Asymmetric Synthesis of 2-Alkyl(Aryl)-2,3-dihydro-4-pyridones by Addition of Grignard Reagents to Chiral 1-Acyl-4-methoxypyridinium Salts

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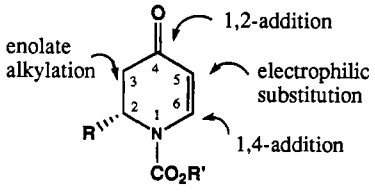
Abstract: The asymmetric synthesis of 2-alkyl(aryl)-2,3-dihydro-4-pyridones **3** by addition of various Grignard reagents to chiral 1-acyl-4-methoxypyridinium salts was studied in detail. Chiral pyridinium salts formed from 4-methoxy-3-(triisopropylsilyl)pyridine (**2f**), and (–)-8-arylmenthyl chloroformates, or (–)-*trans*-2-(α-cumyl)cyclohexyl chloroformate, gave the best results, with diastereomeric selectivities ranging from 60 to 94%. When 4-methoxy-3-(trialkylstannyl)pyridines were used, destannylated 2-alkyl-2,3-dihydropyridones **3a** resulted in good yield. The size of the C-3 substituent, the auxiliary, the solvent, the reaction temperature, and the structure of the Grignard reagent were varied to determine their effect on the yield and the degree of asymmetric induction. The chiral auxiliary and the C-3 triisopropylsilyl group can be removed from **3f**, and the auxiliary recovered, on treatment with sodium methoxide in methanol followed by aqueous acid. The resulting 2,3-dihydropyridones **8** are useful chiral building blocks for the enantioselective synthesis of various alkaloids.

Introduction

Dihydropyridones of the type **1** are interesting heterocycles and attractive building blocks for alkaloid synthesis. The enone moiety within **1** can be utilized as a Michael acceptor,[1] or 1,2-addition to the enone carbonyl can be effected by choosing the proper conditions.[2] The C-5 position of the heterocycle is



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susceptible to electrophilic substitution,[3a] and alkylation at C-3 can be carried out via the enolate.[3b] Due to A(1,3) strain, the C-2 substituent of **1** is forced axial, providing a conformational bias in the molecule.[4] This conformational bias can be used to control the stereochemical outcome of 1,2- and 1,4-additions to the enone of **1**, as well as alkylations at C-3. In addition to these synthetically useful properties, 1-acyldihydropyridones **1** are readily prepared in one step by the addition of organometallics to 1-acyl salts of 4-methoxypyridine.[1a] We have reported that dihydropyridones **1** are useful intermediates for the stereoselective preparation of racemic indolizidine,[3] quinolizidine,[5] piperidine,[6,7] and *cis*-decahydroquinoline[8] alkaloids. Recently, we enhanced the scope of this chemistry by describing a method for preparing heterocycles **1** enantiomerically pure by the addition of Grignard reagents[9] or metallo enolates[10] to homochiral 1-acylpyridinium salts. The synthetic potential of this asymmetric modification has been demonstrated by us in the enantioselective syntheses of the various alkaloids depicted in Figure 1.[10,11]

Dihydropyridones **1** can be used as precursors to 1-acyl-1,2-dihydropyridines, which are also very useful building blocks for alkaloid synthesis.[12,13] Two methods for converting enantiopure **1** to 1,2-dihydropyridines have been developed in our laboratories.[11b,14] The considerable synthetic utility of 1-acyl-2,3-dihydro-4-pyridones prompted us to thoroughly examine their preparation from Grignard reagents and homochiral 1-acylpyridinium salts. The results of our studies on the asymmetric synthesis of dihydropyridones **1** are detailed below.

Results and Discussion

The asymmetric reaction is carried out by adding a Grignard reagent to a chiral 1-acylpyridinium salt, formed in situ from

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(1) (a) Comins, D. L.; Brown, J. D. *Tetrahedron Lett.* **1986**, *27*, 4549. (b) Comins, D. L.; Killpack, M. O. *J. Am. Chem. Soc.* **1992**, *114*, 10972 and references cited therein.

(2) Hydride reduction: (a) Comins, D. L.; Hong, H.; Salvador, J. M. *J. Org. Chem.* **1991**, *56*, 7197. (b) See ref 1b. Alkyl nucleophiles: (c) Organocerium reagents undergo preferentially 1,2-addition. Comins, D. L.; Bieda, K.; Joseph, S. P. Unpublished results.

(3) (a) Comins, D. L.; Morgan, L. A. *Tetrahedron Lett.* **1991**, *32*, 5919. (b) Comins, D. L.; Zeller, E. *Tetrahedron Lett.* **1991**, *32*, 5889.

(4) For reviews on A(1,3) strain, see: (a) Hoffman, R. W. *Chem. Rev.* **1989**, *89*, 1841–1860. (b) Johnson, F. *Chem. Rev.* **1968**, *68*, 375–413.

(5) (a) Brown J. D.; Foley, M. A.; Comins, D. L. *J. Am. Chem. Soc.* **1988**, *110*, 7445. (b) Comins, D. L.; LaMunyon, D. H. *Tetrahedron Lett.* **1989**, *30*, 5053. (c) Al-awar, R. S.; Joseph, S. P.; Comins, D. L. *J. Org. Chem.* **1993**, *58*, 7732. (d) Also see: Beckwith, A. L. J.; Joseph, S. P.; Mayadunne, R. T. A. *J. Org. Chem.* **1993**, *58*, 4198.

(6) Comins, D. L.; Foley, M. A. *Tetrahedron Lett.* **1988**, *29*, 6711.

(7) Chiral piperidines have been prepared from *N*-alkyl-2,3-dihydro-4-pyridones; see: (a) Pfrengle, W.; Kunz, H. *J. Org. Chem.* **1989**, *54*, 4261. (b) Waldmann, H.; Braun, M.; Drager, M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1468. (c) Hattori, K.; Yamamoto, H. *J. Org. Chem.* **1992**, *57*, 3264 and references cited therein.

(8) (a) Comins, D. L.; Dehghani, A. *Tetrahedron Lett.* **1991**, *32*, 5697. (b) Comins, D. L.; Al-awar, R. S. *J. Org. Chem.* **1992**, *57*, 4098.

(9) Comins, D. L.; Goehring, R. R.; Joseph, S. P.; O'Connor, S. *J. Org. Chem.* **1990**, *55*, 2574.

(10) (a) Comins, D. L.; Hong, H. *J. Am. Chem. Soc.*, **1993**, *115*, 8851. (b) Comins, D. L.; Hong, H. *J. Org. Chem.* **1993**, *58*, 5035.

(11) (a) Comins, D. L.; Hong, H. *J. Am. Chem. Soc.* **1991**, *113*, 6672. (b) Al-awar, R. S.; Joseph, S. P.; Comins, D. L. *Tetrahedron Lett.* **1992**, *33*, 7635. (c) Comins, D. L.; LaMunyon, D. H. *J. Org. Chem.* **1992**, *57*, 5807. (d) Comins, D. L.; Dehghani, A. *J. Chem. Soc., Chem. Commun.* **1993**, 1838. (e) Comins, D. L.; Radi Benjelloun, N. *Tetrahedron Lett.* **1994**, *35*, 829.

(12) For reviews on dihydropyridines, see: Stout, D. M.; Meyers, A. I. *Chem. Rev.* **1982**, *82*, 223. Sausins, A.; Duburs, G. *Heterocycles* **1988**, *27*, 291. Also see: Comins, D. L.; O'Connor, S. *Adv. Heterocycl. Chem.* **1988**, *44*, 199.

(13) (a) Yamaguchi, R.; Hata, E.; Matsuki, T.; Kawanisi, M. *J. Org. Chem.* **1987**, *52*, 2094. (b) Comins, D. L.; Myoung, Y. C. *J. Org. Chem.* **1990**, *55*, 292. (c) Ogawa, M.; Natsume, M. *Heterocycles* **1985**, *23*, 831. (d) Natsume, M.; Utsunomiya, I.; Yamaguchi, K.; Sakai, S. *Tetrahedron* **1985**, *41*, 2115 and references cited therein. (e) Yamaguchi, R.; Nakazono, Y.; Matsuki, T.; Hata, E.; Kawanisi, M. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 215. (f) Comins, D. L.; Weglarz, M. A. *J. Org. Chem.* **1991**, *56*, 2506.

(14) Comins, D. L.; Hong, H.; Salvador, J. M. *J. Org. Chem.* **1991**, *56*, 7197.

