

SYNTHESIS AND REACTIONS OF ENANTIOPURE 1-ACYL-2-[TRIARYL(ALKYL)SILYL]-2,3-DIHYDRO-4-PYRIDONES

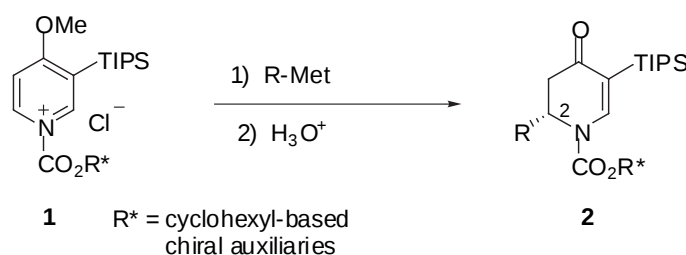
Daniel L. Comins,^{a*} Michael O. Killpack,^b Emilie Despagnet,^a and Emmanuel Zeller^a

^aDepartment of Chemistry, North Carolina State University, Raleigh, NC 27695-8204, USA

^bDepartment of Chemistry and Biochemistry, Utah State University, Logan, UT 84322-0300, USA

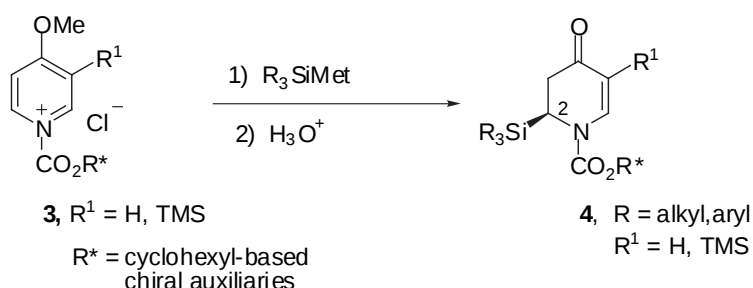
Abstract – The addition of triphenylsilyl- or dimethylphenylsilylmagnesium bromide to certain chiral 1-acylpyridinium salts affords C-2 silylated dihydro-4-pyridones in good yield and high diastereoselectivity (84 – 96% de). Reduction and substitution reactions of these heterocycles were examined to explore their utility as chiral building blocks. Several highly stereoselective transformations were observed.

For several years we have been exploring the utility of enantiopure *N*-acyl-2,3-dihydro-4-pyridones as chiral building blocks for the stereocontrolled synthesis of various alkaloids and natural products.¹ These dihydropyridones are prepared by the addition of Grignard reagents or metallo enolates to chiral 1-acylpyridinium salts.² For example, the reaction of enantiopure 1-acylpyridinium salt (**1**), prepared in situ from 4-methoxy-3-triisopropylsilylpyridine and the chloroformate of (-)-*trans*-2-(α -cumyl)cyclohexanol (TCC),³ with aliphatic Grignard reagents provides dihydropyridones (**2**) in high yield and 85-95% de (Scheme 1).



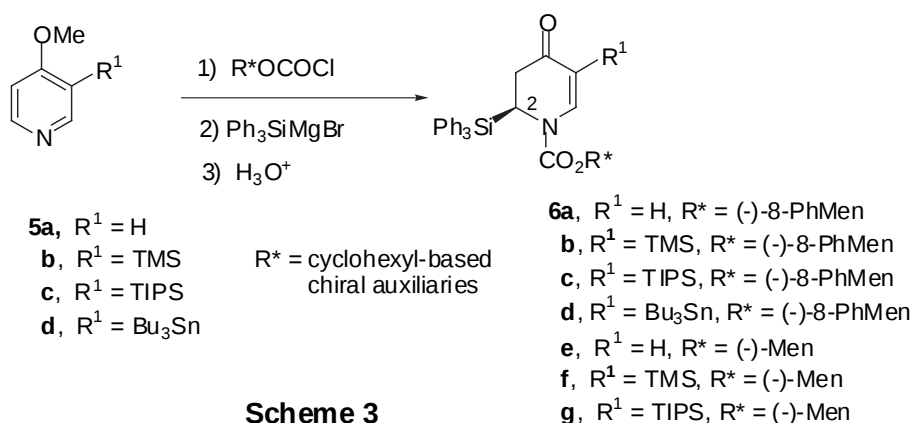
Scheme 1

The absolute stereochemistry at C-2 of the major diastereomer (**2**) was shown to be the (*R*) configuration. Interestingly, in contrast to carbanions, silicon nucleophiles add to the corresponding 1-acylpyridinium salts (**3**) from the opposite face to give the dihydropyridones (**4**) with the (*S*) configuration at C-2 (Scheme 2).⁴ Reported herein is a study of this unique asymmetric reaction and synthetic transformations of the resulting silylated dihydropyridones (**4**).



Scheme 2

The reaction of triphenylsilylmagnesium bromide⁵ with various chiral 1-acylpyridinium salts to give dihydropyridones (**6**) was investigated (Scheme 3). The pyridinium salts were prepared from 4-methoxypyridine, 4-methoxy-3-trimethylsilylpyridine,⁶ 4-methoxy-3-tributylstannylpyridine² or 4-methoxy-3-triisopropylsilylpyridine,² and the chloroformate of (-)-menthol (Men) or (-)-8-phenylmenthol (8-PhMen).² The results of this study are shown in Table 1.



Scheme 3

Poor de's were observed when (-)-menthol was the chiral auxiliary (Entries 1-3). When the corresponding 8-phenylmenthol-derived pyridinium salts were used, excellent de's were obtained for most reactions. It was interesting that pyridine (**5c**), which gives the best results with Grignard reagents,² afforded product (**6c**) with a low de (Entry 4). When the TIPS group was replaced with a TMS or Bu₃Sn group or a proton, an excellent degree of asymmetric induction was observed (Entries 5-8). In contrast to

our earlier work with Grignard reagents and enolates as nucleophiles, a large trialkylsilyl blocking group is not needed at C-3 of the pyridinium salt in order to obtain excellent de's. Also, the direction of asymmetric induction is opposite to that observed in the corresponding reactions with carbanions. The stereochemical assignment was confirmed by single-crystal X-Ray analysis⁷ of **6a** (R* = 8-PhMen) and by conversion of **6b** to **6a** with HBr/HOAc. The reversal in stereochemistry might be a result of chelation control as shown in Figure 1.

Table 1. Preparation of 1-Acyl-2-triphenylsilyl-2,3-dihydropyridones (**6**).

Entry ^a	R ¹	R*	Solvent	Diastereomer Ratio ^b	Yield ^d (%)
1	H	Men	THF	56 : 42	63
2	TMS	Men	THF	63 : 37	65
3	TIPS	Men	THF	73 : 27	68
4	TIPS	8-PhMen	THF	58 : 42	65
5	TMS	8-PhMen	THF	93: 7	62
6	TMS	8-PhMen	Toluene/THF	92: 8	73
7	Bu ₃ Sn	8-PhMen	Toluene/THF	92: 8 ^c	40
8	H	8-PhMen	Toluene/THF	98 : 2	88

^aAll reactions were performed on a 1 mmol scale. ^bRatio was determined by HPLC analysis of the crude product. ^cAcidic workup removed the Bu₃Sn group to give the same diastereomeric products as Entry 8.

^dYield of products obtained from radial PLC (silica gel, EtOAc/hexanes).

