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Asymmetric Synthesis of (+)-Deoxoprosopinine

Daniel L. Comins,* Matthew J. Sandelier, and
Teresa Abad Grillo

*Department of Chemistry, North Carolina State University,
Raleigh, North Carolina 27695-8204*

daniel_comins@ncsu.edu

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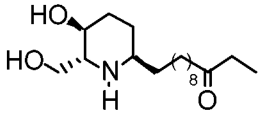
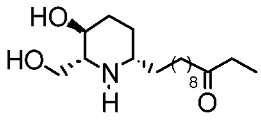
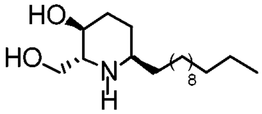
Several 2,6-disubstituted piperidin-3-ol alkaloids have been isolated from *Prosopis africana*,[1] whose leaves have been used in Africa to treat toothaches.[2] Among these various naturally occurring compounds are (+)-prosopinine (**1**) and (±)-prosophylline (**2**). These alkaloids possess antibiotic and anesthetic properties and have attracted considerable interest as synthetic targets.[3] A reduction analogue of prosopinine, (+)-deoxoprosopinine (**3**), also exhibits similar biological properties, and a number of syntheses of this derivative have been reported.[4]



(+)-prosopinine (**1**)

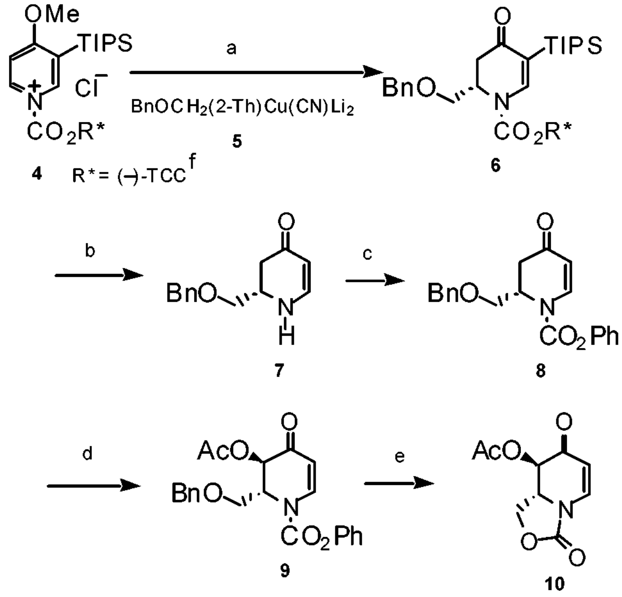


(±)-prosophylline (**2**)



(+)-deoxoprosopinine (**3**)

Scheme 1[a]



[a] Reagents and conditions: (a) **5** (2-Th = 2-thienyl), THF, −78 °C; 10% HCl (70%). (b) NaOMe, MeOH, reflux; HCl, *i*-PrOH (100%). (c) *n*-BuLi, PhOCOCl, THF, −78 °C (94%). (d) Pb(OAc)$_4$, toluene, reflux (57%). (e) HCO$_2$H, reflux, 3.5 h; then NH$_3$, MeOH, 0 °C (73%). (f) (−)-TCC = (1*R*,2*S*)-2-(1-methyl-1-phenylethyl)cyclohexanol.

We describe here a short and efficient total synthesis of enantiopure **3**, which bears a 2,3-*trans*-3,6-*cis* configuration. The synthetic utility of chiral *N*-acyl-2,3-dihydro-4-pyridones has been well-established in the past through the asymmetric syntheses of various indolizidine,[5] quinolizidine,[6] and piperidine[7] alkaloids. This study further demonstrates that utility through the asymmetric synthesis of **3** via the key intermediate dihydropyridone **9**.