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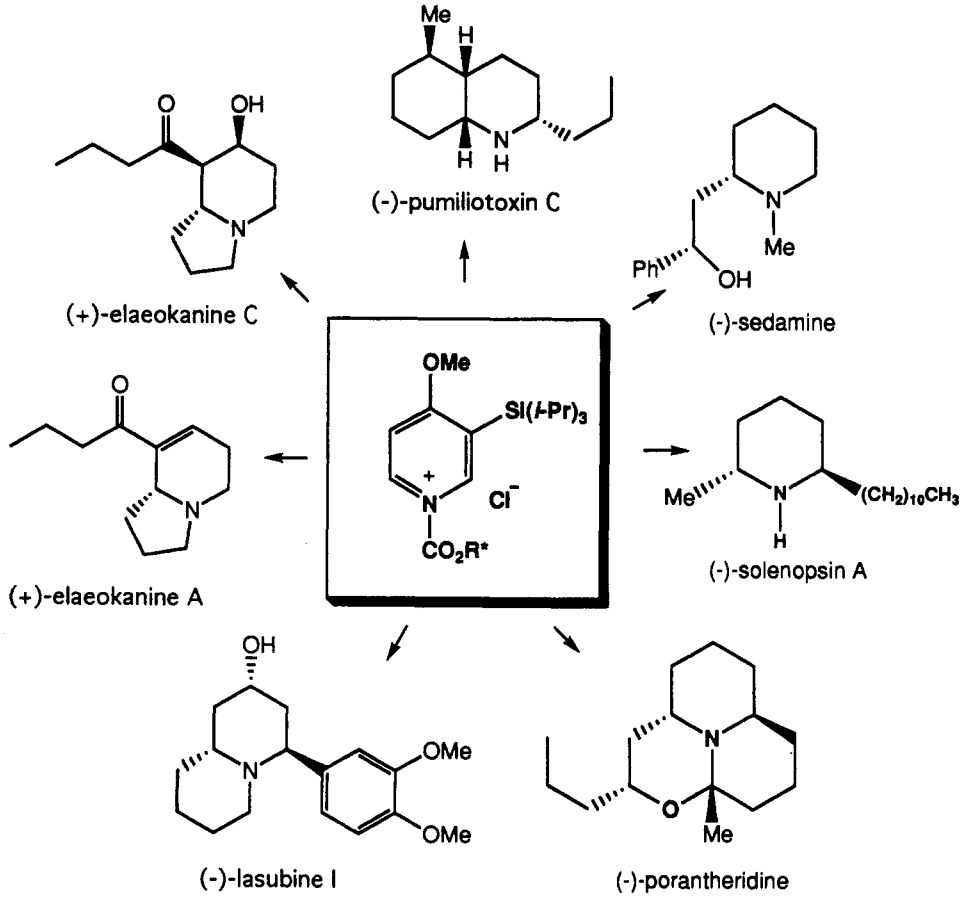
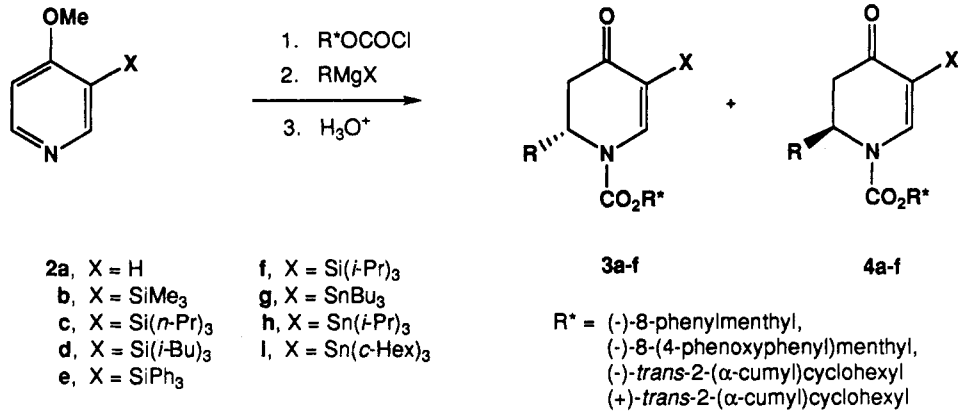


Figure 1.

Scheme 1



2a, X = H
b, X = $SiMe_3$
c, X = $Si(n\text{-}Pr)_3$
d, X = $Si(i\text{-}Bu)_3$
e, X = $SiPh_3$
f, X = $Si(i\text{-}Pr)_3$
g, X = $SnBu_3$
h, X = $Sn(i\text{-}Pr)_3$
I, X = $Sn(c\text{-}Hex)_3$

3a-f **4a-f**

R* = (-)-8-phenylmenthyl,
(-)-8-(4-phenoxyphenyl)menthyl,
(-)-*trans*-2-(α-cumyl)cyclohexyl
(+)-*trans*-2-(α-cumyl)cyclohexyl

pyridine **2** and a homochiral chloroformate, and hydrolyzing the resulting 4-methoxy-1,2-dihydropyridines with 10% HCl in the workup to give a diastereomeric mixture of 1-acyl-2,3-dihydropyridones **3** and **4** (Scheme 1). As part of our initial studies, we treated 4-methoxypyridine (**2a**) with (–)-8-phenylmenthyl chloroformate and phenylmagnesium chloride. After quenching with aqueous acid, a mixture of diastereomeric dihydropyridones **3a** and **4a** (R = Ph, R* = 8-phenylmenthyl) was isolated in high yield with a diastereomeric excess (de) of 30%. The chiral 1-acylpyridinium salt of **2a** is susceptible to nucleophilic attack at either α-position on the pyridine ring. We reasoned that an easily removable, bulky substituent at C-3 of the 4-methoxypyridine would direct the nucleophile to C-6,[15] causing, by reducing the number of reactive positions, an increase in diastereoselectivity. Accordingly, the chiral salt prepared from 3-(trimethylsilyl)-4-methoxypyridine (**2b**) and (–)-8-phenylmenthyl chloroformate was treated with phenylmagnesium chloride under the same reaction conditions, and as anticipated, the diastereoselectivity increased considerably to 65%. Encouraged by this result, we prepared various 4-methoxypyridines with a bulky trisubstituted tin or silicon substituent at the C-3 position using ortho metalation chemistry.[16] This was easily accomplished by treating 4-methoxypyridine with LDA and the appropriate silyl or stannyl chloride (Table 1). All the 3-substituted 4-methoxypyridines **2b-i** were subjected to reaction with an aryl Grignard reagent and (–)-menthyl or (–)-8-phenylmenthyl chloroformate under the usual conditions, as shown in Scheme 1, and the results obtained are given in Table 2. The best diastereoselectivity (94%) was obtained when 4-methoxy-3-(triisopropylsilyl)pyridine (**2f**) was treated with (–)-8-phenylmenthyl chloroformate and phenylmagnesium chloride (entry e). The less bulky 3-(trialkylsilyl)-4-methoxy-

(15) Comins, D. L.; Mantlo, N. B. *Tetrahedron Lett.* **1983**, *24*, 3683. Comins, D. L.; Myoung, Y. C. *J. Org. Chem.* **1990**, *55*, 292.

(16) Comins, D. L.; LaMunyon, D. H. *Tetrahedron Lett.* **1988**, *29*, 773.

Table 1. Preparation of 3-Substituted 4-Methoxypyridines from **2a**

2	X	conditions	yield,[a] %
a	H		
b	$SiMe_3$	LDA, THF, RT, 12 h	61
c	$SiPr_3$	LDA, THF, RT, 12 h	62
d	$Si(i\text{-}Bu)_3$	LDA, THF, RT, 12 h	53
e	$SiPh_3$	LDA, THF, RT, 22 h	46
f	$Si(i\text{-}Pr)_3$	LDA, THF, RT, 12 h	69
g	$SnBu_3$	LDA, THF, RT, 16 h	77
h	$Sn(i\text{-}Pr)_3$	LDA, THF, RT, 12 h	16[b]
i	$Sn(c\text{-}Hex)_3$	LDA, THF, RT, 18 h	45

[a] Products were purified by radial preparative-layer chromatography, with the exception of **2f,g**, which were purified by distillation. [b] This compound decomposed significantly during chromatography. No attempts were made to improve the yield.