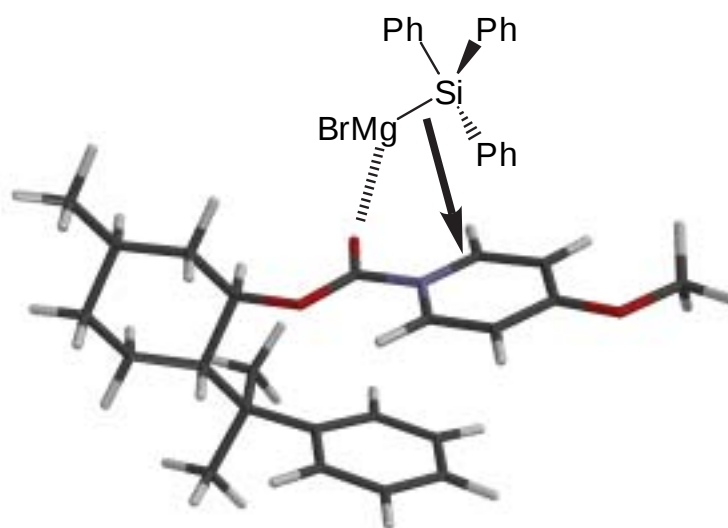
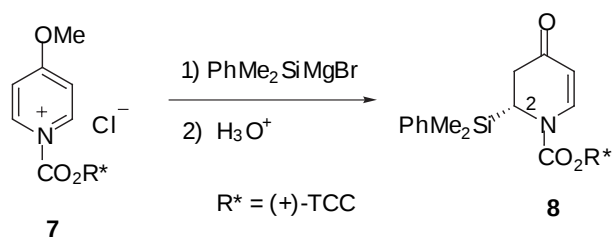


Figure 1. Working model derived from molecular mechanics

To determine if a smaller silyl nucleophile would also afford a high degree of asymmetric induction in this reaction, dimethylphenylsilylmagnesium bromide⁸ was prepared and added to chiral 1-acylpyridinium salt (**7**) (Scheme 4). Remarkably, a 90% yield of dihydropyridone (**8**) was isolated. The diastereoselectivity of this reaction was determined to be 98% by HPLC analysis of the crude product.



Scheme 4

Synthetic transformations of dihydropyridones (**6a**) and (**8**) were investigated (Scheme 5). The copper-mediated addition of methyl Grignard to **6a** afforded a 78% yield of 2,6-*trans*-piperidone (**9**). The *trans* stereochemistry of **9** was anticipated based on the low-energy conformation of **6a** found by molecular modeling⁹ (Figure 2) and X-Ray analysis.⁷ Due to $A^{(1,3)}$ strain,¹⁰ the Ph_3Si group of **6a** occupies the axial position shielding the top face of the molecule.

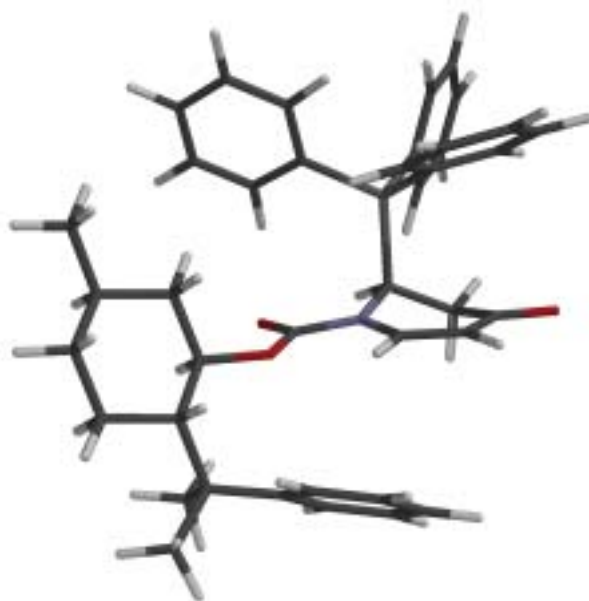
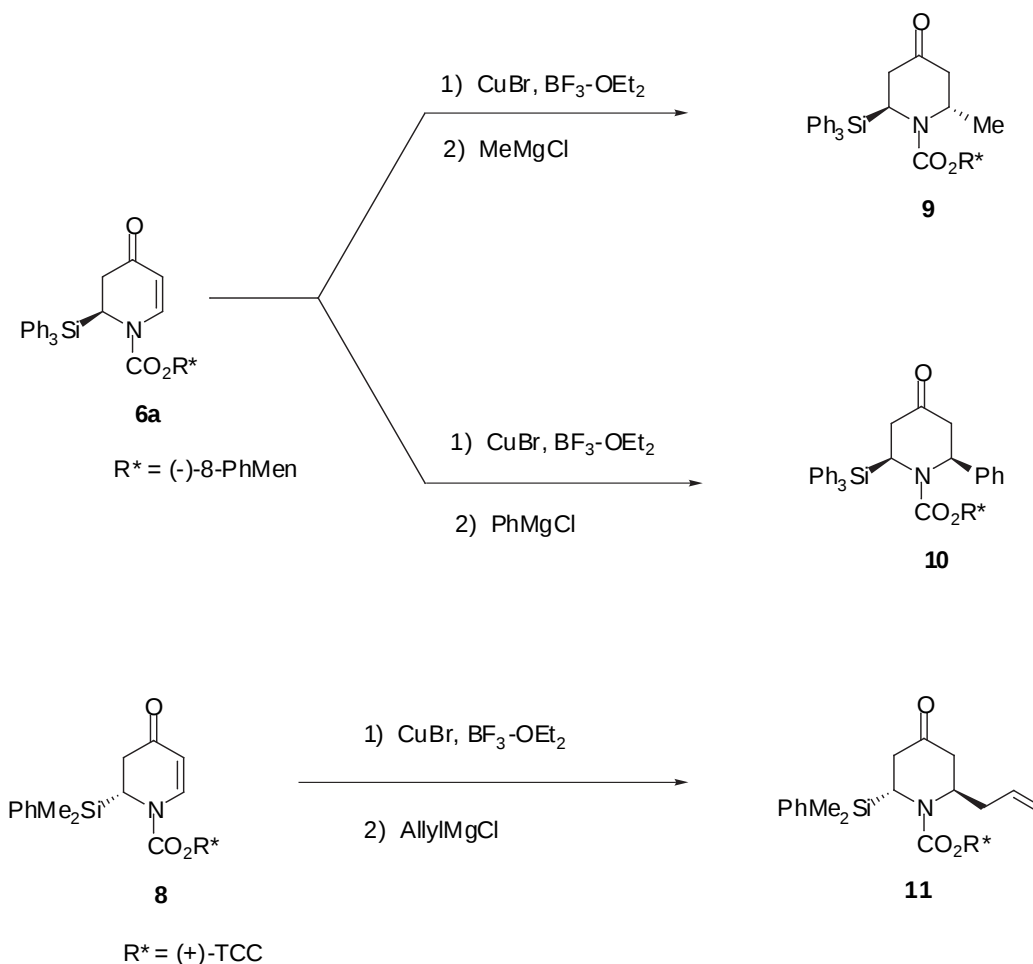


Figure 2. Low energy conformation of **6a** (MMFF)

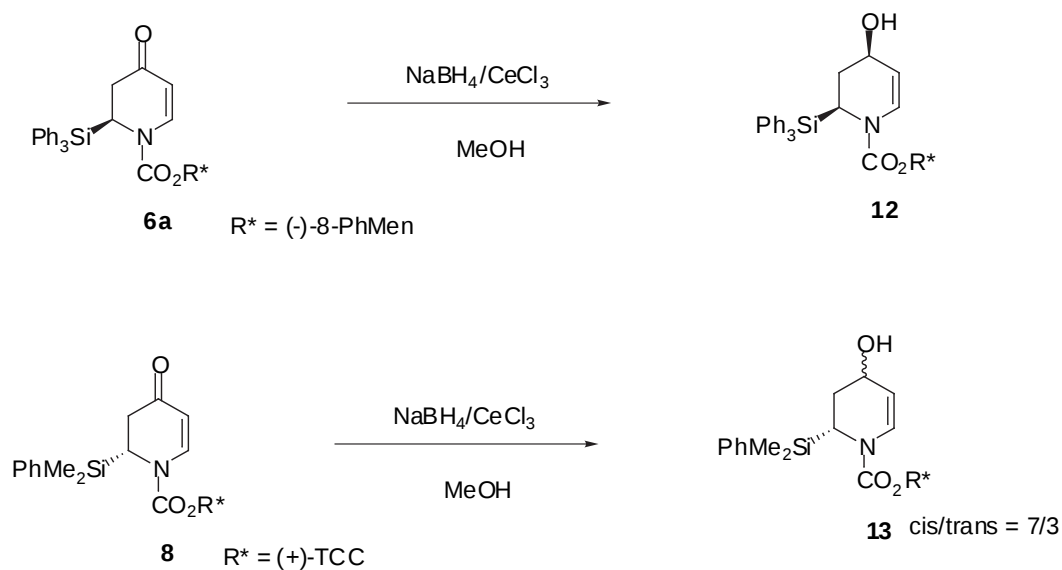
In contrast, the analogous reaction of **6a** using phenylmagnesium chloride gave a 65% yield of the *cis* product (**10**). At this time, we do not have an explanation for this reversal of stereoselectivity. When dihydropyridone (**8**) was treated with allyl Grignard/CuBr, the *trans* piperidone (**11**) was isolated as the sole product in 85% yield.



