Chiral and Stereoselective Total Synthesis of (−)-Deoxoprosopinine and (−)-Deoxoprosophylline. Intramolecular Aminomercuration of an ε,ζ-Unsaturated Amine[1,2]

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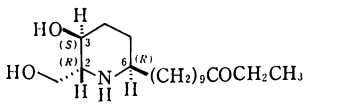
L-Serine was transformed in 8 steps into (4*R*,5*S*)-2,2-dimethyl-4-[(*Z*)-3-pentadecenyl]-1,3-dioxan-5-amine. This chiral ε,ζ-unsaturated amine was subjected to intramolecular aminomercuration and then acid hydrolysis to give (−)-deoxoprosopinine and (−)-deoxoprosophylline.

Seven piperidine alkaloids have been isolated from *Prosopis africana* TAUB. and their structures have been determined, (+)-(2*R*,3*S*,6*R*)-prosopinine (**1**) and (±)-prosophylline (**2**) being two representatives of these Prosopis alkaloids.[3] Although some approaches to the synthesis of Prosopis alkaloids have been reported,[4] no chiral synthesis has yet been accomplished. Recently, an intramolecular aminomercuration[5] was successfully applied to the synthesis of (±)-solenopsin A and (±)-isosolenopsin A, piperidine derivatives related to fire ant venom.[6] This paper deals with a chiral and stereoselective total synthesis of (−)-deoxoprosopinine (**3**) [an enantiomer of (+)-deoxoprosopinine derived from natural **1**] and (−)-deoxoprosophylline (**4**) starting from L-serine (**5**) by a route involving the intramolecular aminomercuration of an ε,ζ-unsaturated amine (**6**).

(2*S*)-3-Acetoxy-2-phthalimidopropanal (**7**) was prepared from L-serine (**5**) *via* (2*S*)-3-acetoxy-2-phthalimidopropanoic acid (**8**) by the known procedure.[7] The carbon chain of the aldehyde (**7**) was elongated by C_{15}-unit by the Grignard reaction. A C_{15}-bromide (**9**) was prepared as follows. Hydrogenation of 3-pentadecyn-1-ol[8] in ethanol in the presence of a palladium–barium sulfate catalyst deactivated with quinoline[9] gave (*Z*)-3-pentadecen-1-ol (**10**) in a quantitative yield. The alcohol (**10**) was brominated with dibromotriphenylphosphine in dichloromethane to afford (*Z*)-3-pentadecenyl bromide (**9**) in 89% yield.



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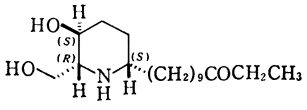
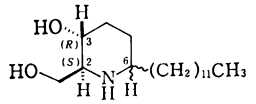
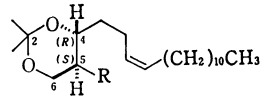


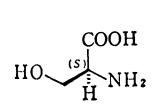
2 (racemic)



3 (6*S*) : 6β-H
4 (6*R*) : 6α-H



6 R = NH_2
15 R = N=Phth



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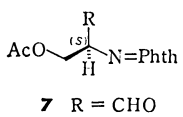
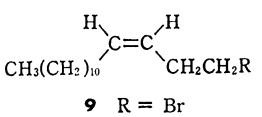


7 R = CHO
8 R = COOH

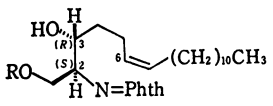


9 R = Br
10 R = OH

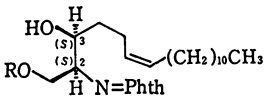
(Phth : phthaloyl)

The chiral aldehyde (**7**) in a mixture of tetrahydrofuran and ether was treated with the Grignard reagent prepared from **9** at −70 °C and then at −45 °C to give a mixture of diol monoacetates (**11** and **12**), the separation of which by column and thin-layer chromatographies was unsuccessful. Acid hydrolysis of this mixture afforded, after separation by silica gel column chromatography, (2*S*,3*R*,6*Z*)-2-phthalimido-6-octadecene-1,3-diol (**13**) and (2*S*,3*S*,6*Z*)-2-phthalimido-6-octadecene-1,3-diol (**14**) in 16.5 and 2.4% yields from **8**, respectively. On treatment with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid, the diols **13** and **14** gave their acetonides **15** and **16** in 97% and 70% yields, respectively. The coupling constant between a C-4 proton and a C-5 proton was determined by ^{1}H-NMR measurements to be 10 and 5 Hz for **15** and **16**, respectively; this led to the *erythro* and *threo* configurations for **13** and **14**, respectively. The formation of **13** and **14** from **7** in a *ca.* 7 : 1 ratio showed that a stereoselective attack[7] of the Grignard reagent to the aldehyde (**7**) was effected preferentially from the less hindered side of **7** to give predominantly the desired *erythro* derivative (**11**).