Table 2. Addition of Aryl Grignard Reagents to Chiral 1-Acylpyridinium Salts

entry[a]	pyridine	chiral auxiliary	RMgX	yield,[b] %	de[c]
a	**2a**	(–)-menthol	PhMgCl	79	34
b	**2b**	(–)-menthol	PhMgCl	88	50[d]
c	**2a**	(–)-8-phenylmenthol	PhMgCl	83	30
d	**2b**	(–)-8-phenylmenthol	PhMgCl	82	65
e	**2f**	(–)-8-phenylmenthol	PhMgCl	88	94
f	**2b**	(–)-8-phenylmenthol	*o*-MePhMgCl	90	30
g	**2f**	(–)-8-phenylmenthol	*o*-MePhMgCl	81	60
h	**2c**	(–)-8-phenylmenthol	*o*-MePhMgCl	88	40
i	**2d**	(–)-8-phenylmenthol	*o*-MePhMgCl	89	34
j	**2e**	(–)-8-phenylmenthol	*o*-MePhMgCl	85	18
k	**2g**	(–)-8-phenylmenthol	PhMgCl	84	60
l	**2h**	(–)-8-phenylmenthol	PhMgCl	80	84
m	**2i**	(–)-8-phenylmenthol	PhMgCl	75	80

[a] The reactions were generally performed on a 0.5-mmol scale and quenched with aqueous 10% HCl. [b] Combined yield of purified products **3** and **4** obtained from radial preparative-layer chromatography. [c] Unless indicated, the diastereomeric excess (de) was determined by HPLC. [d] The de was determined by 300-MHz ^1H NMR analysis of the crude reaction products.

pyridines **2c,d** and *o*-tolyl Grignard gave 40 and 34% de, respectively. When 4-methoxy-3-(triphenylsilyl)pyridine (**2e**) and *o*-tolyl Grignard were subjected to the same reaction, the diastereomeric excess observed was only 18%. At this time we do not have an explanation as to why the bulky **2e** gives such poor results. All these reactions gave good to excellent yields (79–90%) of the expected products.

The reactions of 4-methoxy-3-(trialkylstannyl)pyridines **2g-i** and phenyl Grignard exhibited similar reactivity, resulting in good yields (75–84%) of destannylated products with good de (60–84%). Treatment of 4-methoxy-3-(tributylstannyl)pyridine (**2g**) with (–)-8-phenylmenthyl chloroformate and phenylmagnesium chloride, followed by acid hydrolysis, produced destannylated dihydropyridones **3a** and **4a** in 84% yield and with a de of 60%. The 3-(triisopropylstannyl)- and 3-(tricyclohexylstannyl)-4-methoxypyridines (**2h,i**) under the same reaction conditions gave dihydropyridones **3a** and **4a** in good yield with 84 and 80% de, respectively (entries l and m).

The diastereoselectivity was found to be solvent dependent, as shown in Table 3. When the reaction of phenylmagnesium chloride, pyridine **2f**, and (–)-8-phenylmenthyl chloroformate was carried out in THF, the de obtained was 72%. The analogous reaction in dichloromethane gave only 66% de. When the reaction was carried out in toluene/ether (5:1), the chemical yield decreased but the de increased to 84%. The best yield and diastereoselectivity were obtained when a 0.5 M solution of the pyridinium salt in toluene was treated with 1.3 equiv of a 1 M solution of the Grignard reagent in THF (entry d).[17]

(17) Recent results suggest that adding the Grignard reagent to a solution of the chiral 1-acylpyridinium salt in a toluene/THF mixture (4:1) at –78 °C is advantageous in most cases.

Table 3. Effect of Solvent on Diastereoselectivity

entry[a]	RMgX[b]	solvent	temperature	yield,[c] %	de[d]
a	PhMgCl	CH_2Cl_2	–78 °C	53	66
b	PhMgCl	THF	–78 °C	86	72
c	PhMgCl	toluene/ether	–78 °C	62	84
d	PhMgCl	toluene/THF	–78 °C	88	94

[a] The chiral 1-acylpyridinium salt was prepared from pyridine **2f** and (–)-8-phenylmenthyl chloroformate. [b] The reactions were generally performed on a 0.5 mmol scale using 1.3 equiv of Grignard reagent. [c] Combined yield of the two diastereomers **3f** and **4f** obtained from radial preparative-layer chromatography. [d] The diastereomeric excess (de) was determined by HPLC.

Table 4. Diastereoselective Formation of Dihydropyridones **3** from **2f**

entry[a]	pyridine	RMgX	yield,[b] %	de[c]
a	**2f**	PhMgCl	80	94
b	**2f**	*p*-MePhMgBr	75	82
c	**2f**	*o*-MePhMgCl	66	60
d	**2f**	*p*-MeOPhMgBr	68	73
e	**2f**	*p*-ClPhMgBr	67	81
f	**2f**	MeMgCl	85	91
g	**2f**	*i*-BuMgBr	86	92
h	**2f**	*c*-HexMgBr	83	81
i	**2f**	*n*-PrMgCl	88	91[d]
j	**2f**	1-hexynylMgCl	74	83
k	**2f**	vinylMgCl	75	85

[a] The reactions were generally performed on a 0.5-mmol scale and quenched with aqueous 10% HCl. The chiral 1-acylpyridinium salt was prepared using (–)-8-phenylmenthyl chloroformate. [b] Yield of purified major diastereomer **3** obtained from radial preparative-layer chromatography. [c] The diastereomeric excess (de) was determined by HPLC analysis of the crude product. [d] See ref 5c.

In contrast to many other chiral auxiliary mediated reactions, changing the temperature of the 1-acylpyridinium salt reaction mainly affects the chemical yield. A limited study using phenylmagnesium bromide, **2f**, and (–)-8-phenylmenthyl chloroformate showed little variation in the diastereoselectivity between –23 and –78 °C. However, as the temperature was raised, the amount of side products increased, thus lowering the yield. It appears that at higher temperatures the reaction of a Grignard reagent with the *N*-acyl carbonyl competes with addition to the pyridinium ring.

We studied the reaction of various Grignard reagents with the 1-acylpyridinium salt prepared from 4-methoxy-3-(triisopropylsilyl)pyridine (**2f**) and (–)-8-phenylmenthyl chloroformate (Table 4). The diastereomeric excess was found to be dependent on both the steric and electronic nature of the Grignard reagent. The reaction with *o*-tolylmagnesium chloride under standard conditions resulted in the lowest selectivity, giving the corresponding dihydropyridones **3f** and **4f** in good yield and 60% de. It is not clear at this time as to why an ortho substituent on the aryl Grignard adversely affects the stereoselectivity. The reaction using *p*-anisylmagnesium bromide gave 73% de and 77% yield of the two diastereoisomers. The reactions of *p*-chloro and *p*-tolyl Grignard reagents proceeded with 81 and 82% de, respectively. The aliphatic Grignard reagents gave similar selectivities (81–92% de) and excellent yields (81–95%). The representative examples of the acetylenic and vinylic Grignard reagents (entries j, k) gave good yields with 85 and 83% de, respectively.

The choice of chiral auxiliary was found to be crucial for effecting high asymmetric induction in these reactions. The various chiral auxiliaries studied were the chloroformates of (–)-menthol, (–)-8-phenylmenthol,[18] (–)-8-cyclohexylmenthol,[19] (–)-8-(4-phenoxyphenyl)menthol,[20] and (–)-*trans*-2-(α-cumyl)-

(18) Ort, O. *Org. Synth.* **1987**, *65*, 203.
(19) Whitesell, J. K.; Lawrence, R. M.; Chen, H.-H. *J. Org. Chem.* **1986**, *51*, 4779.
(20) d'Angelo, J.; Maddaluno, J. *J. Am. Chem. Soc.* **1986**, *108*, 8112.

Table 5. Effect of the Chiral Auxiliary

entry[a]	pyridine	chiral auxiliary	RMgX	yield,[b] %	de[c]
a	**2b**	(–)-menthol	PhMgCl	88	50
b	**2b**	(–)-8-phenylmenthol	PhMgCl	82	65
c	**2f**	(–)-menthol	PhMgCl	87	44
d	**2f**	(–)-8-phenylmenthol	PhMgCl	88	94
e	**2f**	(–)-8-cyclohexylmenthol	PhMgCl		60
f	**2f**	(–)-8-phenylmenthol	*o*-MePhMgCl	81	60
g	**2f**	(–)-8-(4-phenoxyphenyl)menthol	*o*-MePhMgCl	78	78
h	**2f**	(–)-8-phenylmenthol	*c*-HexMgBr	90	81
i	**2f**	(–)-8-(4-phenoxyphenyl)menthol	*c*-HexMgBr	67	90
j	**2f**	(–)-8-phenylmenthol	*p*-MeOPhMgBr	77	73
k	**2f**	(–)-8-(4-phenoxyphenyl)menthol	*p*-MeOPhMgBr	88	90
l	**2f**	(–)-8-phenylmenthol	vinylMgBr	81	85
m	**2f**	(–)-8-(4-phenoxyphenyl)menthol	vinylMgBr	80	88
n	**2f**	(–)-8-phenylmenthol	*n*-PrMgCl	88	91[d]
o	**2f**	(–)-*trans*-2-(α-cumyl)cyclohexanol	*n*-PrMgCl	98	90
p	**2f**	(+)-*trans*-2-(α-cumyl)cyclohexanol	PhMgCl	90	92

[a] The reactions were generally performed on a 0.5-mmol scale and quenched with aqueous 10% HCl. [b] Combined yield of purified products **3** + **4** obtained from radial preparative-layer chromatography. [c] The diastereomeric excess (de) was determined by HPLC. [d] See ref 5c.