Scheme 5

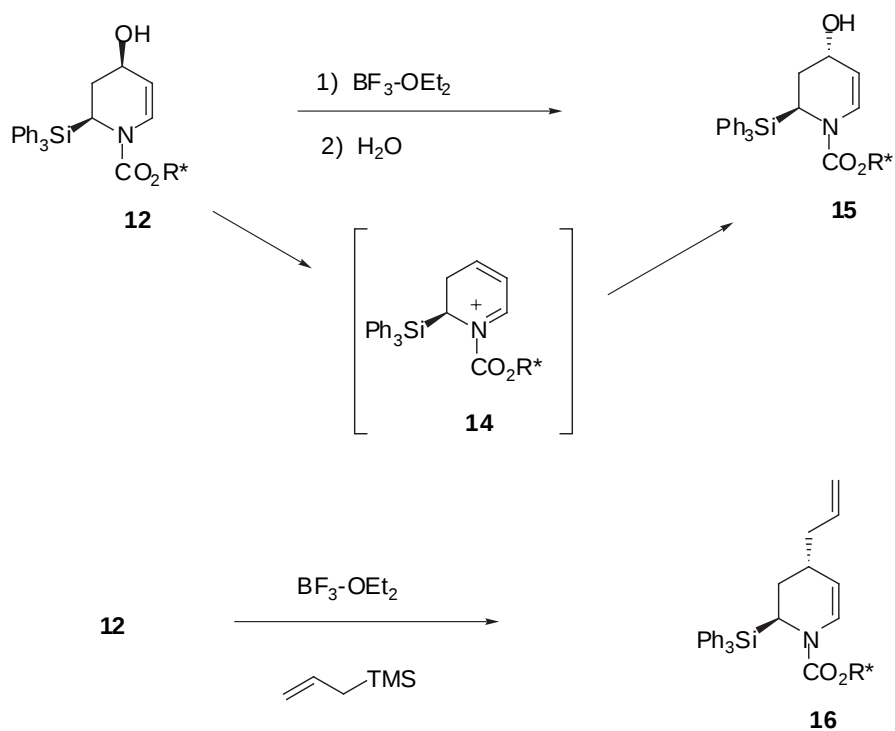
Luche reduction of the C-4 carbonyl group of **6a** and **8** was investigated (Scheme 6). Treatment of **6a** with $\text{NaBH}_4/\text{CeCl}_3$ afforded a 98% yield of the *cis* alcohol (**12**). The exclusive formation of the axial alcohol clearly demonstrates the effective top-face shielding of the carbonyl by the C-2 Ph_3Si group. When **8** was reduced under the same conditions, a mixture of alcohols (**13**) was observed. Obviously, the smaller Me_2PhSi group is less effective at blocking hydride attack at the C-4 carbonyl.

The alcohols (**12**) and (**13**) are *N*-acyliminium ion precursors.¹¹ When **12** in toluene was treated with $\text{BF}_3\text{-OEt}_2$, followed by addition of water, a near quantitative yield of epimeric alcohol (**15**) was formed (Scheme 7). This reaction proceeds *via* the iminium ion (**14**) which is attacked by water at C-4 on the face anti to the Ph_3Si group. Treatment of **12** with $\text{BF}_3\text{-OEt}_2$ and allyltrimethylsilane in CH_2Cl_2 afforded ene carbamate (**16**) in high yield. The regio- and stereoselectivity of this reaction was determined to be greater than 96% by NMR spectral analysis.

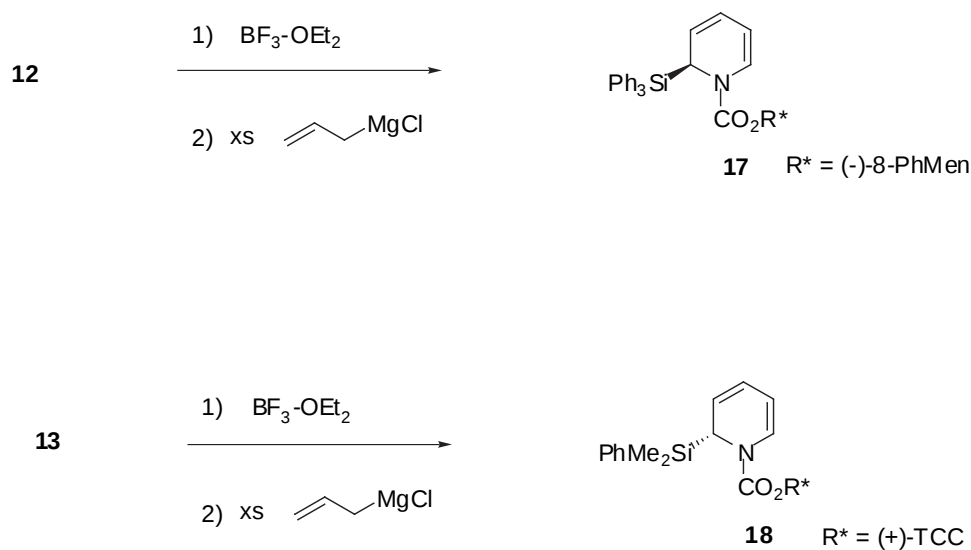


Scheme 6

Interestingly, when alcohols (**12**) and (**13**) are treated with $\text{BF}_3 \cdot \text{OEt}_2$ and allylmagnesium chloride, the unique dihydropyridines (**17**) and (**18**) result (Scheme 8). The Grignard reagent must act as a base which deprotonates iminium ion (**14**) to give the observed products.

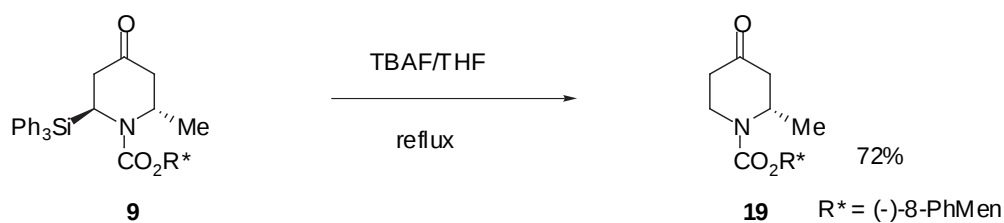


Scheme 7



Scheme 8

Once the C-2 R_3Si group has completed its usefulness as a chiral controller, it can be removed from the piperidine ring by treatment with tetrabutylammonium fluoride. For example, silane (**9**) was converted to piperidone (**10**) in good yield using this simple procedure (Scheme 9).



Scheme 9

In summary, enantiopure C-2 silylated dihydropyridones and dihydropyridines have been prepared by efficient asymmetric synthesis, and various chemical reactions of these heterocycles have been examined. These compounds and their derivatives have potential as chiral building blocks for various natural products and biologically active compounds.

EXPERIMENTAL

All reactions were performed in oven-dried glassware under a N₂ atmosphere. Tetrahydrofuran (THF) was dried by distillation from sodium/benzophenone ketyl prior to use. Pyridine and substituted pyridines were distilled from calcium hydride and stored over 4 Å molecular sieves under N₂. Other solvents and reagents from commercial sources were stored over 3 Å molecular sieves and used without further purification. Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were recorded on a Varian XL-300, Gemini-300, or Mercury-400 spectrometers. Radial preparative-layer chromatography (Radial PLC) was carried out by using a chromatotron (Harris Associates, Palo Alto, CA). IR spectra were recorded on a Perkin-Elmer model 7500 spectrophotometer. Elemental analyses were carried out by Atlantic Microlab, Inc. (Norcross, GA).