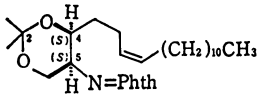
Hydrazinolysis of the *N*-protective phthaloyl group of **15** gave (4*R*,5*S*)-2,2-dimethyl-4-[(*Z*)-3-pentadecenyl]-1,3-dioxan-5-amine (**6**) in a quantitative yield. The ε,ζ-unsaturated amine (**6**) was subjected to aminomercuration with mercury(II) acetate in methanol at room temperature and then demercuration with sodium borohydride to afford two piperidine acetonides, (1*R*,6*S*,8*S*)-8-dodecyl-3,3-dimethyl-2,4-dioxa-7-azabicyclo[4.4.0]decane (**17**) and its (1*R*,6*S*,8*R*)-diastereomer (**18**), in 3.3 and 76% yields, respectively; this shows that the reaction proceeded stereoselectively. The 8*S* and 8*R* stereochemistry was shown for **17** and **18** by their conversion into **3** and **4**, respectively, as described below. In the ^{1}H-NMR spectrum (270 MHz) of **17** in deuteriochloroform the proton on C-8 resonated at δ 2.99 as a broad signal with a half-band width ($W_{1/2}$) 21 Hz, while in the spectrum of **18** in deuteriobenzene the C-8 proton signal appeared at δ 2.33 as a broad signal with $W_{1/2}$=25 Hz. These $W_{1/2}$ values are in line with those ($W_{1/2}$=18 Hz[3b] and $W_{1/2}$=24 Hz[3c]) observed for the corresponding proton signals of *O*,*O*′-benzylidene



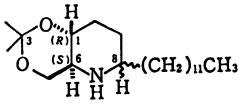
11 R = Ac
13 R = H



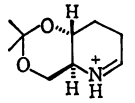
12 R = Ac
14 R = H



16



17 (8S) : 8β-H
18 (8R) : 8α-H



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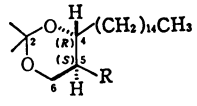

20 R = NH_2
21 R = N=Phth

derivatives of deoxoprosopinine[3b] and deoxoprosophylline,[3c] respectively. A peak at *m/e* 170 (**19**) due to a loss of the side chain was observed as a base peak in the mass spectra of both **17** and **18**.

Finally, the acetonides **17** and **18** were hydrolyzed to afford (−)-deoxoprosopinine (**3**) and (−)-deoxoprosophylline (**4**) in 58 and 86% yields, respectively. The two synthetic piperidines **3** and **4** were found to be identical, except for optical property, with authentic (+)-deoxoprosopinine[3a,b] and (±)-deoxoprosophylline[3c] derived from natural (+)-prosopinine (**1**)[3a,b] and (±)-prosophylline (**2**),[3c] respectively. Since the absolute value of optical rotation ($[\alpha]_D$ −14.7°) of the synthetic deoxoprosopinine (**3**) is almost the same as that ($[\alpha]_D$ +12°) of deoxoprosopinine derived from natural **1**, no racemization occurred during the course of synthesis.

Thus, (−)-deoxoprosopinine (**3**) and (−)-deoxoprosophylline (**4**) were synthesized from L-serine (**5**) in overall yields of 0.12 and 4.3%, respectively. This constitutes the first example of stereoselective total synthesis of optically active Prosopis alkaloids, presenting a useful synthetic route applicable to the other piperidine alkaloids.

Experimental

Melting points were measured on a Mel-temp capillary melting point apparatus (Laboratory Devices) and are uncorrected. IR spectra were measured with a Hitachi EPI-G2, a Hitachi 260-30, or a JEOL JIR-03F (FT) spectrometer, ^{1}H-NMR spectra with a Hitachi R-20B (60 MHz), a Varian EM-390 (90 MHz), a JEOL PS-100 (100 MHz), or a Brucker WH 270 (270 MHz, FT) spectrometer in deuteriochloroform solution containing tetramethylsilane as an internal standard, low resolution mass spectra with a Hitachi RMU-6-Tokugata mass spectrometer with a direct inlet system operating at 70 eV, high resolution mass spectra and chemical ionization mass spectra (CI-MS) with a JEOL JMS-D300 mass spectrometer. Measurenents of optical rotation were carried out with JASCO DIP-SL and DIP-4 polarimeters. Vaper-phase chromatographic (VPC) analyses were performed on Shimadzu gas chromatographs GC-4A PF and GC-6A PF. Thin-layer chromatography (TLC) was carried out on Kieselgel GF_{254} (E. Merck, Darmstadt) and Alumina B-10F (Wako Pure Chemical Industries) in 0.25 mm thickness for analytical use and in 1 mm thickness for preparative use. Wakogel C-200 and Aluminiumoxid Woelm (neutral; M. Woelm, Eschwege) were used for column chromatography.