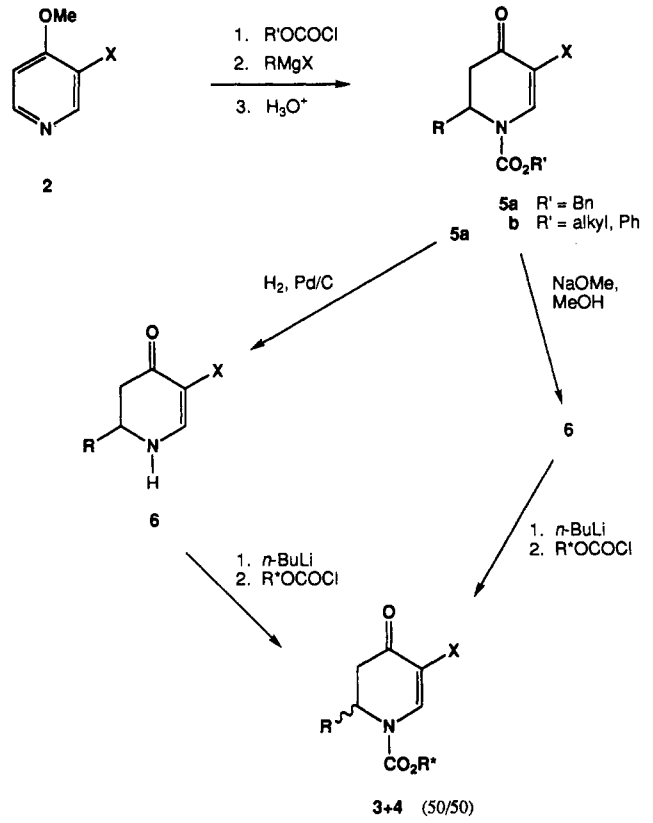
cyclohexanol.[21] The results obtained using methoxypyridines **2b,f** are given in Table 5. As anticipated, use of the chloroformate derived from (–)-menthol gave the lowest diastereomeric excess. Good to excellent diastereoselectivity was obtained when (–)-8-phenylmenthol and (–)- or (+)-*trans*-(α-cumyl)cyclohexanol were the chiral auxiliaries (Tables 4 and 5). With phenyl Grignard and **2f**, the diastereoselectivity decreased to 60% when (–)-8-cyclohexylmenthol was used as compared to (–)-8-phenylmenthol (94% de). In most cases the diastereoselectivity increased significantly when (–)-8-(4-phenoxyphenyl)menthol was used as the auxiliary (Table 5).

These results show that the 4-phenoxyphenyl substituent at C-8 of the menthyl system has a favorable effect on the stereoselectivity of this reaction. Whether this is a steric effect, an electronic effect, or a combination of the two will have to be determined through additional studies. The diastereoselectivity increased in the order (–)-menthol < (–)-8-cyclohexylmenthol < (–)-8-phenylmenthol ≈ (–)-*trans*-(α-cumyl)cyclohexanol < (–)-8-(4-phenoxyphenyl)menthol.

For all reactions performed, the diastereomeric excess was determined by HPLC analysis of the crude reaction products. A 1:1 mixture of the major and minor diastereomers **3** and **4** was prepared as shown in Scheme 2. The 1-acylpyridinium salt was prepared by treating the appropriate chloroformate with a methoxypyridine **2**. Addition of a Grignard reagent at –23 °C and an acidic workup afforded the dihydropyridones **5**. Hydrogenation of the *N*-(benzyloxycarbonyl)-2,3-dihydropyridones **5a** over 10% Pd/C gave the 2,3-dihydropyridones **6**. Alternatively, the dihydropyridones **6** were obtained by heating **5** with NaOMe/MeOH at reflux. The vinylogous amides **6** were treated with *n*-BuLi and the appropriate homochiral chloroformate to give a 1:1 mixture of diastereomeric dihydropyridones **3** and **4**. These crude mixtures were used as such as standards for HPLC analysis.

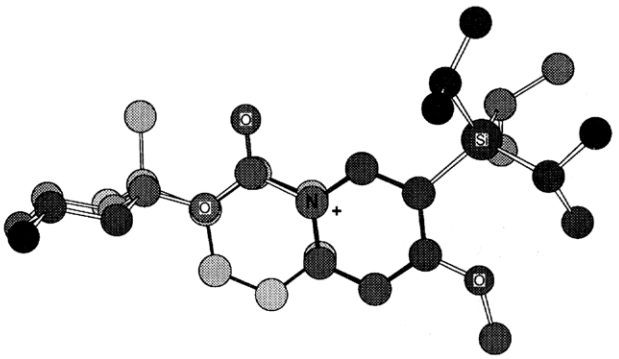
The absolute stereochemistry of the dihydropyridone products was determined by single crystal X-ray analysis of compounds **3b** (R = Ph)[9] and **3f** (R = Me)[9] and by comparing the NMR data of these compounds with corresponding spectral data from the other major diastereomers. The ^{1}H NMR spectra of the two diastereomers are quite different. In the major diastereomer, the C-2-H is shielded by the aromatic ring of the chiral auxiliary. In contrast, the C-6-H of the minor diastereomer is shielded by the aromatic ring. For the 2-alkyl derivatives, the major diastereomers exhibit a ^{1}H NMR signal for C-2-H in the range 2.4–2.8 ppm. The signal for C-2-H of the minor diastereomers appears between 4.0 and 4.5 ppm. Similarly, the 2-aryl derivatives show a C-2-H ^{1}H resonance in the range 3.5–4.5 ppm for the major diastereomers and a C-2-H signal at 5.4–5.7 ppm for the minor isomers. The C-6-H proton of both the 2-alkyl and 2-aryl derivatives resonates at 7.7–8.1 ppm for the major diastereomers and at 7.0–7.5 ppm for the minor isomers. The absolute configuration of certain major diastereomers was further confirmed through their use as intermediates in the synthesis of various naturally occurring alkaloids with known absolute configuration.[10,11]

Scheme 2

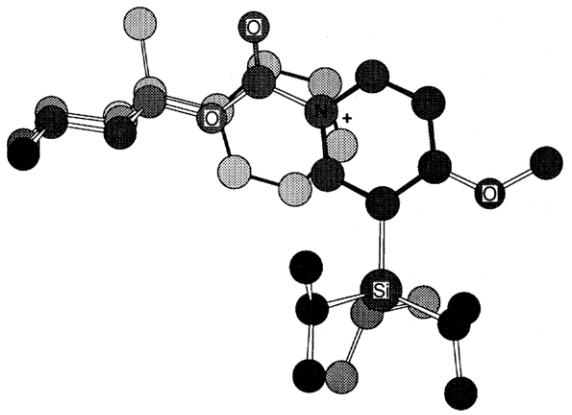


A working model that explains the observed stereoselectivity was presented in our initial communication. It is believed that the aryl substituent at C-8 of the chiral auxiliary is blocking one face of the pyridinium salt, thus favoring nucleophilic attack from the opposite face.[9] This explanation is complicated somewhat by the lack of double-bond character at the carbonyl carbon–nitrogen bond, which may allow free rotation in the ground state. Figure 2 shows two possible rotamers, **A** and **B**, which on nucleophilic attack at C-6 from the less sterically hindered top face would give the observed major and minor diastereomers, respectively. Molecular mechanics calculations (MMX),[22] which

(21) (a) Comins, D. L.; Salvador, J. *Tetrahedron Lett.* **1993**, *34*, 801. (b) Comins, D. L.; Salvador, J. *J. Org. Chem.* **1993**, *58*, 4656.