Preparation of Triphenylsilylmagnesium Chloride. Freshly cut lithium metal (8 mmol, 0.05 g) (excess lithium may be added to reduce the reaction time) was placed in a 25-mL flask under N₂ and washed with hexanes (10 mL). THF (10 mL) was added followed by the addition of chlorotriphenylsilane (1.5 mmol, 0.442 g). The solution was stirred for 4-12 h at rt (the solution first forms a white precipitate, then a brown milky mixture, and finally a homogeneous, dark black solution of triphenylsilyllithium). When prepared on a larger scale, it may take as long as 2 days for the reaction to turn black. In a separate 50-mL flask containing THF (10 mL) and magnesium turnings (4 mmol, 0.10 g) was added 1,2-dibromoethane (0.16 mL, 2.5 mmol), and the mixture was refluxed for 3 h. The heating mantle was removed and the black solution of triphenylsilyllithium was transferred by syringe into the solution of MgBr₂/THF at rt forming a purple solution. The mixture was stirred for 30 min at rt and then added directly to the 1-acylpyridinium salt *via* a syringe.

Preparation of (-)-1-((1*R*,2*S*,5*R*)-8-Phenylmenthoxycarbonyl)-(S)-2-triphenylsilyl-2,3-dihydro-4-pyridone (6a). **General Procedure for the Preparation of Chiral 2-Triphenylsilyl-2,3-dihydropyridones.** To a 100-mL flask equipped with a mechanical stirrer was added (-)-8-phenylmenthyl chloroformate (2.19 g, 7.44 mmol), toluene (40 mL), and 4-methoxypyridine (0.89 mL, 8.2 mmol) at -23 °C. After 15 min, the solution was cooled to -85 °C (Et₂O/CO₂) and then Ph₃SiMgCl, (prepared from 3.30 g (11.1 mmol) of Ph₃SiCl, was added dropwise over 15 min. The mixture was stirred for an additional 30 min at -85 °C and then the cooling bath was removed. The mixture was allowed to come to rt over 30 min followed by the addition of a saturated aqueous solution of oxalic acid (40 mL). The mixture was stirred at rt for 5 min, was extracted with Et₂O (2 x 30 mL), and washed with brine (30 mL). The solution was dried (MgSO₄), concentrated, and checked by HPLC (m-Porasil, 10% EtOAc/hexanes) for diastereomeric excess (96%). The crude product was purified by radial PLC (5-30% EtOAc/hexanes) to give 4.03 g (88%) of a white foam. The product was further purified by recrystallization from 5% EtOAc/hexanes to give **6a** as clear colorless crystals, mp 163.5-164.5 °C. IR (neat) 2959, 2922, 1712, 1672, 1595, 1429, 1362, 1260, 1107 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.55 – 7.00 (m, 20 H), 6.43 (d, 1H, *J* = 8.1 Hz), 5.02 (d, 1 H, *J* = 8.1 Hz), 4.74 (d, 1 H, *J* = 8.4 Hz), 4.53 (dt, 1 H, *J* = 4.5, 10.5 Hz), 2.83 (dd, 1 H, *J* = 8.4, 17.1 Hz), 2.61 (d, 1 H, *J* = 17.1 Hz), 2.10 – 0.40 (m, 17 H); ¹³C NMR (75 MHz, CDCl₃) δ 191.82, 151.81, 150.75, 142.86, 136.26, 131.56, 129.95, 127.89, 125.25,

124.69, 107.00, 77.37, 50.47, 43.41, 41.06, 39.03, 37.49, 34.27, 30.98, 29.96, 26.05, 22.12, 21.58. Anal. Calcd for $C_{40}H_{43}NO_3Si$: C, 78.26; H, 7.06; N, 2.28. Found C, 78.40; H, 6.98; N, 2.30. $[\alpha]_D^{20}$ -60.0° (c = 1, CH_2Cl_2).

Spectral data. **1-((1*R*,2*S*,5*R*)-8-Phenylmenthoxycarbonyl)-(R)-2-triphenylsilyl-2,3-dihydro-4-pyridone (epi-6a, 2*R*).** IR (neat) 3049, 2958, 1709, 1672, 1601, 1427, 1321, 1261, 1190, 1107 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, 1 H, J = 8.1 Hz), 7.70 – 6.95 (m, 20 H), 4.98 (d, 1 H, J = 8.1 Hz), 4.68 (dt, 1 H, J = 4.5, 10.5 Hz), 3.70 (d, 1 H, J = 8.4 Hz) 2.64 (dd, 1 H, J = 8.4, 17.4 Hz), 2.26 (d, 1 H, J = 17.4 Hz), 2.20 – 0.20 (m, 17 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.35, 152.47, 152.06, 143.21, 136.42, 131.35, 130.14, 128.26, 128.00, 125.03, 108.48, 78.02, 50.05, 42.69, 39.76, 39.26, 38.16, 34.12, 30.97, 30.52, 26.27, 22.13, 21.55. Anal. Calcd for $C_{40}H_{43}NO_3Si$: C, 78.26; H, 7.06; N, 2.28. Found: C, 78.16; H, 7.21; N, 2.29. $[\alpha]_D^{20}$ – 18.7° (c = 1, CH_2Cl_2).

1-((1*R*,2*S*,5*R*)-8-Phenylmenthoxycarbonyl)-5-trimethylsilyl-(S)-2-triphenylsilyl-2,3-dihydro-4-pyridone (6b). IR (neat) 2953, 1710, 1656, 1571, 1362, 1305, 1256, 1109 cm^{-1} . 1H NMR (300 MHz, $CDCl_3$) δ 7.90 – 6.90 (m, 20 H), 6.70 (s, 1 H), 4.98 (d, 1 H, J = 7.8 Hz), 4.58 (dt, 1 H, J = 4.5, 10.5 Hz), 2.79 (dd, 1 H, J = 8.4, 16.8 Hz), 2.61 (d, 1 H, J = 16.8 Hz), 2.00 – 0.40 (m, 17 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.69, 151.77, 150.96, 147.26, 136.37, 134.96, 131.56, 129.92, 127.87, 125.25, 124.73, 114.50, 76.89, 50.77, 43.82, 41.20, 39.12, 38.14, 34.17, 31.54, 31.02, 29.71, 26.10, 22.61, 22.31, 21.60, 14.10, - 1.64. Anal. Calcd for $C_{43}H_{51}NO_3Si_2$: C, 75.28; H, 7.49; N, 2.04. Found: C, 75.33; H, 7.44; N, 1.89. $[\alpha]_D^{20}$ - 48.9° (c = 1, CH_2Cl_2).

1-((1*R*,2*S*,5*R*)-8-Phenylmenthoxycarbonyl)-5-trimethylsilyl-(R)-2-triphenylsilyl-2,3-dihydro-4-pyridone (epi-6b, 2*R*). IR (neat) 2956, 2924, 1713, 1656, 1575, 1457, 1386, 1324, 1300, 1256, 1227, 1109 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.78 (s, 1 H), 7.65 – 7.05 (m, 20 H), 4.70 (dt, 1 H, J = 4.5, 10.5 Hz), 3.65 (d, 1 H, 8.4 Hz), 2.60 (dd, 1 H, J = 8.4, 16.8 Hz), 2.25 (d, 1 H, J = 16.8 Hz), 2.15 – 0.50 (m, 17 H), -0.80 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.41, 152.48, 148.02, 136.52, 131.58, 130.04, 128.31, 128.01, 125.09, 116.93, 78.05, 49.94, 42.98, 39.74, 39.33, 38.88, 34.14, 31.05, 30.33, 29.70, 26.37, 22.41, 21.58, - 1.59. HRMS Calcd for 685.3407 $[M + H]^+$. Found: 685.3407.

1-((1*R*,2*S*,5*R*)-8-Phenylmenthoxycarbonyl)-5-triisopropylsilyl-(S)-2-triphenylsilyl-2,3-dihydro-4-pyridone (6c). IR (neat) 2949, 2865, 1713, 1660, 1563, 1361, 1304, 1258, 1110 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.60 – 7.00 (m, 21 H), 5.03 (d, 1 H, J = 8.1 Hz), 4.57 (dt, 1 H, J = 4.2, 10.5 Hz), 2.93 (dd, 1 H, J = 8.1, 16.5 Hz), 2.78 (d, 1 H, J = 16.5 Hz), 2.40 – 0.40 (m, 38 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.91, 50.96, 44.05, 41.33, 39.83, 38.01, 34.14, 31.09, 27.42, 26.73, 25.89, 21.61, 18.88, 11.32. Anal. Calcd for $C_{49}H_{63}NO_3Si_2$: C, 76.41; H, 8.24; N, 1.82. Found: C, 76.27; H, 8.21; N, 1.78.