The 1-acylpyridinium salt **4**[8] was treated with higher order cyanocuprate **5**[9] to afford dihydropyridone **6** in 70% yield (Scheme 1). Reaction with sodium methoxide followed by aqueous acid provided dihydropyridone **7** in quantitative yield. N-Acylation of **7** with *n*-BuLi and phenyl chloroformate gave a 94% yield of enantiopure carbamate **8**.

Treatment of **8** with Pb(OAc)$_4$[10] afforded **9** in 57% yield (>98% de; $J_{\mathrm{H2-3}} = 1.5$ Hz). Acetoxylation was carried out

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(9) Compound 5 was prepared from benzyl chloromethyl ether by Kaufman's procedure (Kaufman, T. S. *Synlett* **1997**, 1377), followed by transmetalation to the organolithium and then to **5**. All attempts at forming the corresponding α-hetero-Grignard reagent were unsuccessful.

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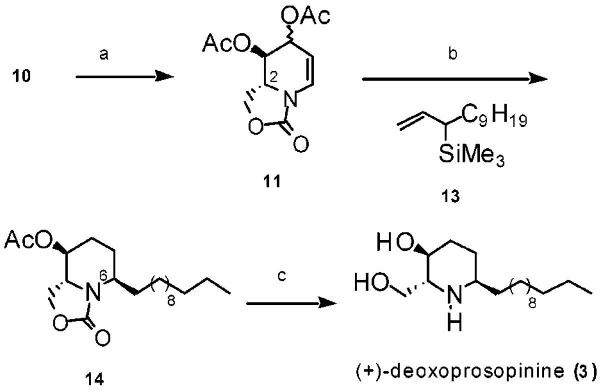
Scheme 2[a]



[a] Reagents and conditions: (a) (1) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH, −40 °C; (2) Ac_2O, Et_3N, DMAP, CH_2Cl_2 (98%, two steps). (b) (1) $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78 °C, **13**; (2) H_2, Pt/C, EtOH (71%, two steps). (c) KOH, EtOH, 140 °C (85%).

prior to cyclization of the carbamate ring in order to achieve the required stereochemistry at C-3. The stereoselectivity results because the C-2 substituent of **8** is in an axial position as a result of $A^{(1,3)}$ strain.[10] Cyclization of **9** was effected by a one-pot procedure involving cleavage of the benzyl ether and formation of a formate ester via refluxing formic acid and subsequent treatment with ammonia in MeOH at 0 °C to afford **10** in 73% yield. The oxazolidinone ring in bicyclic compound **10** is critical in controlling the introduction of the final stereocenter at C-6.

The allylic acetate **11** was generated in 98% yield by selective 1,2-reduction[11] of enone **10** and subsequent acylation (Scheme 2). The bicyclic system in **11** forces the 2-substituent into a pseudoequatorial orientation, and thus the subsequent C-6 addition occurs via a stereoelectronically controlled axial attack[12] to produce the desired *trans*-2,6-product. Lewis acid promoted addition of allylsilane **13**[13] to the *N*-acyliminium ion[14] generated in situ from **11** and $BF_3{\cdot}OEt_2$ afforded **14** in 71% yield after catalytic hydrogenation of the diene intermediate. The addition is completely stereoselective as none of the corresponding cis diastereomer was observed.[15] Finally, saponification in aqueous NaOH of both the acetate ester and the oxazolidinone ring afforded **3** in 85% yield. The mp, $[\alpha]_D$, and ^1H and ^{13}C NMR spectra of our synthetic **3** were in agreement with the literature data.[4b,k]

A highly stereocontrolled asymmetric synthesis of (+)-deoxoprosopinine (**3**) has been carried out in 10 steps from readily available starting materials. The synthetic strategy should be amenable to the preparation of other *Prosopis africana* alkaloids. This synthesis further expands the considerable scope of *N*-acyl-2,3-dihydro-4-pyridones as chiral building blocks for the enantioselective preparation of alkaloid natural products.