(Z)-3-Pentadecen-1-ol (10). 3-Pentadecyn-1-ol[8] (20 g) in methanol (150 ml) was hydrogenated in the presence of a 5% palladium–barium sulfate catalyst (400 mg) deactivated with quinoline[9] at room temperature for 3 h. The reaction was monitored by VPC examination. After filtration of the catalyst, the solvent was removed to give a residue, which was dissolved in hexane (200 ml). The hexane solution was washed with 1.5 M (1 M=1 mol dm^{-3}) hydrochloric acid, saturated aqueous sodium hydrogencarbonate solution, and brine, dried, and evaporated. The residue was chromatographed on a column of silica gel (150 g; elution with benzene) to give **10** (20.4 g) in a quantitative yield. (*Z*)-3-Pentadecen-1-ol (**10**): mp 12—13 °C, bp 105 °C/0.1 kPa; IR (neat) 3350, 3000, 2950, 2850, 1660, 1470, 1380, 1050, 1020, and 720 cm^{-1}; absence of absorption around 965 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.89 (3H, t, *J*=5 Hz, $-CH_2C\underline{H}_3$), 1.27 (18H, s, 9×CH_2), 2.00 (3H, m, $-C\underline{H}_2CH{=}CH-$ and OH), 2.38 (2H, m, $-CH{=}CH-C\underline{H}_2-CH_2OH$), 3.62 (2H, t, *J*=6.5 Hz, $-C\underline{H}_2OH$), and 5.45 (2H, m, $-CH_2-C\underline{H}{=}C\underline{H}-CH_2-$); MS *m/e* 208 [relative intensity (%): 15; $(M-18)^+$], 186 (100), and 141 (95). Found: C, 79.32; H, 13.41%. Calcd for $C_{15}H_{30}O$: C, 79.57; H, 13.36%. On VPC examination (DEGS; 2 m; 205 °C; N_2 50 ml/min), the retention time (R_t) of **10** was found to be 8.8 min; a peak (R_t=7.2 min) due to pentadecan-1-ol was absent.

(Z)-3-Pentadecenyl Bromide (9). A solution of (*Z*)-3-pentadecen-1-ol (**10**; 14.4 g) in dichloromethane (50 ml) was added to a solution of dibromotriphenylphosphine in dichloromethane (380 ml) prepared from triphenylphosphine (52 g) and bromine (26.15 g), and the mixture was stirred at room temperature for 1.5 h. The organic solution was washed with water and brine, and concentrated to 100 ml. Hexane (700 ml) was added to this concentrated solution with vigorous stirring to produce a precipitated mass of triphenylphosphine oxide, which was separated by filtration and washed with hexane (total 200 ml). The filtrate and the washings were combined, and the solvents were removed to give a residue, which was subjected to dry column chromatography (silica gel, 150 g; elution with hexane) and then distillation under reduced pressure, giving **9** (16.3 g) in 89% yield. (*Z*)-3-Pentadecenyl bromide (**9**): a colorless oil, bp 156—156.5 °C/0.4 kPa; IR (neat) 3000, 2950, 2900, 2860, 1660, 1460, 1380, 1310, 1280, 1210, 720, 675, and 640 cm^{-1}; absence of absorption around 965 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.89 (3H, t, *J*=6 Hz, $-CH_2-C\underline{H}_3$), 1.27 (18H, s, 9×CH_2), 2.03 (2H, m, $-C\underline{H}_2CH{=}CH-$), 2.67 (2H, m, $-CH{=}CH-C\underline{H}_2-CH_2Br$), 3.35 (2H, t, *J*=6.5 Hz, $-CH_2Br$), and 5.44 (2H, m, $-CH_2-C\underline{H}{=}C\underline{H}-CH_2-$; a coupling constant between the two olefinic protons was determined to be 10.5 Hz by decoupling experiments, indicating a (*Z*)-olefin stereochemistry); MS *m/e* 290 and 288 (each 6.5; M^+), 186 (88), and 149 (100). Found: C, 62.09; H, 10.07%. Calcd for $C_{15}H_{29}Br$: C, 62.28; H, 10.10%.

When a part of **9** was left at room temperature for 6 months, **9** isomerized into (*E*)-3-pentadecenyl bromide: a colorless oil; IR (neat) 3000, 2950, 2920, 2850, 1660, 1460, 1380, 1260, 1200, 1070, 965, 800, 720, 665, and 640 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.90 (3H, t-like, $-CH_2C\underline{H}_3$), 1.27 (18H, s, 9×CH_2), 2.00 (2H, m, $-C\underline{H}_2CH{=}CH-$), 2.59 (2H, m, $-CH{=}CH-C\underline{H}_2-CH_2Br$), 3.37 (2H, t, *J*=7 Hz, $-CH_2Br$), and 5.44 (2H, m, $-CH_2C\underline{H}{=}C\underline{H}-CH_2-$; decoupling experiments showed a

coupling constant between the two olefinic protons to be 15 Hz, indicating an (*E*)-olefin structure).