1-((1*R*,2*S*,5*R*)-8-Phenylmenthoxycarbonyl)-5-triisopropylsilyl-(R)-2-triphenylsilyl-2,3-dihydro-4-pyridone (epi-6c, 2*R*). IR (neat) 2949, 2865, 1713, 1660, 1571, 1385, 1298, 1259, 1227, 1109 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.85 (s, 1 H), 7.40 – 7.00 (m, 20 H), 4.74 (dt, 1 H, J = 4.8, 10.5 Hz), 3.80 (d, 1 H, J = 8.4 Hz), 2.66 (dd, 1 H, J = 8.4, 15.3 Hz), 2.34 (d, 1 H, J = 15.6 Hz), 2.20 – 0.60 (m, 38 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.20, 152.15, 149.24, 136.52, 131.48, 130.02, 127.94, 125.16, 111.20, 77.92, 50.21, 42.43, 40.01, 39.34, 38.30, 34.09, 31.54, 31.03, 30.08, 26.33, 22.57, 21.51, 18.75, 14.08, 11.09. Anal. Calcd for $C_{49}H_{63}NO_3Si_2$: C, 76.41; H, 8.24; N, 1.82. Found: C, 76.55; H, 8.06; N, 1.65.

1-((1*R*,2*S*,5*R*)-Menthoxycarbonyl)-(S)-2-triphenylsilyl-2,3-dihydro-4-pyridone (6e). IR (neat) 2956, 1717, 1673, 1599, 1337, 1312, 1260, 1194 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.80 – 7.00 (m, 16 H), 5.29 (d, 1 H, J = 7.8 Hz), 5.09 (d, 1 H, J = 5.09 Hz), 4.41 (dt, 1 H, J = 3.6, 10.5 Hz), 3.01 (dd, 1 H, J = 8.4, 7.1 Hz), 2.71 (d, 1 H, J = 17.1 Hz), 2.00 – 0.40 (m, 18 H); ^{13}C NMR (75 MHz, CDCl_3) δ 192.08, 142.85, 136.36, 130.11, 128.02, 107.80, 77.89, 46.80, 43.73, 40.57, 37.79, 31.99, 31.16, 26.30, 23.33, 21.85, 20.61, 16.44. Analysis was performed on a mixture of both (2*R*) and (2*S*) isomers (56:42 ratio by HPLC). Anal. Calcd for $\text{C}_{34}\text{H}_{39}\text{NO}_3\text{Si}$: C, 75.94; H, 7.31; N, 2.60. Found: C, 75.97; H, 7.47; N, 2.69.

1-((1*R*,2*S*,5*R*)-Menthoxycarbonyl)-(R)-2-triphenylsilyl-2,3-dihydro-4-pyridone (epi-6e, 2*R*).

IR (neat) 2957, 2870, 1718, 1673, 1601, 1429, 1329, 1317, 1263, 1242, 1192 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.00 – 7.20 (m, 16 H), 5.30 – 4.90 (m, 2 H), 4.42 (dt, 1 H, J = 4.20, 10.50 Hz), 3.00 (dd, 1 H, J = 8.7, 17.4 Hz), 2.70 (d, 1 H, J = 17.4 Hz), 2.10 – 0.40 (m, 18 H); ^{13}C NMR (75 MHz, CDCl_3) δ 192.07, 143.52, 163.32, 133.55, 130.13, 128.03, 108.50, 77.96, 46.92, 43.95, 41.80, 39.00, 37.84, 33.88, 31.00, 26.68, 23.40, 21.78, 20.83, 16.43.

1-((1*R*,2*S*,5*R*)-Menthoxycarbonyl)-5-trimethylsilyl-(S)-2-triphenylsilyl-2,3-dihydro-4-pyridone (6f).

IR (neat) 2954, 2870, 1718, 1658, 1574, 1429, 1300, 1255, 1109 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.10 – 7.50 (m, 16 H), 5.50 – 5.20 (m, 1 H), 4.80 – 4.50 (m, 1 H), 3.20 (dd, 1 H, J = 8.7, 16.8 Hz), 2.95 (d, 1 H, J = 16.8 Hz), 2.40 – 0.60 (m, 17 H), 0.03 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 194.8, 147.5, 136.4, 131.6, 130.0, 127.9, 77.8, 46.9, 44.0, 40.5, 38.4, 33.9, 31.1, 26.6, 23.5, 21.8, 20.8, 16.6, 1.7. Anal. Calcd for $\text{C}_{37}\text{H}_{47}\text{NO}_3\text{Si}_2$: C, 72.86; H, 7.76; N, 2.30. Found: C, 73.04; H, 7.82; N, 2.36.

1-((1*R*,2*S*,5*R*)-Menthoxycarbonyl)-5-triisopropylsilyl-(S and R)-2-triphenylsilyl-2,3-dihydro-4-

pyridone (6g). IR (neat) 2958, 2866, 1718, 1661, 1567, 1462, 1370, 1333, 1303, 1258, 1110 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.10 – 7.00 (m, 16 H), 5.20 – 5.00 (m, 1 H), 4.50 – 4.20 (m, 1 H), 3.10 – 2.80 (m, 2 H), 2.20 – 0.40 (m, 39 H); ^{13}C NMR (75 MHz, CDCl_3) δ 194.87, 152.25, 148.50, 136.43, 131.48, 130.01, 127.93, 111.00, 77.60, 46.90, 43.92, 41.00, 38.14, 33.89, 31.06, 26.40, 23.25, 21.81, 20.94, 18.76, 16.49, 11.12. Anal. Calcd for $\text{C}_{43}\text{H}_{59}\text{NO}_3\text{Si}_2$: C, 74.37; H, 8.56; N, 2.02. Found: C, 74.41; H, 8.59; N, 1.91.

Preparation of 2-Dimethylphenylsilanyl-4-oxo-3,4-dihydro-2*H*-pyridine-1-carboxylic acid 2-(1-methyl-1-phenylethyl)cyclohexyl ester (8). Toluene (5.5 mL), (+)-TCC chloroformate (1 mmol) and 4-methoxypyridine (0.11 mL, 1.1 mmol) were stirred under Argon and at $-23\text{ }^\circ\text{C}$ for 15 min. The solution of pyridinium salt was then cooled to $-85\text{ }^\circ\text{C}$ ($\text{Et}_2\text{O}/\text{CO}_2$) and dimethylphenylsilylmagnesium chloride was added dropwise over 15 min. The mixture was stirred for 30 min at $-85\text{ }^\circ\text{C}$ and allowed to come to rt for another 30 min. A saturated solution of oxalic acid (5.5 mL) was then added, and the mixture was stirred for 5 min at rt, and then extracted with ether. The combined organic layers were washed with water (2 x) and brine, dried over MgSO_4 and concentrated. Purification of the crude product by radial PLC (5% EtOAc /hexanes) yielded 400 mg (88%) of **8** as a white foam. The product was crystallized from 5% EtOAc /hexanes to give white crystals, mp $115\text{--}116\text{ }^\circ\text{C}$. IR (neat) 2928, 1712, 1669, 1593, 1256, 1190 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.45–7.01 (m, 10 H), 6.41 (d, 1 H, J = 8.2 Hz), 4.80 (d, 1 H, J = 8.2 Hz), 4.73 (dd, 1 H, J = 4, 10.5 Hz), 4.32 (d, 1 H, J = 9 Hz), 2.76 (dd, 1 H, J = 9, 16.8 Hz), 2.31 (d, 1 H, J = 16.8 Hz), 2.18–1.70 (m, 5 H), 1.30 (s, 5 H), 1.17 (s, 5 H), 0.32 (s, 3 H), 0.22 (s, 3 H); ^{13}C NMR (75

MHz, CDCl₃) δ 199.39, 151.88, 151.001, 142.61, 135.27, 134.02, 129.60, 128.02, 127.84, 125.30, 124.78, 106.47, 77.89, 51.17, 44.30, 39.35, 36.73, 33.28, 30.08, 26.74, 25.86, 24.59, 22.15, -3.55. Anal. Calcd for C₂₉H₃₇NO₃Si: C, 73.22; H, 7.84; N, 2.94. Found: C, 73.41; H, 7.95; N, 2.93. HRMS Calcd for C₂₉H₃₇NO₃Si: 476.2621 [M+H]⁺. Found: 476.2639 [M+H]⁺. $[\alpha]_D^{23} = -18.9^\circ$ ($c = 1$, CH₂Cl₂).