Experimental Section

All reactions described in this section were performed using oven-dried glassware under an argon or dry nitrogen atmosphere. THF, toluene, and diethyl ether were dried by distillation from sodium/benzophenone. Other reagents and solvents were stored over molecular sieves under argon and used directly. Radial PLC was done using a model 7924T Chromatotron (Harrison Research, Palo Alto, CA) using thin layers of silica gel-gypsum. Elemental analyses were performed by Atlantic Microlabs, Norcross, GA.

(2*S*-1-[(1*R*,2*S*)-*trans*-2-(α-Cumyl)cyclohexyloxycarbonyl]-2-(benzyloxymethyl)-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (6). To a stirred solution of benzyloxymethyltributylstannane (308 mg, 0.75 mmol) in THF cooled to −78 °C was added 0.375 mL of *n*-butyllithium (2.0 M solution in hexanes). After 30 min of stirring at −78 °C, 3.0 mL of lithium 2-thienylcyanocuprate (0.25 M solution in diethyl ether) was added dropwise. The mixture was allowed to stir for an additional 30 min at −78 °C. In a separate flask, a stirred solution of 4-methoxy-3-(triisopropylsilyl)pyridine (132.8 mg, 0.50 mmol) in toluene was cooled to −30 °C, and 0.52 mL of (−)-TCC chloroformate[8] (1.0 M solution in toluene) was added dropwise. This solution was allowed to stir at −30 °C for 1 h, and then it was cooled to −78 °C. Through a double-tipped stainless steel needle, surrounded by a layer of dry ice, the cuprate solution was slowly transferred to the pyridinium salt solution. The resulting mixture was stirred for 1 h, at which point TLC showed complete disappearance of starting material. The reaction was quenched with 10% aqueous hydrochloric acid, and the mixture was stirred for 1 h. The solution was diluted with EtOAc and then washed with water and brine. The combined aqueous layers were extracted twice with EtOAc, and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification by radial PLC (2−10% EtOAc/hexanes) yielded a colorless oil that solidified upon standing. Recrystallization from methanol afforded 215 mg (70%) of **6** as a white solid, mp 84−85 °C. A small amount (16 mg, 5%) of the minor diastereomer was also isolated. HPLC analysis of the crude reaction mixture showed a de of 82%. $[\alpha]_D^{23}$ −30.9 (*c* 0.12, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.10−7.31 (m, 10H), 4.79 (m, 1H), 4.32 (s, 2H), 2.97−3.10 (m, 3H), 2.40 (m, 1H), 2.18 (m, 2H), 2.00 (m, 1H), 1.61−1.74 (m, 4H), 1.17−1.35 (m, 9H), 0.99−1.04 (m, 22H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.2, 152.5, 147.7, 137.7, 128.4, 128.0, 127.9, 127.7, 125.2, 110.1, 77.8, 73.0, 58.4, 51.0, 50.9, 39.4, 38.1, 33.1, 30.8, 26.7, 25.8, 24.6, 21.5, 18.9, 11.2; IR (thin film, NaCl) 2942, 2863, 1716, 1659 cm^{-1}. Anal. Calcd for $C_{38}H_{55:}NO_4Si$: C, 73.86; H, 8.97; N, 2.27. Found: C, 73.92; H, 9.17; N, 2.34. HRMS calcd for $C_{38}H_{55}NO_4Si$ 618.3979 $(M + H)^+$, found 618.3986.