(2S)-3-Acetoxy-2-phthalimidopropanal (7). According to the procedure described by Newman,[7] L-serine (**5**) was converted into (2*S*)-3-acetoxy-2-phthalimidopropanoic acid (**8**) in 41% yield, which was then transformed into the aldehyde (**7**) in 95% yield. Because of an unstability of the aldehyde (**7**), **7** was used immediately for the following Grignard reaction.

Grignard Reaction of (2S)-3-Acetoxy-2-phthalimidopropanal (7) with (Z)-3-Pentadecenylmagnesium Bromide. A solution of (*Z*)-3-pentadecenylmagnesium bromide (4.96 mmol) in ether (62 ml) [prepared from the bromide (**9**) and magnesium in ether by the usual procedure] was added dropwise to a solution of the aldehyde (**7**; 1.298 g; 4.97 mmol) in a mixture of tetrahydrofuran (10 ml) and ether (5 ml) with stirring under an argon atmosphere at a temperature between −72 and −70 °C. After the mixture had been stirred at this temperature for 1 h and then at −45 °C for 1 h, a saturated aqueous solution (50 ml) of ammonium chloride was added at −45 °C. The reaction mixture was treated in the usual way to give a residue (2.75 g) which was chromatographed on a column of silica gel (100 g). Elution with hexane–ethyl acetate (17 : 3) gave a mixture (760 mg; 32% yield from **7**; 30% yield from **8**) of diol monoacetate (**11** and **12**). However, separation of each of two diastereomers (**11** and **12**) by column and thin-layer chromatographies was unsuccessful. Mixture of **11** and **12**: an oil; IR (neat) 3450, 2900, 1770, 1740, 1705, 1380, 1230, 1040, 720, and 675 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.89 (3H, t-like, $-CH_2C\underline{H}_3$), 1.24 (18H, broad s, $9\times CH_2$), 1.60 (2H, m, $-\underline{C}H(OH)-C\underline{H}_2CH_2-$), 1.95 (3H, s, CH_3CO-), 2.10 (4H, broad m, allylic H's), *ca.* 3.5 (1H, broad signal, OH), 4.15 (1H, m, $HO-\underline{C}H-$), 4.55 (3H, m, $AcO-C\underline{H}_2-\underline{C}H-\underline{N}-$), 5.36 (2H, m, $-CH_2-C\underline{H}=C\underline{H}-CH_2-$), and 7.83 (4H, m, aromatic H's).

Acid Hydrolysis of the Mixture of Diol Monoacetates (11 and 12). The mixture of diol monoacetates (**11** and **12**; 838 mg) was added to a solution (20 ml) prepared from 1 M hydrochloric acid and methanol (1 : 9 v/v), and the whole mixture was refluxed for 4 h. After the solvent had been removed under reduced pressure, the mixture was extracted with ether. The ethereal solution was washed with saturated aqueous sodium hydrogencarbonate solution and brine, dried (Na_2SO_4), and evaporated to give an oil, which was chromatographed on a column of silica gel (15 g). Elution with hexane–ethyl acetate (7 : 3) gave a mixture of **13** and **14**, and then pure **13** (306 mg). This mixture was subjected to separation by TLC to afford **13** (116 mg) and **14** (59 mg; 2.6% yield from **7**; 2.4% yield from **8**). The *erythro*-diol (**13**; total 422 mg) was obtained in 17.6% yield from **7** (16.5% yield from **8**). (2*S*, 3*R*, 6*Z*)-*erythro*-2-Phthalimido-6-octadecene-1,3-diol (**13**): mp 32.5—34.5 °C [purified by molecular distillation: 110—130 °C (bath temperature)/13 Pa], $[\alpha]_D^{19}$ −15° (*c* 0.20; $CHCl_3$); IR (Nujol) 3450, 1780, and 1705 cm^{-1}; absence of absorption around 965 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.89 (3H, t-like, $-CH_2C\underline{H}_3$), 1.26 (18H, broad s, $9\times CH_2$), 1.55 (2H, m, $HO-\underline{C}H-C\underline{H}_2CH_2-$), 2.10 (4H, broad m, allylic H's), *ca.* 3.1—3.8 (2H, broad signals, $2\times OH$), 4.17 [4H, m, $HO-C\underline{H}_2-C\underline{H}(NPhth)-C\underline{H}(OH)-$], 5.35 (2H, m, $-CH_2-C\underline{H}=C\underline{H}-CH_2-$), and 7.82 (4H, m, aromatic H's). Found: C, 72.74; H, 9.17; N, 3.45%. Calcd for $C_{26}H_{39}NO_4$: C, 72.69; H, 9.15; N, 3.26%. (2*S*, 3*S*, 6*Z*)-*threo*-2-Phthalimido-6-octadecene-1,3-diol (**14**): an oil [purified by molecular distillation: 110—130 °C (bath temperature)/13 Pa], $[\alpha]_D^{19}$ +5° (*c* 0.23; $CHCl_3$); IR (Nujol) 3450, 1770, and 1700 cm^{-1}; absence of absorption around 965 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.89 (3H, t-like, $-CH_2C\underline{H}_3$), 1.27 (18H, broad s, $9\times CH_2$), 1.50 (2H, m, $HO-\underline{C}H-C\underline{H}_2-CH_2-$), 2.05 (4H, broad m, allylic H's), *ca.* 3.2—3.8 (2H, broad signals, $2\times OH$; disappeared on addition of D_2O), 4.16 (3H, m, $HO-C\underline{H}_2-\underline{C}H-\underline{N}-$ and $HO-\underline{C}H-$), 4.40 (1H, t-like, J=*ca.* 6 Hz, $HO-CH_2-\underline{C}H-\underline{N}-$), 5.37 (2H, m, $-CH_2-C\underline{H}=C\underline{H}-CH_2-$), and 7.88 (4H, m, aromatic H's). Found: *m/e* 429.2883. Calcd for $C_{26}H_{39}NO_4$: M, 429.2878.