Preparation of (S)-6-Methyl-1-((1R,2S,5R)-8-phenylmenthoxy carbonyl)-(R)-2-triphenylsilyl-4-oxopiperidine (9). To a 50-mL flask containing **6a** (0.613 g, 1.00 mmol) was added CuBr•Me₂S (0.615 g, 3.0 mmol) and THF (20 mL). The heterogeneous mixture was cooled to -78 °C and BF₃•OEt₂ (0.42 mL, 3 mmol) was added. After stirring for 5 min, MeMgCl (1.0 mL 3.0 mmol) was added dropwise. The solution turned brown and then a golden yellow. The solution was stirred for 4 h at -78 °C and then poured directly into an aqueous solution of 20% NH₄OH/NH₄Cl (50:50) (50 mL) and Et₂O (50 mL). The organic layer was washed with H₂O (30 mL) and brine (30 mL). The mixture was dried (K₂CO₃) and concentrated under reduced pressure to give 0.710 g of a viscous foam as the crude product. Purification by radial PLC (5-30% EtOAc/hexanes) gave 0.476 g (76%) of **9** and 0.062 g (10%) of starting material (**6a**), mp 164-165 °C. IR (neat) 2955, 2922, 1709, 1655, 1570, 1305, 1255, 1109 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.70 – 7.10 (m, 20 H), 4.60 (dt, 1 H, $J = 4.2, 10.8$ Hz), 4.24 – 4.10 (m, 1 H), 3.73 (d, 1 H, $J = 13.2$ Hz), 2.76 (dd, 1 H, $J = 13.2, 14.4$ Hz), 2.54 (d, 1 H, $J = 14.4$ Hz), 2.47 (dd, 1 H, $J = 6.6, 14.4$ Hz), 2.19 (d, 1 H, $J = 14.4$ Hz), 1.68 – 0.80 (m, 20 H); ¹³C NMR (75 MHz, CDCl₃) δ 207.81, 154.68, 151.68, 136.19, 135.83, 128.85, 127.51, 125.24, 124.91, 76.17, 50.37, 49.38, 47.09, 43.10, 42.22, 40.14, 39.58, 34.40, 34.01, 30.96, 26.55, 26.34, 26.25, 22.24, 21.72, 19.29, 13.99. Anal. Calcd for C₄₁H₄₇NO₃Si: C, 78.18; H, 7.52; N, 2.22. Found: C, 78.20; H, 7.61; N, 2.16. $[\alpha]_D^{20} + 52.9^\circ$ ($c = 1$, CH₂Cl₂).

Preparation of (2S, 6S)-6-Phenyl-1-[(1R,2S,5R)-(8-phenylmenthoxy carbonyl)]-2-triphenylsilyl-4-piperidone (10). In a similar manner to the preparation of **9**, dihydropyridone (**6a**) and PhMgCl/CuBr/BF₃•OEt₂ afforded a 65% yield of piperidone (**10**) as a white solid, mp 194-195 °C (EtOAc/hexane). IR (neat) 2960, 2438, 1686, 1513, 1426, 1282, 1095 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.0-7.5 (m, 25 H), 5.67 (d, 1 H, $J = 4.5$ Hz), 4.75 (dt, 1 H, $J = 4.6, 10.6$ Hz), 3.58 (dd, 1 H, $J = 2.4, 13.2$ Hz), 3.05 (d, 1 H, $J = 15.7$ Hz), 2.81 (dd, 1 H, $J = 13.2, 15.5$ Hz), 2.70 (dd, 1 H, $J = 7.1, 15.0$ Hz), 2.53 (d, 1 H, $J = 15.1$ Hz), 0.70-2.00 (m, 17 H); ¹³C NMR (75 MHz, CDCl₃) δ 207.68, 155.32, 150.71, 139.11, 135.97, 135.45, 128.96, 128.67, 127.89, 127.48, 125.48, 125.19, 76.62, 57.37, 50.54, 43.98, 43.28, 42.64, 41.19, 40.25, 34.32, 31.20, 30.40, 27.08, 23.14, 21.80. Anal. Calcd for C₄₆H₄₉NO₃Si: C, 79.84; H, 7.14; N, 2.02. Found: C, 79.96; H, 7.20; N, 1.98. $[\alpha]_D^{20} + 81.94^\circ$ ($c = 0.62$, CHCl₃).

Preparation of (2R,6R) 6-Allyl-2-(dimethylphenylsilyl)-4-oxo-piperidine-1-carboxylic acid (1S,2R)-2-(1-methyl-1-phenylethyl)cyclohexyl ester (11). To a solution of **8** (50 mg, 0.1 mmol) in THF (1 mL) was added CuBr•SMe₂ (62 mg, 0.3 mmol). The heterogeneous mixture was cooled to -78 °C and BF₃•OEt₂ (0.05 mL, 0.3 mmol) was added. After stirring for 30 min at -78 °C, allylmagnesium chloride (0.15 mL, 0.3 mmol) was slowly added. The mixture was stirred at -78 °C for 3 h and was allowed to warm to rt for 1 h. A solution of 20% NH₄OH/NH₄Cl (50:50) was added (1 mL) and the aqueous phase was extracted with ether. The combined organic layers were washed with water and brine and then dried

over K_2CO_3 . Purification by radial PLC (5% EtOAc/hexanes) afforded 45 mg (85%) of **11** as a clear oil. IR (neat) 2929, 2858, 1722, 1688, 1403, 1308, 701 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.52–7.00 (m, 10 H), 5.41–5.27 (m, 1 H), 4.97 (d, 1 H, $J = 9.9$ Hz), 4.88–4.73 (m, 2 H), 4.25 (dd, $J = 5.0, 8.0$ Hz), 2.50–1.59 (m, 7 H), 1.32–1.14 (m, 11 H), 0.37 (s, 3 H), 0.33 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 209.04, 154.91, 153.19, 137.13, 134.02, 133.99, 129.47, 127.96, 124.99, 124.77, 117.70, 76.14, 51.07, 49.88, 42.44, 42.24, 41.00, 40.35, 39.39, 33.72, 30.72, 30.58, 26.74, 26.05, 24.71, 21.79, -2.58, -3.94. LRMS Calcd for $\text{C}_{32}\text{H}_{43}\text{NO}_3\text{Si}$: $[\text{M}+\text{H}]^+$ 518.30. Found: $[\text{M}+\text{H}]^+$ 518.35. $[\alpha]_D^{23} = -48.2^\circ$ ($c = 1$, CH_2Cl_2).

Preparation of (R)-4-Hydroxy-1-((1R,2S,5R)-8-phenylmenthoxy-carbonyl)-(S)-

2-triphenylsilyl-1,2,3,4-tetrahydropyridine (12). In a 25-mL flask were placed **6a** (0.495 g, 0.8 mmol), EtOH (10 mL), and $\text{CeCl}_3 \cdot 7 \text{H}_2\text{O}$ (3.3 mL of a 0.3 molar solution in MeOH). The mixture was refluxed until the starting material was completely dissolved. After cooling to 0 $^\circ\text{C}$, NaBH_4 (0.110 g, 2.9 mmol) was slowly added over a 5 min period. The solution was stirred for an additional 30 min at 0 $^\circ\text{C}$ and then 30 min at rt. The solvent was removed under reduced pressure, and to the residue was added CH_2Cl_2 (50 mL), H_2O (40 mL), and 10% aqueous HCl (10 mL). The aqueous layer was extracted with CH_2Cl_2 (40 mL), and the combined organic layers were washed with brine, dried (MgSO_4), and concentrated to give 0.486 g (98%) of **12** as a white foam. By NMR only one diastereomer was detected and no further purification was required for elemental analysis. IR (neat) 2955, 2920, 1691, 1649, 1427, 1390, 1109 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.64 – 7.00 (m, 20 H), 5.90 (d, 1 H, $J = 8.4$ Hz), 4.59 (dd, 1 H, $J = 3.6, 8.4$ Hz), 4.35 – 4.05, (m, 2 H), 3.95 (s, 1 H), 2.25 – 0.40 (m, 19 H); ^{13}C NMR (75 MHz, CDCl_3) δ 151.91, 151.48, 136.34, 134.61, 129.21, 127.77, 127.50, 124.96, 108.66, 76.13, 62.35, 50.40, 41.08, 40.01, 39.43, 34.38, 33.58, 30.85, 27.79, 26.41, 25.08, 21.58. Anal. Calcd for $\text{C}_{40}\text{H}_{45}\text{NO}_3\text{Si}$: C, 78.01; H, 7.36; N, 2.27. Found: C, 78.11; H, 7.42; N, 1.99. $[\alpha]_D^{20} + 7.1^\circ$ ($c = 1$, CH_2Cl_2).