(2*S*)-2-(Benzyloxymethyl)-2,3-dihydro-4-pyridone (7). To a stirred solution of **6** (370 mg, 0.6 mmol) in MeOH (15 mL) was added 1.37 mL of sodium methoxide (4.36 M solution in MeOH). The solution was heated to reflux, and the reaction was stirred for 18 h. The reation mixture was cooled to room temperature, and 6 N HCl in 2-propanol was added dropwise until the solution reached a pH of 1. This solution was allowed to stir at room temperature for 1.25 h, after which the pH was returned to 7 by the slow addition of solid Na_2CO_3. The solution was concentrated in vacuo, and the resulting residue was dissolved in EtOAc and filtered through Celite. Concentration in vacuo and purification by radial PLC (50−100% EtOAc/hexanes) gave 134 mg (100%) of **7** as a white solid, mp 107.8−108.3 °C. $[\alpha]_D^{23}$ +285.3 (*c* 0.38, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.30−7.40 (m, 5H), 7.16 (d, 1H, $J = 7.0$ Hz), 5.34 (br s, 1H), 5.02 (d, 1H, $J = 7.5$ Hz), 4.56 (s, 1H), 3.92 (m, 1H), 3.56 (m, 2H), 2.34 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.7, 150.8, 137.4, 128.6, 128.1, 127.9, 99.5, 73.5, 71.6, 52.8, 38.4; IR (thin film, NaCl) 3255, 3036, 2858, 1619 cm^{-1}. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.58; H, 6.92; N, 6.37.

(2*S*)-2-(Benzyloxymethyl)-1-(phenoxycarbonyl)-2,3-dihydro-4-pyridone (8). To a solution of **7** (16 mg, 0.0736 mmol)

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(15) The C2, C6 trans stereochemistry in **14** was confirmed by the observation of an NOE interaction between the C6 side chain protons and the C2 proton.

in 1.0 mL of THF, cooled to −78 °C, was added 0.03 mL of *n*-butyllithium (2.5 M solution in hexanes), and the mixture was stirred for 20 min. Phenyl chloroformate (0.010 mL, 0.078 mmol) was added, and the solution was stirred for 30 min. The reaction was quenched with saturated $NaHCO_3$ and then warmed to room temperature. The solution was extracted with EtOAc, washed with water (3×), dried over $MgSO_4$, and concentrated in vacuo. Purification by radial PLC (10−20% EtOAc/hexanes) gave 23.2 mg (94%) of **8** as colorless oil. $[\alpha]_D^{23}$ −44.4 (*c* 2.17, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.0 Hz, 1H), 7.21−7.38 (m, 8H), 7.05 (m, 2H), 5.39 (d, *J* = 8.2 Hz, 1H), 4.95 (m, 1H), 4.51 (q, *J* = 11.9 Hz, 2H), 3.72 (m, 1H), 3.60 (m, 1H), 2.92 (dd, *J* = 6.9, 16.6 Hz, 1H), 2.62 (d, *J* = 16.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.4, 151.5, 150.6, 141.7, 137.6, 129.6, 128.6, 127.9, 126.4, 121.4, 108.0, 73.5, 68.5, 52.9, 37.5; IR (thin film, NaCl) 3064, 2864, 1738, 1674, 1608 cm^{-1}. Anal. Calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.19; H, 5.67; N, 4.08.

(2*R*,3*R*)-3-Acetoxy-2-(benzyloxymethyl)-1-(phenoxycarbonyl)-2,3-dihydro-4-pyridone (9). To a flask containing **8** (27 mg, 0.080 mmol) under a dry nitrogen atmosphere was added $Pb(OAc)_4$ (92 mg, 0.21 mmol, freshly recrystallized from glacial acetic acid and dried in vacuo). Toluene (15 mL) was added, and the mixture was heated at reflux for 18 h. By TLC, the reaction was not complete, and no active $Pb(OAc)_4$ appeared to be present. Additional $Pb(OAc)_4$ (35 mg, 0.080 mmol) was added, and refluxing was resumed for another 6 h. After cooling to room temperature, the solution was filtered through silica gel with EtOAc and concentrated in vacuo. Purification by radial PLC (20% EtOAc/hexanes) gave 18 mg (57%) of **9** as a colorless oil. $[\alpha]_D^{23}$ +88.5 (*c* 2.055, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, 1H, *J* = 8.4 Hz), 7.25−7.42 (m, 10H), 7.07 (m, 2H), 5.50 (d, 1H, *J* = 8.6 Hz), 5.29 (s, 1H), 4.91 (br s, 1H), 4.53 (s, 2H), 3.77 (m, 2H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.6, 169.6, 150.5, 142.7, 137.3, 129.8, 128.7, 128.1, 127.9, 126.7, 121.4, 106.5, 73.7, 70.1, 67.5, 58.1, 21.2; IR (thin film, NaCl) 3076, 2920, 2858, 1745, 1677 cm^{-1}. Anal. Calcd for $C_{22}H_{21}NO_6$: C, 66.83; H, 5.35; N, 3.54. Found: C, 66.77; H, 5.34; N, 3.49.