Acetalization of the erythro-*Diol (13).* The *erythro*-diol (**13**; 176 mg) was dissolved in 2,2-dimethoxypropane (10 ml) containing a trace of *p*-toluenesulfonic acid, and the solution was stirred at room temperature for 12 h. The reaction mixture was treated in the usual way to give a residue, which was purified by chromatography on a column of silica gel [3 g; elution with hexane–ethyl acetate (19 : 1)] giving an acetonide (**15**; 119 mg) in 62% yield. When the reaction was carried out for 10 d, **15** was obtained in 97% yield. (4*R*, 5*S*)-2,2-Dimethyl-4-[(*Z*)-3-pentadecenyl]-5-phthalimido-1,3-dioxane (**15**): mp 47—48 °C (crystallized from ethanol), $[\alpha]_D^{19}$ −6° (*c* 0.23, $CHCl_3$); IR (Nujol) 1780, 1720, 1705, 1110, and 1070 cm^{-1}; absence of absorption around 965 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.88 (3H, t-like, $-CH_2C\underline{H}_3$), 1.24 (18H, broad s, $9\times CH_2$), 1.45 and 1.64 [each 3H, s, $(CH_3)_2\underline{C}-$], 1.48 (2H, m, $-O-\underline{C}H-C\underline{H}_2-CH_2-$), 2.00 (4H, broad m, allylic H's), 3.70 (1H, dd, J=10 and J=5 Hz, $C_{(6\alpha)}-H$), 4.20 (1H, td, J=10 and J=5 Hz, $C_{(5\alpha)}-H$), 4.51 (1H, t, J=10 Hz, $C_{(6\beta)}-H$), 4.65 (1H, m, $C_{(4\beta)}-H$), 5.26 (2H, m, $-CH_2-C\underline{H}=C\underline{H}-CH_2-$), and 7.80 (4H, m, aromatic H's). Found: C, 74.37; H, 9.20; N, 3.23%. Calcd for $C_{29}H_{43}NO_4$: C, 74.16; H, 9.23; N, 2.98%.

Acetalization of the threo-*Diol (14).* A soltuion of the *threo*-diol (**14**; 34 mg) in 2,2-dimethoxypropane (1 ml) containing a trace of *p*-toluenesulfonic acid was stirred at room temperature for 10 d. The reaction mixture was treated in the usual way to give a residue, which was chromatographed on a column of silica gel [elution with hexane–ethyl acetate (2 : 1)] giving the corresponding acetonide (**16**; 26.2 mg) in 70% yield, besides unchanged **14** (8.5 mg). (4*S*, 5*S*)-2,2-Dimethyl-4-[(*Z*)-3-pentadecenyl]-5-phthalimido-1,3-dioxane (**16**): mp 56—56.5 °C, $[\alpha]_D^{19}$ +2° (*c* 0.43; $CHCl_3$); IR (Nujol) 1775, 1720, 1705, 1260, 1110, and 1060 cm^{-1}; absence of absorption around 965 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.89 (3H, t-like, $-CH_2C\underline{H}_3$), 1.26 (18H, broad s, $9\times CH_2$), 1.44 and 1.61 [each 3H, s, $(CH_3)_2\underline{C}-$], 1.46 (2H, m, $-O-\underline{C}H-C\underline{H}_2-CH_2-$), 2.05 (4H, broad m, allylic H's), 3.95 (1H, dd, J=11 and J=7 Hz, $C_{(6)}-H$), 4.15 (1H, dt, J=9 and J=5 Hz, $C_{(4\alpha)}-H$), 4.38 (1H, dd, J=11 and J=7 Hz, $C_{(6)}-H$), 4.67 (1H, td, J=7 and J=5 Hz, $C_{(5\alpha)}-H$), 5.26 (2H, m, $-CH_2-C\underline{H}=C\underline{H}-CH_2-$), and 7.81 (4H, m, aromatic H's). Found: *m/e* 469.3205. Calcd for $C_{29}H_{43}NO_4$: M, 469.3192.