Preparation of (S)-4-Hydroxy-1-((1R,2S,5R)-8-phenylmenthoxy-carbonyl)-(S)-2-

triphenylsilyl-1,2,3,4-tetrahydropyridine (15). To a solution of **12** (0.109 g, 0.18 mmol) in toluene (3 mL) at -23 $^\circ\text{C}$ was added $\text{BF}_3 \cdot \text{OEt}$ (0.05 mL, 0.36 mmol). After stirring for 5 min, H_2O (20 mL) was added and the mixture was allowed to come to rt over 15 min. The solution was extracted with Et_2O (40 mL), and the organic layer was washed with brine, dried (MgSO_4), and concentrated under reduced pressure to give 0.108 g (99%) of **15** as a viscous oil. The product was used without further purification. A small sample was recrystallized from hexanes for elemental analysis, mp 149–150.5 $^\circ\text{C}$ (hexanes). IR (neat) 2957, 2920, 1693, 1647, 1427, 1390, 1109 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.60 – 7.00 (m, 20 H), 5.87 (d, 1 H, $J = 8.1$ Hz), 4.76 (dt, 1 H, $J = 4.2, 10.5$ Hz), 4.25 – 4.17 (m, 1 H), 4.01 (dd, 1 H, $J = 2.4, 8.1$ Hz), 2.83 (s, 1 H), 1.82 – 0.20 (m, 19 H); ^{13}C NMR (75 MHz, CDCl_3) δ 151.83, 151.36, 136.23, 134.36, 129.34, 127.97, 127.70, 126.99, 125.24, 106.91, 76.12, 65.72, 50.65, 41.31, 40.58, 39.74, 34.43, 30.94, 30.12, 26.89, 26.67, 26.23, 21.64. Anal. Calcd for $\text{C}_{40}\text{H}_{45}\text{NO}_3\text{Si}$: C, 78.01; H, 7.36; N, 2.27. Found: C, 78.07; H, 7.38; N, 2.28. $[\alpha]_D^{20} - 155.5^\circ$ ($c = 1$, CH_2Cl_2).

Preparation of (S)-4-Allyl-1-((1R,2S,5R)-8-phenylmenthyl-carbonyl)-(S)-2-triphenylsilyl-1,2,3,4-

tetrahydropyridine (16). To **12** (0.470 g, 0.760 mmol) and allyl-trimethylsilane (0.48 mL, 3.0 mmol) in CH_2Cl_2 (8 mL) at -42 $^\circ\text{C}$ was added $\text{BF}_3 \cdot \text{OEt}_2$ (0.18 mL, 1.5 mmol), and the solution was allowed to come to rt over 30 min. Water (30 mL) was added and the mixture was extracted with CH_2Cl_2 (40 mL). The combined organic layers were washed with brine, dried (MgSO_4), and concentrated under reduced pressure to give 0.512 g of a viscous foam as the crude product. Purification by radial PLC (5%

EtOAc/hexanes) gave 0.364 g (74%) of **16** as a white solid, mp 158.5-159.5 °C. IR (neat) 2920, 2881, 1678, 1427, 1410, 1309, 1107 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.53 – 6.84 (m, 20 H), 5.56 – 5.42 (m, 1 H), 5.40 – 5.20 (m, 1 H), 5.16 (d, 1 H, *J* = 7.8 Hz), 5.08 (d, 1 H, *J* = 7.8 Hz), 4.88 – 4.76 (m, 2 H), 4.51, (d, 1 H, *J* = 17.4 Hz), 2.50 – 2.45 (m, 2 H), 2.30 (dd, 1 H, *J* = 6.0, 17.4 Hz), 2.10 – 0.80 (m, 17 H); ¹³C NMR (75 MHz, CDCl₃) δ 152.63, 136.44, 135.18, 134.14, 129.46, 127.95, 127.65, 126.72, 124.86, 122.96, 116.69, 75.23, 50.97, 49.93, 42.42, 39.31, 38.00, 34.67, 31.30, 29.95, 26.42, 25.87, 22.55, 22.00. Anal. Calcd for C₄₃H₅₁NO₂Si: C, 80.70; H, 7.72; N, 2.19. Found: C, 80.59; H, 7.74; N, 2.10. [α]_D²⁰ – 15.7° (*c* = 1, CH₂Cl₂).

Preparation of 1-((1*R*,2*S*,5*R*)-8-Phenylmenthoxy carbonyl)-(S)-2-triphenylsilyl-1,2,-dihydropyridine (17). To a 25-mL flask containing **12** (0.234 g, 0.38 mmol) in toluene (10 mL) at -78 °C was added BF₃•OEt₂ (0.10 mL, 0.76 mmol). The solution was stirred at -78 °C for 1.5 h followed by the addition of allylmagnesium chloride (0.57 mL, 1.14 mmol). After 15 min, the mixture was poured into a flask containing cold H₂O (40 mL), and the mixture was extracted with Et₂O (2 x 30 mL). The combined organic layers were washed with brine (30 mL), dried (MgSO₄), and concentrated under reduced pressure to give a thick yellow oil. The crude product was purified by radial PLC (5-30% EtOAc/hexanes) to give 0.185 g (82%) of **17** as a viscous foam. IR (neat) 2955, 2920, 1693, 1427, 1325, 1265, 1111 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.72 – 7.00 (m, 20 H), 6.96 (d, 1 H, *J* = 7.5 Hz), 5.66 – 5.52 (m, 3 H), 4.80 – 4.72 (m, 1 H), 4.52 (dt, 1 H, *J* = 4.2, 10.5 Hz), 1.90 – 0.48 (m, 17 H); ¹³C NMR (75 MHz, CDCl₃) δ 151.55, 151.24, 136.47, 132.58, 129.55, 127.88, 127.62, 126.06, 125.13, 127.00, 120.70, 108.72, 76.20, 50.76, 47.04, 41.77, 39.77, 34.51, 31.13, 27.08, 26.84, 26.13, 21.76. Anal. Calcd for C₄₀H₄₃NO₂Si: C, 80.36; H, 7.25; N, 2.34. Found: C, 80.12; H, 7.30; N, 2.20.

Desilylation of 9. To a solution of 40 mg (0.635 mmol) of compound (**9**) in 1 mL of THF was added quickly 0.064 mL (0.65 mmol) of TBAF. The solution turned yellow immediately and was refluxed for 50 min. Completion of the reaction was checked by TLC. The solution was then diluted with Et₂O, washed with water, and dried over MgSO₄. The residue after evaporation was purified by flash chromatography on silica gel (hexanes/Et₂O, 80:20) to yield 17 mg (72%) of desilylated compound (**19**) as an oil. ¹H NMR (300 MHz, CDCl₃): A complex spectrum due to rotamers; only a few characteristic peaks are reported: δ 7.40 - 7.12 (m, 5 H), 4.82 (td, 1 H, *J* = 4.4, 10.7 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 208.41, 154.42, 152.18, 127.99, 125.7, 125.41, 125.22, 125.05, 50.55, 48.03, 47.00, 42.54, 40.63, 39.86, 38.01, 34.65, 31.42, 28.51, 21.89, 18.92, 18.73.