Rotamer A



Rotamer B

Figure 2.

do not measure π–π stacking interactions, indicate that the rotamers have an insufficient energy difference to explain the observed high degree of asymmetric induction. Our results suggest there is a strong possibility of π stacking between the phenyl group of the 8-phenylmenthyl auxiliary and the pyridine ring of the pyridinium salt that could favorably affect the rotamer population by stabilizing rotamer A. This hypothesis is supported by the observation that the diastereoselectivity decreased significantly when the chloroformate of (–)-8-cyclohexylmenthol was used as compared to the analogous reaction with the chloroformate of (–)-8-phenylmenthol (Table 5). Further support is present in the single-crystal X-ray analysis of a 4-methoxy-1-[((1*R*,4*S*,5*R*)-8-phenylmenthoxy)carbonyl]pyridinium salt, which indicates the presence of π–π stacking interactions between the phenyl and pyridine rings.[23] Stabilization of rotamer B through π–π stacking appears to be less favorable due to steric interactions between the TIPS group and the phenyl ring of the chiral auxiliary. Additional studies are underway to help shed more light on the mechanistic aspects of this efficient and practical asymmetric reaction.

Our efforts to convert the chiral dihydropyridones **3** to useful synthetic intermediates have been fruitful. The trialkylsilyl group of **3** can be removed on treatment with HBr/HOAc in dichloromethane at room temperature to give **7** in high yield (Scheme 3). The chiral auxiliary can be removed and recovered in near quantitative yield by refluxing a solution of **3** or **7** in NaOMe/MeOH (Table 6). There was no racemization observed under these conditions. This was confirmed by reintroducing the chiral auxiliary as previously described and analyzing by HPLC. The

(22) Molecular modeling was performed using PCMODEL (Serena Software, Bloomington, IN) and Chem3D (Cambridge Scientific Computing, Inc., Cambridge, MA).

(23) Singh, P.; Comins, D. L.; Joseph, S. P. *Acta Crystallogr.* **1994**, *C50*, 25.

Scheme 3

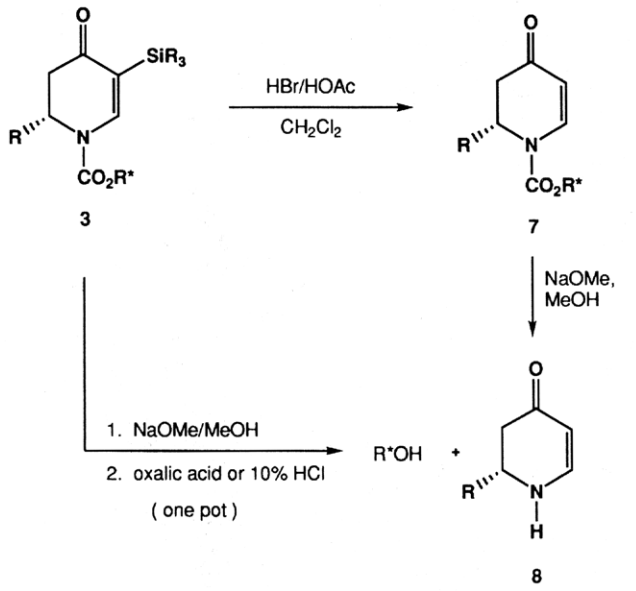


Table 6. Removal of Chiral Auxiliary from **3**

X[a]	R	R*-OH	method[b]	yield,[c] %
H	Ph	8-phenylmenthol	A	85
$(i\text{-Pr})_3$Si	*i*-Bu	8-phenylmenthol	A	92
$(i\text{-Bu})_3$Si	*o*-tolyl	8-phenylmenthol	B	85
$(i\text{-Pr})_3$Si	*c*-Hex	8-(4-phenoxyphenyl)menthol	B	81
$(i\text{-Pr})_3$Si	*o*-tolyl	8-phenylmenthol	B	88

[a] The reactions were generally performed on a 0.5-1.0-mmol scale. [b] Method A: NaOMe/MeOH, reflux. Method B: NaOMe/MeOH followed by oxalic acid or aqueous HCl. [c] Yield of purified product obtained from radial preparative-layer chromatography; the chiral auxiliaries were also isolated in high yield.

enantiopure dihydropyridones **8** can also be obtained from **3** via a one-pot reaction (Scheme 3). A solution of the major diastereomer **3** in NaOMe/MeOH was heated at reflux for 8–12 h, cooled to room temperature, and treated with oxalic acid or 10% HCl to obtain the enantiopure dihydropyridones **8** (Table 6). The enantiomeric purity was checked as described before and was found to be >99%.

Conclusion

We have developed a simple procedure for the enantioselective preparation of synthetically useful 2-substituted 2,3-dihydro-4-pyridones via Grignard addition to homochiral 1-acylpyridinium salts. Both enantiomers of the dihydropyridones **8** can be prepared using the readily available chiral auxiliaries, (–)-8-phenylmenthol[18] or (–)- and (+)-*trans*-(α-cumyl)cyclohexanol (TCC).[21] The synthesis of **8** can be carried out in two easy steps from 4-methoxy-3-(triisopropylsilyl)pyridine via intermediate **3**. Dihydropyridones **3** are generally white crystalline solids that can be obtained diastereomerically pure by simple chromatography or recrystallization. The chiral auxiliary is easily removed and can be recovered in high yield and recycled. The utility of enantiopure dihydropyridones of the type **8** as chiral building blocks for alkaloid synthesis has already been demonstrated in our laboratories and others. We are confident that our ongoing studies will make this methodology even more practical, expand the scope of its synthetic utility, and further open the door to the concise, enantioselective preparation of numerous natural products.

Experimental Section

General. All reactions were performed in oven-dried glassware under an argon atmosphere and were stirred magnetically. Tetrahydrofuran (THF) was dried by distillation from sodium benzophenone ketyl prior

to use. Methylene chloride, toluene, and diisopropylamine were distilled from calcium hydride and stored over 3-Å molecular sieves under N_2. Methanol was distilled from magnesium and stored over 3-Å molecular sieves under N_2. Other solvents were generally stored over 3-Å molecular sieves and used without further purification. *n*-Butyllithium was titrated periodically against diphenylacetic acid according to the procedure of Kofron and Baclawski.[24] Melting points were determined in open capillary tubes with a Meltemp melting point apparatus and are uncorrected. Radial preparative-layer chromatography (radial PLC) was performed with a Chromatotron (Harris Associates, Palo Alto, CA). High-pressure liquid chromatography (HPLC) was carried out using M-Porasil columns with a Waters Model 501 pump and a Model 440 absorbance detector. Optical rotations were determined with an Autopol II automatic polarimeter (Rudolph Research, Flanders, NJ). Combustion analyses were performed by Atlantic Microlabs, Inc., Norcross, GA. High-resolution mass spectral analyses (HRMS) were carried out at North Carolina State University. Infrared spectra were recorded on a Perkin-Elmer Model 1430 spectrophotometer. NMR spectra were recorded on a GN 300 spectrometer.

General Procedure for the Preparation of 3-Substituted 4-Methoxypyridines 2b-i. 4-Methoxy-3-(triisopropylsilyl)pyridine (2f). A solution of LDA was prepared at −23 °C from diisopropylamine (0.77 mL, 5.50 mmol) and 1.55 M *n*-butyllithium (3.55 mL, 5.50 mmol) in 10 mL of THF. After 15 min, 4-methoxypyridine (0.546 g, 5.00 mmol) was added, and the resulting mixture was stirred at −23 °C for 30 min. Triisopropylsilyl chloride (1.25 g, 6.50 mmol) was added, and the reaction mixture was stirred at −23 °C for 15 min and at room temperature for 1 h. Water (10 mL) and 10 mL of Et_2O were added, and the layers were separated. The aqueous phase was extracted with Et_2O (3 × 25 mL). The combined organic extracts were washed with 25-mL portions of water and brine. After drying over anhydrous K_2CO_3, the solvent was removed in vacuo to give the crude product. Purification by radial PLC (SiO_2, 25% EtOAc/hexanes) gave 0.918 g (69%) of **2f** as white crystals: mp 66–7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (d, 1 H, J = 6.0 Hz), 8.45 (s, 1 H), 6.75 (d, 1 H, J = 6.0 Hz), 3.79 (s, 3 H), 1.46 (sept, 3 H, J = 7.2 Hz), 1.06 (d, 18 H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.21, 156.45, 151.83, 117.90, 105.24, 54.12, 18.49, 11.12; IR ($CHCl_3$) 2950, 2870, 1573, 1550, 1470, 1460, 1396, 1290, 1275, 1030, 880, 812 cm^{-1}. Anal. Calcd for $C_{15}H_{27}NOSi$: C, 67.87; H, 10.25; N, 5.28. Found: C, 67.63; H, 1036; N, 5.20.