Hydrazinolysis of the Acetonide (15) Derived from erythro-*Diol Phthalimide (13).* Hydrazine hydrate (100%; 40.9 mg; 0.82 mmol; *ca.* 3 equivalent moles) was added to a solution of the acetonide (**15**; 132 mg; 0.28 mmol) in ethanol (5 ml), and the mixture was refluxed under an argon atmosphere for 2.5 h. The reaction mixture was extracted with dichloromethane (total 30 ml) after addition of water (3 ml) and potassium hydroxide (*ca.* 0.2 g). The organic layer was treated in the usual way to give an *erythro*-amine (**6**; 99 mg; 0.29 mmol) in a quantitative yield. (4*R*, 5*S*)-2,2-Dimethyl-4-[(*Z*)-3-pentadecenyl]-1,3-dioxan-5-amine (**6**): an oil; IR (neat) 3350, 2930, 1660, 1460, 1380, 1270, 1200, 1160, 1070, 860, 720, and 660 cm^{-1}; absence of absorption around 965 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.88 (3H, t-like, $-CH_2C\underline{H}_3$), 1.27

(18H, broad s, 9×CH_2), 1.38 and 1.40 [each 3H, s, $(CH_3)_2\underline{C}$–], 1.70 (2H, m, –O–$\underline{CH}$–$C\underline{H}_2$–CH_2–), 2.00 (4H, m, allylic H's), 2.60 (1H, m, $C_{(5\alpha)}$–H), *ca.* 3.0—3.9 (3H, m, $C_{(4\beta)}$–H, $C_{(6\beta)}$–H, and $C_{(6\alpha)}$–H), and 5.34 (2H, m, –CH_2–$C\underline{H}$=$C\underline{H}$–CH_2–); MS *m/e* 339 (27; M^+), 324 (81), 281 (38), 267 (40), 264 (32), 250 (34), 170 (98), 101 (100), and 100 (92); peaks at *m/e* 341 and 326 due to its dihydro derivative (**20**) were not observed (*vide infra*). Found: *m/e* 339.3134. Calcd for $C_{21}H_{41}NO_2$: M, 339.3135.

When the hydrazinolysis of **15** was carried out with 8 equivalent moles of hydrazine hydrate under reflux for 2 h, a mixture of **6** and its dihydro derivative (**20**) was obtained. Although separation of these products by means of various techniques including VPC was unsuccessful, the mass spectrum showed that the mixture consisted of **6** [*m/e* 339 (M^+) and 324 ($M-15)^+$] and **20** [*m/e* 341 (M^+) and 326 ($M-15)^+$] in a ratio of *ca.* 7 : 6. The formation of **20** could be explained by reduction of **6** with diimide, which may be produced from hydrazine by oxidation with oxygen present in the system, even when the reaction was carried out under an argon atmosphere.