(8*R*,9*R*)-8-Acetoxy-8,8a-dihydro-1*H*-oxazolo[3,4-α]pyridine-3,7-dione (10). A solution of **9** (342 mg, 0.865 mmol) in formic acid (9 mL) was refluxed for 3.5 h. The solution was concentrated in vacuo. The residue was dissolved in MeOH and cooled to 0 °C. To this solution was added 0.432 mL of ammonia (2.0 M solution in methanol), and the mixture was stirred for 30 min. The ammonia was then quenched with a few drops of glacial acetic acid, and the solution was concentrated in vacuo. Purification by radial PLC and recrystallization from EtOAc afforded 134 mg (73%) of **10** as a white solid, mp 180.8−182.0 °C. $[\alpha]_D^{23}$ +374.5 (*c* 0.235, MeOH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, 1H, *J* = 7.8 Hz), 5.56 (d, 1H, *J* = 7.7 Hz), 5.42 (d, 1H, *J* = 13.0 Hz), 4.69 (t, 1H, *J* = 13.0 Hz), 4.69 (t, 1H, *J* = 8.0 Hz), 4.48 (m, 1H), 4.34 (t, 1H, *J* = 9.2 Hz), 2.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.4, 169.7, 151.9, 139.2, 107.4, 72.7, 67.9, 55.1, 20.7; IR (thin film, NaCl) 2915, 2849, 1777, 1752, 1677 cm^{-1}. Anal. Calcd for $C_9H_9NO_5$: C, 51.19; H, 4.30; N, 6.63. Found: C, 51.27; H, 4.50; N, 6.35.

Acetic Acid (2*R*,8*R*)7-Acetoxy-3-oxo-1,7,8,8a-tetrahydro-oxazolo[3,4-a]pyridin-8-yl Ester (11). Solid $CeCl_3 \cdot 7H_2O$ (353 mg, 0.94 mmol) was added to a solution of **10** (100 mg, 0.47 mmol) in anhydrous MeOH (29 mL). Once homogeneous, $NaBH_4$ (53.8 mg, 1.42 mmol) was added to the resulting solution at −40 °C. After 30 min of stirring at −40 °C, the reaction was quenched by addition of acetone (1 mL) and allowed to warm to room temperature. The mixture was concentrated ,and dry CH_2Cl_2 (5 mL) was added under Ar. Triethylamine (0.19 mL, 1.41 mmol) was added followed by Ac_2O (0.13 mL, 1.41 mmol) and DMAP (catalytic amount) at room temperature. After 12 h the mixture was concentrated, and the residue was purified by chromatography (silica gel, 15% EtOAc/hexanes) to give **11** as a diastereomeric mixture of acetate esters (118 mg, 98%). Major diastereomer: ^1H NMR ($CDCl_3$, 300 MHz) δ 6.69 (dd, *J* = 2.0, 7.8 Hz, 1H), 5.64 (d, *J* = 7.8 Hz, 1H), 5.18 (dd, *J* = 8.1, 10.2 Hz, 1H), 4.95 (dd, *J* = 2.1, 8.1 Hz, 1H), 4.51 (t, *J* = 9.0 Hz, 1H), 4.27 (t, *J* = 9.0 Hz, 1H), 4.13 (m, 1H), 2.10 (s, 3H), 2.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 170.3, 153.2, 123.6, 105.95, 71.2, 70.25, 67.15, 54.1, 21.1, 20.8. Minor diastereomer: ^1H NMR ($CDCl_3$, 300 MHz) δ 6.73 (dd, *J* = 2.1, 8.1 Hz, 1H), 5.65 (d, *J* = 2.4 Hz, 1H), 5.47 (d, *J* = 2.4 Hz, 1H), 4.87 (d, *J* = 8.8 Hz, 1H), 4.49 (t, *J* = 8.1 Hz, 1H), 4.43 (m, 1H), 4.05 (t, *J* = 8.1 Hz, 1H), 2.16 (s, 3H), 2.05 (s, 3H). EIMS (*m/z*) 256 $(M)^+$ (100); HRMS calcd for $C_{11}H_{23}NO_3$ 256.0821, found 256.0812.