4-Methoxy-3-(trimethylsilyl)pyridine (2b): colorless oil (61%): bp 85 °C (2 mmHg) (Kugelrohr); IR (film) 3034, 2964, 2912, 2872, 1565, 1482, 1405, 1400, 1314, 1291, 1264, 1202, 1186, 1134, 1053, 869, 844, 801, 783, 658 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.49 (d, 1 H, J = 6.0 Hz), 8.39 (s, 1 H), 6.73 (d, 1 H, J = 6.0 Hz), 3.85 (s, 3 H), 0.29 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.10, 154.90, 152.40, 122.50, 105.30, 54.80, −1.00. Anal. Calcd for $C_9H_{15}NOSi$: C, 59.62; H, 8.34; N, 7.73. Found: C, 59.45; H, 8.41; N, 7.62.

4-Methoxy-3-(tri-*n*-propylsilyl)pyridine (2c): colorless oil (62%); IR (neat) 2950, 2920, 2865, 1570, 1470, 1390, 1295, 1270, 1065, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.47 (d, 1 H, J = 6 Hz), 8.35 (s, 1 H), 6.71 (d, 1 H, J = 6 Hz), 3.83 (s, 3 H), 1.2–1.4 (m, 6 H), 1.0 (t, 9 H), 0.75–0.9 (m, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.21, 155.67, 152.18, 120.58, 105.24, 54.64, 18.46, 17.36, 14.97; HRMS exact mass calcd for $C_{15}H_{27}NOSi$ 265.1862 (M^+), found 265.1860.

4-Methoxy-3-(triisobutylsilyl)pyridine (2d): colorless oil (53%); IR (neat) 2950, 2870, 1570, 1465, 1390, 1295, 1270, 1220, 1165, 1090, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.47 (d, 1 H, J = 6 Hz), 8.39 (s, 1 H), 6.70 (d, 1 H, J = 6 Hz), 3.84 (s, 3 H), 1.6–1.8 (m, 3 H), 0.8–0.9 (m, 24 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.05, 155.48, 152.15, 121.94, 105.21, 54.58, 26.40, 24.79, 23.5; HRMS exact mass calcd for $C_{18}H_{33}NOSi$ 307.2332 (M^+), found 307.2328.

4-Methoxy-3-(triphenylsilyl)pyridine (2e): white solid (46%); mp 126–7 °C; IR (KBr) 3070, 3050, 3010, 1570, 1555, 1470, 1425, 1395, 1295, 1275, 1185, 1110, 1015 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.57 (d, 1 H, J = 6 Hz), 8.25 (s, 1 H), 7.3–7.6 (m, 15 H), 6.80 (d, 1 H, J = 6 Hz), 3.56 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.05, 158.35, 153.41, 136.09, 133.67, 129.44, 127.69, 117.90, 105.92, 54.67; HRMS exact mass calcd for $C_{24}H_{21}NOSi$ 367.1393 (M^+), found 367.1393.

4-Methoxy-3-(tri-*n*-butylstannyl)pyridine (2g): (77%) bp 142–4 °C (0.06 mmHg); IR ($CHCl_3$) 2958, 2925, 2873, 2855, 1562, 1463, 1434, 1392, 1373, 1288, 1265, 1028, 809, 802 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.44 (d, 1 H, J = 6.0 Hz), 8.35 (s, 1 H), 6.72 (d, 1 H, J = 6.0 Hz), 3.81 (s, 3 H), 1.48–1.66 (m, 6 H), 1.24–1.37 (m, 6 H), 1.03–1.09 (m, 6 H), 0.84–0.87 (m, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.50, 156.00, 151.10, 124.20, 104.80, 54.24, 28.65, 26.70, 13.22, 9.32. Anal. Calcd for $C_{18}H_{33}NOSn$: C, 54.30; H, 8.35; N, 3.52. Found: C, 54.29; H, 8.39; N, 3.51.

4-Methoxy-3-(triisopropylstannyl)pyridine (2h): (16%) IR ($CHCl_3$) 2940, 2860, 1570, 1465, 1440, 1400, 1295, 1275, 1185, 1160, 1035, 995, 870, 820, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.46 (d, 1 H, J = 5.9 Hz), 8.40 (s, 1 H), 6.74 (d, 1 H, J = 5.9 Hz), 3.83 (s, 3 H), 1.71 (sept, 3 H, J = 7.3 Hz), 1.31 (d, 18 H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.85, 156.90, 151.40, 124.00, 105.40, 54.61, 22.04, 15.06. Anal. Calcd for $C_{15}H_{27}NOSn$: C, 50.60; H, 7.64; N, 3.93. Found: C, 50.75; H, 7.67; N, 3.90.

4-Methoxy-3-(tricyclohexylstannyl)pyridine (2i): white solid (45%); mp 96–8 °C; IR ($CHCl_3$) 2930, 2855, 1570, 1470, 1436, 1400, 1295, 1275, 1170, 1035, 995, 820, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.43 (d, 1 H, J = 5.1 Hz), 8.39 (s, 1 H), 6.72 (d, 1 H, J = 5.1 Hz), 3.82 (s, 3 H), 1.20–2.20 (m, 33 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.76, 156.90, 151.18, 124.04, 105.27, 54.45, 32.03, 29.18, 27.21, 27.05. Anal. Calcd for $C_{24}H_{39}NOSn$: C, 60.53; H, 8.25; N, 2.94. Found: C, 60.40; H, 8.19; N, 2.93.

General Procedure for the Preparation of 8-Arylmenthyl Chloroformates. (1*R*,2*S*,5*R*)-8-Phenylmenthyl Chloroformate. Caution: Phosgene is highly toxic. All procedures involving phosgene should be carried out in a well-ventilated hood! To a mixture of (−)-8-phenylmenthol (1.278 g, 5.50 mmol) and quinoline (1.60 mL, 13.54 mmol) in 20 mL of toluene cooled to 0 °C was added a 1.92 *M* solution (4.60 mL, 8.88 mmol) of phosgene in toluene over a period of 5 min. After stirring an additional 30 min, the bath was removed and stirring was continued at room temperature for 16 h. The reaction mixture was diluted with 10 mL of ether and 15 mL of 10% HCl. After stirring at room temperature for 5 min, the layers were separated and the aqueous phase was extracted with ether (2 × 10 mL). The combined organic extracts were washed with 10 mL of brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to give 1.62 g (*ca.* 100%) of the chloroformate as a thick orange oil: $[\alpha]^{23}$D −30.6° (*c* 2.32, $CHCl_3$); IR ($CHCl_3$) 2965, 2930, 1765, 1453, 1172, 1157, 838, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.10–7.34 (m, 5 H), 4.76 (dt, 1 H, J = 4.2, 10.2 Hz), 1.92–2.08 (m, 1 H), 1.50–1.67 (m, 1 H), 1.35 (s, 3 H), 1.28 (s, 3 H), 0.85 (d, 3 H, J = 6.6 Hz), 0.75–1.30 (m, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.51, 149.42, 128.00, 125.38, 125.16, 83.56, 50.27, 40.73, 39.55, 33.87, 31.13, 26.64, 26.41, 24.46, 21.43; HRMS exact mass calcd for $C_{17}H_{23}ClO_2$ 294.138 64 (M^+), found 294.138 60.

(1*R*,2*S*,5*R*)-8-(4-Phenoxyphenyl)menthyl chloroformate: viscous oil (*ca.* 100%); $[\alpha]^{23}$D −25.1° (*c* 0.78, $CHCl_3$); IR ($CHCl_3$) 2960, 2920, 1765, 1590, 1505, 1488, 1240, 1173, 1160, 840, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.93–7.35 (m, 9 H), 4.78 (dt, 1 H, J = 6.0, 9.0 Hz), 1.36 (s, 3 H), 1.29 (s, 3 H), 0.90 (d, 3 H, J = 9.0 Hz), 0.79–2.10 (m, 8 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 187.69, 154.77, 144.91, 129.63, 126.66, 122.94, 118.65, 118.58, 83.88, 50.57, 40.94, 39.36, 34.09, 31.38, 27.34, 26.66, 26.31, 21.59; HRMS exact mass calcd for $C_{23}H_{27}ClO_3$ 386.164 86 (M^+), found 386.164 74.