Aminomercuration of the ε,ζ-Unsaturated Amine (6). A solution of mercury(II) acetate (486 mg) in methanol (20 ml) was added to a solution of the ε,ζ-unsaturated amine (**6**; 266 mg) in methanol (15 ml), the whole solution being stirred at room temperature for 2 weeks. After addition of a solution of sodium borohydride (72 mg) in 2 M aqueous sodium hydroxide solution (5 ml), the aqueous methanol solution was separated from a white precipitate of mercury by decantation. This aqueous methanol solution was evaporated under reduced pressure, and extracted with dichloromethane (total 30 ml) after addition of water (10 ml). The organic layer was washed with brine, dried ($MgSO_4$), and evaporated, giving an oil, which was chromatographed on a column of alumina (5 g). Elution with hexane–ether (6 : 1) afforded an (8*R*)-acetonide (**18**; 202 mg) in 76% yield. Successive elution with ether gave an (8*S*)-acetonide (**17**; 8.9 mg) in 3.3% yield. (1*R*, 6*S*, 8*S*)-8-Dodecyl-3,3-dimethyl-2,4-dioxa-7-azabicyclo[4.4.0]decane (**17**): an oil, $[\alpha]_D^{19}$ +2° (*c* 0.10; $CHCl_3$); IR (neat) 3300, 2920, 1460, 1380, 1270, 1200, 1160, 1095, 1060, 960, and 855 cm^{-1}; ^{1}H-NMR (270 MHz; $CDCl_3$) δ 0.89 (3H, t, *J*=7 Hz, –$CH_2C\underline{H}_3$), 1.42 and 1.51 [each 3H, s, $(CH_3)_2\underline{C}$–], 2.80 (1H, m, $C_{(6\alpha)}$–H), 2.99 (1H, broad signal, $W_{1/2}$=21 Hz, $C_{(8\beta)}$–H), 3.58 (1H, td, *J*=10 and *J*=4 Hz, $C_{(1\beta)}$–H), 3.68 (1H, dd, *J*=12.6 and *J*=10 Hz, $C_{(5)}$–H), and 3.70 (1H, dd, *J*=10 and *J*=2.5 Hz, $C_{(5)}$–H); MS *m/e* 339 (0.3; M^+), 324 (6), 264 (8), 224 (23), and 170 (100). Found: *m/e* 339.3090. Calcd for $C_{21}H_{41}NO_2$: M, 339.3135. The fragment ion peak due to **19** was observed at *m/e* 170.1200. Calcd for $C_9H_{16}NO_2$: M−$C_{12}H_{25}$, 170.1180. (1*R*, 6*S*, 8*R*)-8-Dodecyl-3,3-dimethyl-2,4-dioxa-7-azabicyclo-[4.4.0]decane (**18**): mp 45—47.5 °C (crystallized from hexane–ether), $[\alpha]_D^{23}$ +9° (*c* 0.27; $CHCl_3$); IR (Nujol) 3550, 3300, 1270, 1200, 1090, 1060, 855, and 760 cm^{-1}; ^{1}H-NMR (270 MHz; C_6D_6) δ 0.92 (3H, t, *J*=6.5 Hz, –$CH_2C\underline{H}_3$), 1.40 and 1.56 [each 3H, s, $(CH_3)_2\underline{C}$–], 2.33 (1H, broad signal, $W_{1/2}$=25 Hz, $C_{(8\alpha)}$–H); 2.56 (1H, td, *J*=10 and *J*=4.9 Hz, $C_{(6\alpha)}$–H), 3.47 (1H, ddd, *J*=10.5. *J*=10, and *J*=4 Hz, $C_{(1\beta)}$–H), 3.59 (1H, dd, *J*=10.7 and *J*=10 Hz, $C_{(5\beta)}$–H), and 3.64 (1H, dd, *J*=10.7 and *J*=4.9 Hz, $C_{(5\alpha)}$–H); MS *m/e* 339 (8; M^+), 324 (35), 224 (49), and 170 (100). Found: *m/e* 339.3114. Calcd for $C_{21}H_{41}NO_2$: M, 339.3135. The fragment ion peak due to **19** was observed at *m/e* 170.1193. Calcd for $C_9H_{16}NO_2$: M−$C_{12}H_{25}$, 170.1180.

When a mixture (*ca.* 7 : 6) of **6** and **20** (*vide supra*) was subjected to aminomercuration and then separation by column chromatography as described above, **17**, **18**, and unchanged **20** [elution with ether–methanol (9 : 1)] were obtained in 2, 41, and 46% yields, respectively. The saturated amine (**20**) was found to be identical with an authentic specimen (**20**) described below.

Preparation of the Saturated Amine (20) from its Phthalimide Derivative (21). The known (4*R*, 5*S*)-2,2-dimethyl-4-pentadecyl-5-phthalimido-1,3-dioxane[10] (**21**; *N*-phthaloyldihydrosphingosine acetonide; 25.8 mg) was added to a solution (0.4 ml) prepared from hydrazine hydrate (80%) and ethanol (1 : 7 v/v), and the mixture was refluxed under an argon atmosphere for 1.5 h. The reaction mixture was treated as described for the hydrazinolysis of **15**, giving the saturated amine (**20**; 16.8 mg) in 87% yield. (4*R*, 5*S*)-2,2-Dimethyl-4-pentadecyl-1,3-dioxan-5-amine (**20**): an oil; IR (neat) 3350, 2920, 1265, 1200, 1165, 1090, 860, and 660 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.88 (3H, t-like, –$CH_2C\underline{H}_3$), 1.27 (s, methylene protons in the side chain), 1.38 and 1.43 [each 3H, s, $(CH_3)_2\underline{C}$–], *ca.* 2.4 (1H, m, $C_{(5\alpha)}$–H), 3.44 (2H, m, $C_{(6\beta)}$–H and $C_{(4\beta)}$–H), and 3.85 (1H, dd-like, $C_{(6\alpha)}$–H); MS *m/e* 341 (7; M^+), 326 (100), and 266 (89). Found: *m/e* 341.3282. Calcd for $C_{21}H_{43}NO_2$: M, 341.3292.

