5, 132.5, 132.3, 129.6, 128.4, 128.1, 128.0, 125.3, 76.9, 66.7, 51.4, 47.9, 35.0, 32.6, 31.9, 29.6, 29.5, 29.3, 29.1, 22.6, 20.9, 20.5, 18.9, 14.0; MS (FAB) 604 $[M+Na]^+$; HRMS (FAB) *m*/*z* calcd for $C_{35}H_{51}NO_4NaS$ 604.3436; found 604.3435.

4.1.9. Amidomercuration *21*

To a stirred solution of the acetate **20** (581 mg, 1 mmol) in dry DCM (5 mL) was added $Hg(OCOCF_3)_2$ (853 mg, 2 mmol) at rt. The reaction mixture was stirred for 16 h, diluted with dry THF (5 mL), cooled to −78 °C, and $LiBH_4$ (2 M in THF, 2 mL) was added dropwise over a period of 15 min. The reaction mixture was gradually warmed to 0 °C and the solution was stirred for 30 min. After 30 min the reaction was quenched with aqueous saturated solution of NH_4Cl (2 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (2×10 mL). The combined organic layers were washed with water (2×10 mL), brine (10 mL), dried over Na_2SO_4, and the solvent was evaporated under reduced pressure to yield a viscous oil, which was purified by column chromatography using 10% EtOAc/petroleum ether (v/v) to afford the cyclized compound **21** (404 mg, 0.75 mmol) in 75% yield as a gummy liquid. TLC, R_f (20% EtOAc/hexane) 0.35; $[\alpha]_D^{25}$ +11.0 (*c* 1.0, $CHCl_3$); IR (neat) 3430, 2924, 1638, 1455, 1235 cm^{-1}; ^1H NMR

(300 MHz, $CDCl_3$) δ 7.4–7.2 (m, 7H), 7.2–7.1 (d, J=8.6 Hz, 2H), 5.1 (s, 2H), 4.7–4.5 (m, 1H), 4.2–4.0 (m, 1H), 3.4 (dd, J=10.2, 5.5 Hz, 1H), 3.2–2.9 (m, 2H, H and OH), 2.4 (s, 3H), 2.0 (dd, J=13.3, 2.3 Hz, 1H), 1.7–1.4 (m, 3H), 1.4–1.1 (m, 25H), 0.9 (t, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 138.7, 136.4, 135.0, 129.6, 128.2, 127.7, 127.6, 125.8, 70.4, 67.0, 51.2, 50.4, 44.7, 35.2, 33.7, 31.7, 29.4, 29.3, 29.1, 27.1, 22.5, 20.9, 13.9; MS (FAB) 540 $[M+H]^+$; HRMS (FAB) m/z calcd for $C_{33}H_{50}NO_3S$ 540.3511; found 540.3513.

4.1.10. Deoxocassine **6**

To a solution of the alcohol **21** (108 mg, 0.2 mmol) in absolute ethanol (10 mL) was added Ra-Ni (1.1 g, 10 times by weight) and the mixture stirred at rt under hydrogen atmosphere for 2 h. The reaction mass was filtered through a small pad of silica gel, the filtrate was evaporated under reduced pressure to give deoxocassine **6** (54 mg, 0.19 mmol) in 94% yield as a white solid. Mp 46–47 °C (lit.[7f] mp 47–48 °C); $[\alpha]_D^{25}$ −12.2 (*c* 0.8, $CHCl_3$) (lit.[7f] $[\alpha]_D^{25}$ −12.4 (*c* 0.8, $CHCl_3$)); IR (KBr) 3394, 2916, 2848, 1455 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.5 (m, 1H), 2.8 (q, J=5.5 Hz, 1H), 2.6–2.5 (m, 1H), 2.2–1.6 (m, 2H), 1.6–0.9 (m, 27H), 0.8 (t, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.3, 57.5, 56.0, 37.2, 32.3, 32.1, 30.0, 29.9, 29.8, 29.6, 26.4, 26.0, 22.9, 18.9, 14.3; MS (FAB) 284 $[M+H]^+$; HRMS (FAB) m/z calcd for $C_{18}H_{38}NO$ 284.2953; found 284.2958.