General Procedure for the Addition of Grignard Reagents to Chiral 1-Acylpyridinium Salts. 2(*S*)-Phenyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = Ph, R* = 8-Phenylmenthyl). To a solution of 4-methoxy-3-(triisopropylsilyl)-pyridine (0.107 g, 0.405 mmol) in 3 mL of toluene cooled to −23 °C was added a solution of (−)-8-phenylmenthyl chloroformate (0.118 g, 0.40 mmol) in 2.5 mL of toluene. After 15 min the reaction mixture was cooled to −78 °C, phenylmagnesium chloride (0.46 mmol) in 0.23 mL of THF was added dropwise, and the mixture was stirred at −78 °C for 1 h. The reaction was quenched by the addition of 5 mL of 10% HCl, followed by warming the reaction mixture to room temperature over a period of 10 min. After extracting with ether (3 × 5 mL), the combined organic extracts were washed with brine (5 mL) and dried over $MgSO_4$. Removal of the solvent in vacuo afforded 0.262 g of crude product as a pale yellow crystalline solid. HPLC analysis (5% EtOAc/hexane; 1 mL/min) showed a 97:3 ratio of the two diastereomers (94% de). Radial PLC (SiO_2; 5% EtOAc/hexane) gave 0.210 g (88%) of pure major diastereomer **3f** (R = Ph) as a white solid: mp 131–3 °C; $[\alpha]^{23}$D +24.20° (*c* 1.09, $CHCl_3$); IR ($CHCl_3$) 2970, 2870, 1709, 1650, 1573, 1388, 1300, 1244, 1122, 975, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.93 (s, 1 H), 7.10–7.50 (m, 10 H), 4.73–4.82 (m, 1 H), 3.58 (d, 1 H, J = 5.8 Hz), 2.71 (dd, 1 H, J = 5.8, 14.7 Hz), 2.29 (d, 1 H, J = 14.7 Hz), 0.70–1.79 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz,) δ 195.79, 153.66, 152.11, 146.99, 133.21, 129.11, 128.33, 127.30, 126.05, 125.90, 122.98, 110.25, 77.77, 51.50, 51.02, 40.00, 38.12, 30.70, 26.11, 21.77, 19.15, 18.52, 18.11, 11.52.

(24) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

Anal. Calcd for $C_{37}H_{53}NO_3Si$: C, 75.59; H, 9.09; N, 2.38; Found: C, 75.69; H, 9.12; N, 2.34.

The minor diastereomer 4f (R = Ph): viscous oil; $[\alpha]^{23}D$ +26.70° (*c* 0.97, $CHCl_3$); IR ($CHCl_3$) 2955, 2870, 1710, 1655, 1580, 1297, 1267, 1183, 1115, 1020, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.08–7.30 (m, 1 H), 5.51 (d, 1 H, *J* = 6.0 Hz), 4.92 (br dt, 1 H), 3.04 (dd, 1 H *J* = 9.0, 15.0 Hz), 2.65 (dd, 1 H, *J* = 1.0, 15.0 Hz), 1.00–2.15 (m, 16 H), 1.02 (d, 18 H, *J* = 6.0 Hz), 0.87 (d, 3 H, *J* = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.22, 150.60, 147.62, 138.55, 128.53, 127.83, 127.50, 125.62, 125.46, 125.20, 110.76, 55.48, 50.83, 42.52, 42.14, 39.55, 34.10, 31.26, 26.51, 21.60, 18.79, 18.69, 11.10. Anal. Calcd for $C_{37}H_{53}NO_3Si$: C, 75.59; H, 9.09; N, 2.38. Found: C, 75.42; H, 9.13; N, 2.30.

2(*S*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *o*-tolyl, R* = 8-phenylmenthyl): viscous oil (66%); $[\alpha]^{25}D$ +62.50° (*c* 0.28, $CHCl_3$); IR ($CHCl_3$) 2960, 2860, 1710, 1655, 1570, 1320, 1300, 1240, 1120, 1110, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.05 (s, 1 H), 6.83–7.35 (m, 9 H), 4.76 (m, 1 H), 4.12 (d, 1H, *J* = 8.8 Hz), 2.74 (dd, 1 H, *J* = 8.8, 15.4 Hz), 0.62–2.28 (m, 42 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.25, 152.64, 152.09, 148.98, 138.06, 133.28, 130.50, 127.92, 127.31, 126.08, 125.24, 124.82, 123.65, 110.05, 76.77, 51.99, 51.19, 40.72, 39.13, 34.06, 30.86, 30.67, 25.86, 21.33, 20.88, 19.14, 18.81, 18.68, 11.06. Anal. Calcd for $C_{38}H_{55}NO_3Si$: C, 75.82; H, 9.21; N, 2.33. Found: C, 75.54; H, 9.25; N, 2.27.

2(*R*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *o*-tolyl, R* = 8-phenylmenthyl): viscous oil (15%); $[\alpha]^{25}D$ –40.12° (*c* 0.13, $CHCl_3$); IR ($CHCl_3$) 2935, 2835, 1710, 1655, 1570, 1300, 1255, 1110, 1020, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.99–7.29 (m, 10 H), 5.65 (d, 1 H, *J* = 7.3 Hz), 4.88 (m, 1 H), 3.04 (dd, 1 H, *J* = 7.3, 15.3 Hz), 2.48 (d, 1 H, 15.3 Hz), 2.39 (s, 3 H), 0.844–1.954 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.15, 151.39, 150.56, 148.76, 137.19, 133.38, 131.12, 127.85, 127.66, 126.17, 125.37, 125.30, 123.82, 110.26, 77.13, 52.99, 50.93, 42.24, 41.17, 39.72, 34.16, 31.32, 29.64, 26.70, 21.62, 18.94, 18.81, 11.25; HRMS exact mass calcd for $C_{38}H_{55}NO_3Si$ 601.3951 (M^+), found 601.3951

2(*S*)-(4-Chlorophenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *p*-ClPh, R* = 8-phenylmenthyl): white solid (67%); mp 136–7 °C; $[\alpha]^{25}D$ +30.03° (*c* 0.86, $CHCl_3$); IR (KBr) 2960, 2860, 1710, 1655, 1565, 1380, 1295, 1240, 1120, 1015, 760, 695 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.95 (s, 1 H), 6.74–7.36 (m, 9 H), 4.79 (m, 1 H), 4.47 (d, 1 H, *J* = 7 Hz), 2.67 (dd, 1 H, *J* = 7, 16 Hz), 2.2 (d, 1 H, *J* = 16 Hz), 0.77–2.1 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.21, 153.18, 152.18, 148.02, 137.74, 133.15, 128.57, 128.18, 126.56, 125.17, 124.95, 111.47, 77.81, 53.93, 50.25, 42.88, 40.85, 39.07, 34.26, 31.44, 31.12, 25.98, 21.53, 20.72, 18.81, 18.68, 11.03. Anal. Calcd for $C_{37}H_{52}ClNO_3Si$: C, 71.41; H, 8.42; N, 2.25. Found: C, 71.31; H, 8.45; N, 2.22.

2(*R*)-(4-Chlorophenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *p*-ClPh, R* = 8-phenylmenthyl): viscous oil (7%); $[\alpha]^{25}D$ –4.35° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) 2960, 2870, 1710, 1655, 1570, 1300, 1255, 1115, 1020, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.03–7.5 (m, 10 H), 5.46 (d, 1 H, *J* = 7 Hz), 4.92 (m, 1 H), 3.04 (dd, 1 H, *J* = 7, 16 Hz), 2.6 (dd, 1 H, *J* = 1.5, 16 Hz), 0.88–2.08 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.06, 151.50, 151.41, 150.73, 147.50, 137.38, 133.54, 128.86, 127.95, 127.11, 125.30, 111.02, 77.19, 55.10, 50.96, 42.43, 42.27, 39.65, 34.19, 31.38, 26.89, 26.60, 21.69, 18.88, 18.78, 11.19; HRMS exact mass calcd for $C_{37}H_{52}ClNO_3Si$ 621.345 (M^+), found 621.3406.