Acetic Acid (2*R*,5*R*,8*S*)-5-Dodecyl-3-oxo-hexahydro-oxazolo[3,4-a]pyridin-8-yl Ester (14). A solution of **13** (282.5 mg, 1.17 mmol) in CH_2Cl_2 (4 mL) was added via cannula to a precooled (−78 °C) solution of **11** in CH_2Cl_2 (2.35 mL) under Ar, followed by dropwise addition of $BF_3 \cdot OEt_2$ (0.10 mL, 0.7 mmol). After 1 h at −78 °C, the reaction was gradually warmed to −10 °C over a period of 3 h. The solution was cooled again to −30 °C and then quenched with an aqueous saturated solution of ammonium chloride. The reaction mixture was warmed to room temperature and extracted with CH_2Cl_2 (3 × 5 mL). The combined extracts were washed with brine and dried (Na_2SO_4). The solvent was removed under vacuo to give the crude product, which was unstable on silica gel (^1H NMR ($CDCl_3$, 500 MHz) δ 5.87 (dd, *J* = 2.5, 9.2 Hz, 1H), 5.70 (d, *J* = 10.2 Hz, 1H), 5.17 (dd, *J* = 1.8, 7.6 Hz, 1H), 4.44 (t, *J* = 8.9 Hz, 1H), 4.30 (dd, *J* = 4.8, 9.4 Hz, 1H), 4.22 (m, 1H), 3.70 (m, 1H), 2.35 (t, *J* = 6.7 Hz, 2H), 2.12 (s, 3H), 1.98 (q, *J* = 7.1 Hz, 2H), 1.32 (br s, 14H), 0.85 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.6, 156.9, 135.4, 130.7, 125.5, 124.4, 69.4, 67.6, 52.7, 50.7, 36.9, 32.8, 32.1, 29.9, 29.8, 29.7, 29.6, 22.9, 21.2, 14.3). A solution of the crude product in EtOH (4 mL) was added to a mixture of 5% Pt on carbon (4.6 mg, 0.02 mmol of Pt) in ethanol (7 mL). The mixture was stirred under H_2 (1 atm) for 5 h and then filtered through a Celite pad. The solvent was removed, and the residue was purified by chromatography (silica gel, 20% EtOAc/hexanes) to give **14** as a white solid (61 mg, 71%, 2 steps), mp 77.5−78.5 °C. $[\alpha]_D^{23}$ +20.4 (c 0.225, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.48 (m, 1H), 4.35 (m, 1H), 4.11 (m, 1H), 3.91 (m, 1H), 3.68 (m, 1H), 2.06 (s, 3H), 1.58−1.81 (m, 5H), 1.45 (m, 1H), 1.25 (br s, 20H), 0.88 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 157.0, 72.7, 66.4, 53.9, 49.1, 32.1, 30.0, 29.9, 29.8, 29.7, 29.6, 26.5, 24.9, 22.9, 21.2, 14.3; IR (thin film, NaCl) 2922, 2850, 1738 cm^{-1}; HRMS calcd for $C_{22}H_{38}NO_4$ 368.2801 $(M + H)^+$, found 368.2799.