Lucho reduction of 8 to give alcohols (13). To a solution of **8** (188 mg, 0.396 mmol) in methanol (6 mL) was added CeCl₃•7H₂O (177 mg, 0.475 mmol), and the mixture was stirred at rt until the starting material was dissolved (30 min-1 h). The mixture was cooled to 0 °C and NaBH₄ (23 mg, 0.6 mmol) was slowly added. After stirring for 30 min, the ice bath was removed and the solution was stirred for 1 h at rt. The solvent was removed under reduced pressure, and to the residue was added CH₂Cl₂ (20 mL), water (24 mL) and 10% HCl (6 mL). The aqueous layer was extracted with CH₂Cl₂, and the combined organic layers were washed with brine, dried over MgSO₄ and concentrated. Purification by radial PLC (10% EtOAc/hexanes) yielded 200 mg (100%) of a mixture (7/3) of *cis* (**13a**) and *trans* (**13b**) as a white foam.

13a: IR (neat) 3438, 2962, 1671, 1408, 1260, 1106, 1030 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.47-7.03 (m, 10 H), 6.06 (d, 1 H, J = 8.4 Hz), 4.82-4.77 (m, 1 H), 4.51 (dd, 1 H, J = 4.8, 8.4 Hz), 4.08 (t, 1 H, J = 4.8 Hz), 3.95 (s, 1 H), 2.06 (dt, 1 H, J = 2.4, 12.8 Hz), 1.96-1.59 (m, 6 H), 1.31 (s, 5 H), 1.22 (s, 5 H), 0.39 (s, 3 H), 0.34 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.01, 138.06, 134.16, 133.99, 129.06, 128.00, 127.84, 127.72, 127.26, 125.05, 125.04, 106.89, 76.48, 51.24, 46.10, 40.93, 39.77, 33.76, 32.34, 27.52, 27.11, 25.91, 25.37, 24.67, 11.42, -2.08, -2.33. HRMS Calcd for $\text{C}_{29}\text{H}_{39}\text{NO}_3\text{Si}$: 478.2777 $[\text{M}+\text{H}]^+$. Found: 478.2789 $[\text{M}+\text{H}]^+$. $[\alpha]_D^{23}$ = -81.79° (c = 1, CH_2Cl_2).

13b: IR (neat) 3444, 2930, 1644, 1383, 1337, 1257, 1107 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.49-7.07 (m, 10 H), 5.96 (d, 1 H, J = 8.4 Hz), 4.73 (td, 1 H, J = 4.5, 12 Hz), 4.40 (d, 1 H, J = 8.4 Hz), 4.07 (m, 1 H), 4.02 (dd, 1 H, J = 2.7, 6 Hz), 1.31 (s, 5 H), 1.21 (s, 5 H), 0.32 (s, 6 H); ^{13}C (75 MHz, CDCl_3) δ 152.00, 151.58, 136.91, 133.89, 129.31, 127.98, 127.78, 126.28, 125.16, 125.13, 108.45, 62.83, 51.29, 43.15, 39.81, 33.69, 33.28, 27.55, 27.15, 25.95, 25.43, 24.68, -0.01, -2.83, -3.29. HRMS Calcd for $\text{C}_{29}\text{H}_{39}\text{NO}_3\text{Si}$: 478.2777 $[\text{M}+\text{H}]^+$. Found: 478.2789 $[\text{M}+\text{H}]^+$. $[\alpha]_D^{23}$ = -2.14° (c = 1, CH_2Cl_2).

Preparation of Dihydropyridine (18). To a stirred solution of **5a** (25 mg, 0.05 mmol) in THF (2 mL) cooled at -78 °C was added $\text{BF}_3\cdot\text{OEt}_2$ (0.01 mL, 0.1 mmol) and the resulting mixture was stirred for 30 min at -78 °C. Then, a solution of allylmagnesium chloride in THF (0.075 mL, 0.15 mmol) was added and the reaction mixture was stirred at -78 °C for 3 h and was allowed to warm to rt for 1 h. The reaction mixture was then treated with 5 mL of water and the aqueous phase was extracted with ether. The combined organic layers were washed with brine and dried over MgSO_4 . After evaporation of the solvent *in vacuo*, the crude product was purified by radial PLC (hexanes/TEA) to yield 14 mg (60%) of **18** as a clear oil. IR (neat) 2926, 2863, 1694, 1386, 1249 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.60- 7.08 (m, 10 H), 5.94 (d, 1 H, J = 7.6 Hz), 5.61 (dd, 1 H, J = 5.0, 9.6 Hz), 5.37 (dd, 1 H, J = 6.2, 9.6 Hz), 4.82 (ddd, 1 H, J = 7.6, 5.0, 0.8 Hz), 4.76 (d, 1 H, J = 6.2 Hz), 4.70 (dt, 1 H, J = 8.0, 4.4 Hz), 1.99-0.30 (m, 21 H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.63, 151.26, 134.1, 129.19, 128.46, 127.91, 127.77, 127.64, 126.01, 125.76, 125.24, 125.15, 122.08, 119.78, 107.76, 51.42, 47.75, 39.99, 33.67, 27.37, 27.22, 26.85, 26.35, 26.28, 25.98, 24.69, -0.01, -3.55, -4.54. $[\alpha]_D^{23}$ -207.8° (c = 1, CH_2Cl_2).

ACKNOWLEDGEMENTS

We express appreciation to the National Institutes of Health (Grant GM 34442) for financial support of this research.

REFERENCES AND NOTES

1. D. L. Comins and S. P. Joseph. In *Advances in Nitrogen Heterocycles*, ed. by C. J. Moody, JAI Press Inc., Greenwich, CT, 1996, Vol. 2, pp. 251-294. (b) D. L. Comins and S. P. Joseph. In *Comprehensive Heterocyclic Chemistry*, 2nd ed. by A. McKillop, Pergamon Press, Oxford England, 1996, Vol. 5, pp. 37-89. (c) D. L. Comins, *J. Heterocycl. Chem.*, 1999, **36**, 1491.

2. (a) D. L. Comins, S. P. Joseph, and R. R. Goehring, *J. Am. Chem. Soc.*, 1994, **116**, 4719. (b) D. L. Comins, J. T. Kuethe, H. Hong, F. J. Lakner, T. E. Concolino, and A. L. Rheingold, *J. Am. Chem. Soc.*, 1999, **121**, 2651. (c) J. T. Kuethe and D. L. Comins, *Org. Lett.*, 2000, **2**, 855 and references cited therein.
3. D. L. Comins and J. M. Salvador, *J. Org. Chem.*, 1993, **58**, 4656.
4. For preliminary results, see: D. L. Comins and M. O. Killpack, *J. Am. Chem. Soc.*, 1992, **114**, 10972.
5. The Ph_3SiMgBr was formed by the addition of magnesium bromide to Ph_3SiLi . For the preparation of the lithium reagent, see: M. V. George, D. J. Peterson, and H. Gilman, *J. Am. Chem. Soc.*, 1960, **82**, 403.
6. D. L. Comins and D. H. LaMunyon, *Tetrahedron Lett.*, 1988, **29**, 773.
7. P. Singh, D. L. Comins, and M. O. Killpack, *Acta Crystallogr.*, 1990, **C46**, 1955.
8. $\text{PhMe}_2\text{SiMgBr}$ was prepared via the lithium reagent and MgBr_2 , see reference 5.
9. Molecular modeling program: MacSPARTAN Pro (1.04) by Wavefunction, Inc. Force field, MMFF (conformer distribution).
10. R. W. Hoffman, *Chem. Rev.*, 1989, **89**, 1841; F. Johnson, *Chem. Rev.*, 1968, **68**, 375; M. A. Foley and D. L. Comins, *J. Am. Chem. Soc.*, 1988, **110**, 7445 and references cited therein.
11. (a) A. P. Kozikowski and P.-u. Park, *J. Org. Chem.*, 1984, **49**, 1674. (b) D. L. Comins and A. H. Abdullah, *Tetrahedron Lett.*, 1985, **26**, 43. (c) D. L. Comins and M. A. Foley, *Tetrahedron Lett.*, 1988, **29**, 6711. (d) D. L. Comins, G. Chung, and M. A. Foley, *Heterocycles*, 1994, **37**, 1121.