4.1.11. Bromine displacement product **23**

To a solution of the bromo compound **17** (1.72 g, 2.62 mmol) in dry DMF (13 mL) was added $NaNO_2$ (1.81 g, 26.2 mmol) under nitrogen atmosphere and the mixture heated at 80 °C for 6 h. The reaction mixture was cooled to rt, diluted with ether (40 mL), and washed with water (2×30 mL). The organic layer was separated and the aqueous layer was extracted with ether (3×15 mL). The combined organic layers were washed successively with water (2×30 mL), brine (30 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude reaction mixture was purified by column chromatography using 20% ethyl acetate/petroleum ether (v/v) as the eluent to afford the alcohol **23** (1.3 g, 2.2 mmol) in 80% yield as viscous liquid. TLC, R_f (20% EtOAc/hexane) 0.40; $[\alpha]_D^{25}$ +5.0 (*c* 0.5, $CHCl_3$); IR (neat) 3387, 2925, 2855, 1711, 1516, 1383, 1272, 1057 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4–7.2 (m, 7H), 7.1 (d, J=6.8 Hz, 2H), 5.6–5.3 (m, 2H), 5.3–5.1 (m, 2H), 4.4–3.9 (m, 2H), 3.8–3.6 (m, 2H), 3.1–3.0 (m, 1H), 2.6–2.3 (m, 4H), 2.1–1.9 (m, 2H), 1.8–1.0 (m, 25H), 0.9 (t, J=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 137.1, 134.2, 133.3, 132.3, 131.7, 129.8, 128.6, 128.3, 128.2, 126.3, 95.1, 67.7, 65.2, 63.3, 62.1, 52.2, 36.3, 32.6, 31.9, 29.6, 29.4, 29.2, 27.4, 27.2, 26.3, 26.2, 24.8, 22.7, 21.0, 14.1; MS (FAB) 618 $[M+H]^+$; HRMS (FAB) m/z calcd for $C_{36}H_{53}NO_4NaS$ 618.3587; found 618.3584. *Note*. In the ^{13}C spectrum, the peak for carbonyl carbon could not be picked up.

4.1.12. Aminodiol derivative **24**

To a solution of **23** (595 mg, 1.0 mmol) in methanol (3 mL) was added catalytic amount of (+/−)-camphor-10-sulfonic acid (10 mol %) and the reaction mixture was stirred for 24 h at rt. Few drops of Et_3N were added and the solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography using 20% EtOAC/petroleum ether (v/v) as eluent to afford diol **24** (516 mg, 0.93 mmol) in 93% yield as a gummy liquid. TLC, R_f (30% EtOAc/hexane) 0.30; $[\alpha]_D^{25}$ +24.5 (*c* 0.55, $CHCl_3$); IR (KBr) 3411, 2924, 1628, 1511, 1374, 1253 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4–7.2 (m, 7H), 7.1 (d, J=7.6 Hz, 2H), 5.5–5.4 (m, 2H), 5.3 (d, J=9.1 Hz, 1H), 5.1 (ABq, J=12.8 Hz, 2H), 4.0–3.9 (m, 1H), 3.8–3.6 (m, 2H), 3.6–3.4 (m, 2H), 3.0–2.9 (m, 1H), 2.5–2.3 (m, 4H), 2.2–1.9 (m, 3H), 1.6–1.0 (m, 18H), 0.9 (t, J=7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 138.2, 136.4, 134.2, 133.9, 132.7, 129.9, 128.5, 128.2, 128.0, 125.6, 73.0, 67.0, 65.1, 55.8, 52.0, 33.5, 32.7, 31.9, 29.7, 29.6, 29.4, 29.35, 29.3, 22.7, 21.1, 14.1; MS (FAB) 578 $[M+H]^+$; HRMS (FAB) m/z calcd for $C_{33}H_{49}NO_4NaS$ 578.3274; found 578.3263.

4.1.13. Silyl ether **25**

To a stirred solution of the diol **24** (721 mg, 1.3 mmol) in dry CH_2Cl_2 (2.7 mL) cooled at −15 °C was added 2,6-lutidine (0.68 mL, 5.8 mmol) followed by TBS-OTf (0.67 mL, 0.29 mmol) and the mixture stirred at 0 °C for 1 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with water (2×5 mL), brine (7 mL), and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product, which was purified by column chromatography using 2% EtOAc/petroleum ether (v/v) to yield **25** (940 mg, 1.2 mmol) in 93% yield as gummy liquid. TLC, R_f (10% EtOAc/hexane) 0.50; $[\alpha]_D^{25}$ +5.8 (*c* 2.0, $CHCl_3$); IR (KBr) 3276, 1682, 1566, 1504, 1346, 1267 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4–7.3 (m, 7H), 7.1 (d, J=8.3 Hz, 2H), 5.6–5.4 (m, 2H), 5.3–5.0 (m, 3H), 4.3–4.1 (m, 2H), 3.6 (dd, J=9.8, 5.3 Hz, 1H), 3.4 (t, J=9.8 Hz, 1H), 3.1–3.0 (m, 1H), 2.7–2.5 (m, 1H), 2.4 (s, 3H), 2.1–1.9 (m, 2H), 1.6–1.1 (m, 19H), 1.0–0.8 (m, 21H), 0.2–0.0 (4s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 136.9, 133.0, 132.7, 132.5, 132.0, 129.6, 128.5, 128.0, 127.9, 127.8, 69.7, 66.6, 62.6, 56.1, 52.1, 32.6, 32.5, 31.9, 29.7, 29.6, 29.5, 29.4, 29.2, 25.9, 25.7, 22.7, 21.0, 14.1, −2.9, −4.4, −4.8, −5.4; MS (FAB) 783 $[M+H]^+$; HRMS (FAB) m/z calcd for $C_{45}H_{77}NO_4NaSi_2S$ 806.5009; found 806.4990.