Acid Hydrolysis of the (8S)-Acetonide (17). The (8*S*)-acetonide (**17**; 5.1 mg) was added to a solution (2 ml) prepared from 8 M hydrochloric acid and methanol (1 : 9 v/v), and the mixture was refluxed for 2 h. The reaction mixture was treated in the usual way to give a residue, which crystallized from acetone to afford pure **3**. The mother liquor was evaporated, giving a residue which was subjected to purification by preparative TLC to afford additional **3**. The diol (**3**; total 2.6 mg) was obtained in 58% yield. (−)-Deoxoprosopinine (**3**): mp 89.5 °C, $[\alpha]_D^{20}$ −14.7° (*c* 0.30; $CHCl_3$); MS *m/e* 299 (0.2; M^+), 268 (100), and 250 (55). Found: *m/e* 299.2780. Calcd for $C_{18}H_{37}NO_2$: M, 299.2822. The IR (FT-IR; Nujol) and the ^{1}H-NMR (270 MHz; $CDCl_3$) spectra of **3** were found to be identical with those of (+)-deoxoprosopinine[3b] [an enantiomer of **3**; mp 90.7—91 °C (lit,[3b] 85.5 °C); $[\alpha]_D^{18}$ +13° (*c* 0.31; $CHCl_3$) (lit,[3b] +12°); IR (FT-IR; Nujol) 3370, 3310, 3120, 1153, 1095, 1076, 1061, 1053, 1032, 953, and 864 cm^{-1}; ^{1}H-NMR (270 MHz; $CDCl_3$) δ 0.88 (3H, t, *J*=6 Hz, –$CH_2C\underline{H}_3$), 1.27 (24H, s, 12×CH_2), *ca.* 1.6 (2H, m, $C_{(4\alpha)}$–H and $C_{(4\beta)}$–H), 2.55 (2H, broad signal, 2×OH), 2.77 (1H, broad signal, $C_{(6\alpha)}$–H), 2.85 (1H, m, $C_{(2\beta)}$–H), 3.53 (1H, td, *J*=6.5 and *J*=4 Hz, $C_{(3\alpha)}$–H), 3.62 (1H, dd, *J*=10.6 and *J*=4.8 Hz; A part of ABX-system: HO–$C\underline{H}_2$–$\underline{C}$H–), and 3.66 (1H, dd, *J*=10.6 and *J*=8 Hz; B part of ABX-system: HO–$C\underline{H}_2$–$\underline{C}$H–)], prepared from natural (+)-prosopinine (**1**).[3b]

Acid Hydrolysis of the (8R)-Acetonide (18). The same acid hydrolysis of the (8*R*)-acetonide (**18**; 31 mg) gave a product which crystallized from acetone, affording a diol (**4**; 23.5 mg) in 86% yield. (−)-Deoxoprosophylline (**4**): mp 90.5 °C, $[\alpha]_D^{23}$ −14° (*c* 0.24; $CHCl_3$); IR (Nujol) 3400, 3200, 1260, 1120, 1100, 1070, 1060, 1020, 1000, 935, 910, 890, 865, and 830 cm^{-1}; ^{1}H-NMR (270 MHz; $CDCl_3$) δ 0.88 (3H, t, *J*=6 Hz, –$CH_2C\underline{H}_3$), 1.26 (24H, s, 12×CH_2), 1.75 and 2.05 (each 1H, m, $C_{(4\alpha)}$–H and $C_{(4\beta)}$–H), *ca.* 2.3 (2H, broad signal, 2×OH), 2.50 (1H, broad signal, $C_{(6\alpha)}$–H), 2.56 (1H, m, $C_{(2\alpha)}$–H), 3.44 (1H, td, *J*=6.5 and *J*=4 Hz, $C_{(3\beta)}$–H), 3.71 (1H, dd, *J*=10.8 and *J*=5.3 Hz; A part of ABX-system: HO–$C\underline{H}_2$–$\underline{C}$H–), and 3.83 (1H, dd, *J*=10.8 and *J*=4.6 Hz; B part of ABX-system: HO–$C\underline{H}_2$–$\underline{C}$H–); VPC: R_t=13.0 min (SP-1000; 1.5 m; 175 °C; N_2 37 ml/min), R_t=12.7 min (OV-1; 1 m; 175 °C; N_2 38 ml/min), and R_t=14.8 min (OV-17; 1.5

m; 220 °C; N_2 32 ml/min); MS *m/e* 299 (4; M^+), 250 (90), and 130 (100). Found: *m/e* 299.2800. Calcd for $C_{18}H_{37}NO_2$: M, 299.2822. The ^{1}H-NMR (270 MHz; $CDCl_3$) spectrum and retention times (under the three conditions described above) observed for **4** were found to be identical with those for (±)-deoxoprosophylline[3c] [(±)-**4**; mp 83—83.5 °C (lit,[3c] 83 °C)] derived from natural (±)-prosophylline[3c] [(±)-**2**].

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