(2*R*,3*S*,6*R*)-6-Dodecyl-2-hydroxymethyl-pyperidin-3-ol, (+)-Deoxoprosopinine (3). A solution of **14** (27.5 mg, 0.075 mmol) in a mixture of EtOH (2.7 mL) and 8 M aqueous KOH (2.7 mL) was heated at 140 °C in a sealed tube for 12 h. After cooling to room temperature, the solution was diluted with H_2O (60 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were dried and concentrated in vacuo. The residue was purified by chromatography (silica gel, CH_2Cl_2/MeOH/NH_4OH = 9:1:1) to give **3** (19.3 mg, 86%) as colorless crystals, mp 88.5 °C. $[\alpha]_D^{23}$ +12.2 (*c* 0.015, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 3.60−3.67 (m, 2H), 3.54 (m, 1H), 2.87 (br q, *J* = 6.0 Hz, 1H), 2.76 (br q, *J* = 5.0 Hz, 1H), 2.00 (br s, 3H), 1.47−1.77 (m, 4H), 1.26 (br s, 22H), 0.88 (t, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 68.3, 62.5, 58.3, 50.0, 34.2, 32.2, 29.8, 29.6, 28.8, 27.6, 26.6, 22.9, 14.3; EIMS (*m/z*) 300.0 $(M)^+$ (100); HRMS calcd for $C_{18}H_{37}NO_2$ 300.2903, found 300.2916.

1-Chloro-dodec-2-ene (12).[13] To a solution of *trans*-2-dodecen-1-ol (184.3 mg, 1 mmol) in CH_2Cl_2 (10 mL) at room temperature was added CCl_4 (0.3 mL, 3 mmol) followed by Ph_3P (393.4 mg, 1.5 mmol). After 16 h of stirring, the solvent was removed under reduced pressure, and the residue was purified by chromatography (silica gel, 10% EtOAc/hexanes) to give **12** (183.0 mg, 90%) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.76 (m, 1H), 5.60 (m, 2H), 4.03 (d, *J* = 7.2 Hz, 2H), 2.05 (dd, *J* = 6.2, 13.6 Hz, 2H), 1.26 (br s, 14H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.4, 126.0, 45.6, 32.2, 32.1, 29.7, 29.6, 29.5, 29.3, 29.0, 22.8, 14.2.

Trimethyl-(1-nonyl-allyl)-silane (13).[13] To a stirred solution of hexamethyldisilane (0.46 mL, 2.25 mmol) in HMPA (2.8 mL) at 0 °C was added methyllithium (1.5 mL, 2.25 mmol, 1.5 M MeLi·LiBr complex in ether) dropwise. After 3 min, the red solution was treated with $CuBr \cdot Me_2S$ (462.0 mg, 2.25 mmol) in Me_2S (1 mL), and the resulting black reaction mixture was stirred for 3 min. Ether (5.6 mL) was added, and the reaction mixture was cooled to −60 °C and stirred for 5 min. A solution of **12** (183.0 mg, 0.90 mmol) in ether (0.9 mL) was added dropwise, and the mixture was stirred for 1 h at −60 to −40 °C. The cold solution was poured into a mixture of hexanes (50 mL) and saturated ammonium chloride solution (50 mL, buffered to pH 8 by the addition of ammonium hydroxide), and the mixture was stirred vigorously for 1 h. The aqueous phase was extracted with hexanes, and the combined organic extracts were dried (Na_2SO_4) and concentrated. Purification by chromatography (silica gel, hexanes) gave **13** (129.7 mg, 54%) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.60 (m, 1H), 4.84 (m, 2H), 1.32 (m, 2H), 1.26 (br s, 15H), 0.88 (t, $J = 6.6$ Hz, 3H), −0.03 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 140.8, 111.8, 35.4, 32.4, 30.2, 29.9, 29.8, 29.5, 22.8, 14.3, −2.2.

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Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra for **3**, **11**, and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

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