4.1.14. Amidomercuration product **26**

To a stirred solution of **25** (783 mg, 1 mmol) in dry DCM (5 mL) was added $Hg(OCOCF_3)_2$ (853 mg, 2 mmol) at rt. The reaction mixture was stirred for 16 h, diluted with dry THF (5 mL), cooled to 0 °C, and $LiBH_4$ (2 M in THF, 2 mL) was added dropwise over a period of 15 min. After 30 min the reaction was quenched with aq saturated solution of NH_4Cl (2 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (2×10 mL). The combined organic layers were washed with water (2×10 mL), brine (10 mL), dried over Na_2SO_4, and the solvent was evaporated under reduced pressure to yield a viscous oil, which was purified by column chromatography using 30% EtOAc/petroleum ether (v/v) to afford compound **26** (326 mg, 0.73 mmol) in 73% yield as a gummy liquid. TLC, R_f (30% EtOAc/hexane) 0.30; $[\alpha]_D^{25}$ +52 (*c* 0.25, $CHCl_3$); IR (KBr) 3424, 2924, 1638, 1520, 1422, 1275 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (d, J=8.3 Hz, 2H), 7.1 (d, J=8.3 Hz, 2H), 4.3–4.2 (m, 2H), 3.7–3.4 (m, 4H), 2.5–2.2 (m, 5H), 1.8–1.5 (m, 2H), 1.4–1.0 (m, 20H), 0.9 (t, J=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.5, 137.9, 132.2, 131.8, 130.1, 67.6, 62.8, 56.3, 52.4, 48.8, 31.9, 30.8, 30.3, 29.5, 29.4, 26.7, 22.7, 21.1, 14.1; MS (FAB) 448 $[M+H]^+$; HRMS (FAB) m/z calcd for $C_{26}H_{41}NO_3NaS$ 470.2704; found 470.2683.

4.1.15. Acetate derivative **27**

To a stirred solution of alcohol **26** (18 mg, 0.04 mmol) in dry DCM (0.2 mL) was added Et_3N (0.01 mL, 0.11 mmol) and acetic anhydride (0.005 mL, 0.06 mmol) at 0 °C. The reaction mixture was stirred for 2 h at rt. The mixture was diluted with DCM (10 mL) and washed successfully with water (2×5 mL), brine (5 mL), the organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to yield a viscous oil, which was purified by column chromatography using 15% EtOAc/petroleum ether (v/v) to afford acetate **27** (17.7 mg, 0.036 mmol) in 90% yield as gummy liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.3 (d, J=7.7 Hz, 2H), 7.1 (d, J=8.4 Hz, 2H), 4.9 (t, J=2.3 Hz, 1H), 4.4 (td, J=8.4, 3.1 Hz, 1H), 4.3 (t, J=9.2 Hz, 1H) 3.6 (q, J=3.1 Hz, 1H), 3.6–3.5 (m, 1H), 2.5–2.4 (m, 1H), 2.3 (s, 3H), 2.2–2.1 (m, 4H), 1.8 (td, J=13.8, 2.3 Hz, 1H), 1.7–1.6 (m, 1H), 1.5–1.2 (m, 20H), 0.9 (t, J=8.4, 3H). *Note*. The NOESY spectrum diagnostically revealed NOE between methine protons at C-2 and C-6.

4.1.16. Desulfurization product ***28***

To a solution of the alcohol **26** (89 mg, 0.2 mmol) in absolute ethanol (10 mL) was added Ra-Ni (890 mg, 10 times by weight), and the mixture stirred at rt under hydrogen atmosphere for 2 h. The reaction mass was filtered through a small pad of silica gel, the filtrate was evaporated under reduced pressure to give the product **28** (59 mg, 0.18 mmol) in 90% yield as a semi solid. TLC, R_f (30% EtOAc/hexane) 0.25; $[\alpha]_D^{25}$ −15.5 (*c* 0.3, $CHCl_3$); IR (KBr) 3376, 2928, 2856, 1697, 1385, 1256, 1102 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.5–4.2 (m, 2H), 3.9–3.7 (m, 1H), 3.6 (t, *J*=6.0 Hz, 1H), 3.1–3.0 (m, 1H), 2.5–2.4 (m, 1H), 2.1–2.0 (d, *J*=11.3 Hz, 1H), 1.9–1.2 (m, 24H), 0.9 (t, *J*=6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 64.9, 62.9, 60.9, 57.5, 31.9, 31.2, 31.0, 29.6, 29.3, 26.7, 24.8, 22.6, 14.1; MS (FAB) 326 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{19}H_{36}NO_3$ 326.2689; found 326.2698.

4.1.17. Ketone ***29***

To a solution of the alcohol **28** (59 mg, 0.18 mmol) in EtOAc (1 mL) was added IBX (100 mg, 0.36 mmol) and the mixture was heated at reflux for 6 h. The reaction mixture was filtered through Celite and the filtrate was evaporated under reduced pressure to yield keto compound **29** as a viscous oil. The ketone being unstable to chromatography was used without further purification in the subsequent reduction.

4.1.18. Alcohol ***30***

The crude ketone from the previous step was dissolved in MeOH (1 mL) and $NaBH_4$ (10 mg, 0.27 mmol) was added at 0 °C. The reaction mixture was stirred for 1 h at the same temperature, diluted with 10 mL of diethyl ether, washed with water (5 mL) and brine (5 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to yield a gummy liquid, which was purified by column chromatography using 30% EtOAc/petroleum ether (v/v) to afford alcohol **23** (50 mg, 0.15 mmol) in 86% yield as a gummy liquid. TLC, R_f (30% EtOAc/hexane) 0.25; $[\alpha]_D^{25}$ +24.5 (*c* 0.3, $CHCl_3$); IR (KBr) 3376, 2928, 2856, 1697, 1385, 1256, 1102 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.4–4.1 (m, 2H), 3.5 (ddd, *J*=12.1, 9.1, 3.0 Hz, 1H), 3.3 (ddd, *J*=10.6, 9.1, 3.0 Hz, 1H), 3.0 (q, *J*=7.6 Hz, 1H), 2.5–2.3 (m, 1H), 2.2–2.0 (m, 1H), 1.9–1.0 (m, 24H), 0.9 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9, 69.6, 64.9, 62.6, 57.2, 33.7, 31.9, 30.9, 30.3, 29.8, 29.6, 29.3, 27.0, 26.7, 22.6, 14.0; MS (FAB) 326 $[M+H]^+$; HRMS (FAB) *m*/*z* calcd for $C_{19}H_{36}NO_3$ 326.2689; found 326.2694.

4.1.19. Desoxoprosophylline ***22***

To a stirred solution of the alcohol **30** (25 mg, 0.076 mmol) in ethanol (0.5 mL) was added aq KOH (8 N, 0.5 mL) and the reaction mixture was heated at 95–100 °C for 24 h. The reaction was cooled to rt and extracted with dichloromethane (3×10 mL). The organic layer was successfully washed with water (2×10 mL), brine (10 mL), dried over Na_2SO_4, and evaporated under reduced pressure to furnish the crude product, which was purified by column chromatography using 8% MeOH/$CHCl_3$ (v/v) to afford (+)-desoxoprosophylline **22** (20 mg, 0.068 mmol) in 90% yield as a white solid. Mp 87–88 °C (lit.[17c] mp 89.5–90 °C); TLC, R_f (10% MeOH/$CHCl_3$) 0.25; $[\alpha]_D^{25}$ +12 (*c* 0.22, $CHCl_3$) (lit.[17c] $[\alpha]_D^{25}$ +14.4 (*c* 0.22, $CHCl_3$)); ^1H NMR (300 MHz, $CDCl_3$) δ 3.82 (dd, *J*=10.7, 4.4 Hz, 1H), 3.7 (dd, *J*=10.7, 5.3 Hz, 1H), 3.45 (ddd, *J*=9.2, 8.6, 4.5 Hz, 1H), 2.6–2.4 (m, 2H), 2.4–2.3 (m, 1H), 2.1–1.8 (m, 2H), 1.8–1.6 (m, 2H), 1.4–1.0 (m, 22H), 0.9 (t, *J*=6.7 Hz, 3H); MS (FAB) 300 $[M+H]^+$. HRMS (FAB) *m*/*z* calcd for $C_{18}H_{37}NO_2$ 299.2824; found 299.2843.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.08.031.

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