2(*S*)-(4-Methoxyphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *p*-MeOPh, R* = 8-phenylmenthyl): white solid (68%); mp 152–3 °C; $[\alpha]^{25}D$ +47.69° (*c* 0.13, $CHCl_3$); IR (KBr) 2960, 2860, 1710, 1655, 1570, 1510, 1385, 1300, 1240, 1120, 1030, 765, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.94 (s, 1 H), 7.20–7.36 (m, 5 H), 6.68–6.77 (m, 4 H), 4.77–4.80 (m, 1 H), 3.73 (s, 3 H), 3.53 (d, 1 H, *J* = 6 Hz), 2.67 (dd, 1 H, *J* = 6, 15 Hz), 2.24 (d, 1 H, *J* = 15 Hz), 0.75–2.08 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.83, 158.71, 152.99, 152.41, 148.18, 131.25, 128.11, 126.47, 125.14, 124.91, 113.67, 110.99, 77.58, 55.19, 53.93, 50.25, 43.11, 40.85, 39.10, 34.26, 31.22, 31.10, 25.98, 21.53, 20.94, 18.78, 18.68, 11.06. Anal. Calcd for $C_{38}H_{55}NO_4Si$: C, 73.86; H, 8.97; N, 2.27. Found: C, 73.71; H, 8.99; N, 2.21.

2(*R*)-(4-Methoxyphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *p*-MeOPh, R* = 8-phenylmenthyl): viscous oil (9%); $[\alpha]^{25}D$ +4.32° (*c* 0.182, $CHCl_3$); IR ($CHCl_3$) 2955, 2865, 1710, 1650, 1570, 1510, 1300, 1250, 1175, 1110, 1020, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.75–7.33 (m, 9 H), 5.47 (d, 1 H, *J* = 6.5 Hz), 4.94 (m, 1 H), 3.72 (s, 3 H), 3.03 (dd, 1 H, *J* = 6.5, 15 Hz), 2.63 (dd, 1 H, *J* = 1.5, 15 Hz), 0.87–2.04 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.64, 158.97, 151.60, 150.66, 147.66, 130.89, 127.89, 126.92, 125.33, 113.99, 110.73, 77.19, 55.16, 50.96, 42.75, 42.27, 39.68, 34.19, 31.35, 26.63, 21.66, 18.88, 18.78, 11.19. Anal. Calcd for $C_{38}H_{55}NO_4Si$: C,73.86; H, 8.97; N, 2.27. Found: C, 73.85; H, 8.99; N, 2.21.

2(*S*)-(4-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *p*-tolyl, R* = 8-phenylmenthyl): white solid (75%); mp 116–7 °C; $[\alpha]^{25}D$ +28.96° (*c* 0.23, $CHCl_3$); IR (KBr) 2960, 2860, 1710, 1570, 1380, 1295, 1240, 1115, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.95 (s, 1 H), 6.70–7.35 (m, 9 H), 4.79 (m, 1 H), 3.56 (d, 1 H, *J* = 6 Hz), 2.67 (dd, 1 H, *J* = 6, 15 Hz), 0.74–2.25 (m, 42 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.735, 152.958, 152.506, 152.441, 148.241, 136.868, 136.061, 128.953, 128.113, 125.140, 124.914, 111.054, 77.549, 54.287, 50.248, 43.043, 40.846, 40.749, 39.069, 34.255, 31.089, 26.017, 21.493, 20.976, 20.879, 18.779, 18.682, 11.058. Anal. Calcd for $C_{38}H_{55}NO_3Si$: C, 75.82; H, 9.21; N, 2.33. Found: C, 75.79; H, 9.25; N, 2.31.

2(*R*)-(4-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *p*-tolyl, R* = 8-phenylmenthyl): viscous oil (7%); $[\alpha]^{25}D$ +5.33° (*c* 0.21, $CHCl_3$); IR ($CHCl_3$) 2950, 2860, 1705, 1650, 1565, 1295, 1250, 1110, 1020, 695 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.01–7.26 (m, 10 H), 5.47 (d, 1 H, *J* = 7.3 Hz), 4.92 (m, 1 H), 3.04 (dd, 1 H, *J* = 7.3, 16 Hz), 2.62 (dd, 1 H, *J* = 1.5, 16 Hz), 2.52 (s, 3 H), 0.87–2.00 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.57, 150.70, 147.79, 137.29, 135.80, 129.31, 127.92, 125.53, 125.37, 125.27, 125.14, 110.79, 77.19, 55.48, 50.96, 42.78, 42.27, 39.72, 34.22, 31.38, 29.67, 26.66, 21.69, 20.94, 18.88, 18.78, 11.22. Anal. Calcd for $C_{38}H_{55}NO_3Si$: C, 75.82; H, 9.21; N, 2.33. Found: C, 75.75; H, 9.24; N, 2.33.

2(*S*)-Cyclohexyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *c*-Hex, R* = 8-phenylmenthyl): white solid (83%); mp 147–8 °C; $[\alpha]^{24}D$ –85.27° (*c* 0.218, $CHCl_3$); IR (KBr) 2925, 2860, 1700, 1655, 1570, 1245, 1115, 695 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.78 (s, 1 H), 7.10–7.34 (m, 5 H), 4.86 (m, 1 H), 0.80–2.53 (m, 52 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.48, 152.77, 152.64, 146.28, 128.15, 127.99, 124.88, 110.70, 77.84, 55.81, 50.12, 41.46, 39.33, 39.14, 38.98, 34.45, 31.32, 31.06, 29.57, 28.86, 26.25, 26.08, 26.02, 25.89, 21.69, 21.56, 18.75, 18.69, 11.03. Anal. Calcd for $C_{37}H_{59}NO_3Si$: C, 74.82; H, 10.01; N, 2.36. Found: C, 74.80; H, 10.07; N, 2.33.

(*R*)-Cyclohexyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *c*-Hex, R* = 8-phenylmenthyl): viscous oil (7%); $[\alpha]^{24}D$ +136.92° (*c* 0.13, $CHCl_3$); IR ($CHCl_3$) 2940, 2870, 1710, 1650, 1570, 1260, 1110, 1015, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.04–7.43 (m, 6 H), 4.93 (m, 1 H), 4.18 (m, 1 H), 2.27 (dd, 1 H, *J* = 6, 16 Hz), 2.50 (dd, 1 H, *J* = 1.5, 16 Hz), 0.90–2.06 (m, 49 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.19, 151.86, 150.63, 147.37, 127.92, 125.27, 110.41, 77.19, 57.32, 51.02, 42.30, 39.72, 38.97, 38.46, 34.22, 31.38, 29.31, 29.18, 27.32, 26.66, 26.11, 26.05, 25.92, 25.66, 21.72, 18.88, 18.81, 11.19. Anal. Calcd for $C_{37}H_{59}NO_3Si$: C, 74.82; H, 10.01; N, 2.36. Found: C, 74.97; H, 10.06; N, 2.31.

2(*R*)-Methyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = methyl, R* = 8-phenylmenthyl): white solid (85%); mp 108–9 °C; $[\alpha]^{23}D$ –60.67° (*c* 0.3, $CHCl_3$); IR (KBr) 2960, 2860, 1705, 1650, 1570, 1250, 1100, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.67 (s, 1 H), 7.11–7.34 (m, 5 H), 4.89 (m, 1 H), 0.84–2.77 (m, 44 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.93, 152.57, 146.92, 127.98, 125.08, 124.98, 109.63, 77.32, 50.41, 47.44, 42.43, 41.69, 39.2, 34.42, 31.32, 31.02, 26.18, 21.72, 21.42, 18.84, 18.78, 16.71, 11.09. Anal. Calcd for $C_{32}H_{51}NO_3Si$: C, 73.09; H, 9.78; N, 2.66. Found: C, 72.91; H, 9.81; N, 2.61.

2(*S*)-Methyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = methyl, R* = 8-phenylmenthyl): viscous oil (3%); $[\alpha]^{25}D$ +90.34° (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 2960, 2860, 1705, 1645, 1570, 1300, 1260, 1095, 905, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.10–7.29 (m, 6 H), 4.94 (m, 1 H), 4.47 (m, 1 H), 2.75 (dd, 1 H, *J* = 6.6, 15.4 Hz), 2.20 (dd, 1 H, *J* = 1.5, 15.4 Hz), 0.89–2.21 (m, 41 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.54, 150.66, 146.34, 128.21, 127.85, 125.14, 108.97, 77.16, 50.89, 48.67, 42.30, 42.17, 39.59, 34.16, 31.28, 26.50, 21.62, 18.81, 18.75, 16.42, 11.09. Anal. Calcd for $C_{32}H_{51}NO_3Si$: C, 73.09; H, 9.78; N, 2.66. Found: C, 72.98; H, 9.81; N, 2.67.

2(*S*)-Vinyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = vinyl, R* = 8-phenylmenthyl): white solid (75%); mp 127–8 °C; $[\alpha]^{25}$D –21.37° (*c* 0.36, $CHCl_3$); IR (KBr) 3080, 3050, 2940, 2860, 1710, 1660, 1570, 1390, 1290, 1240, 1120, 980, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.75 (s, 1 H), 7.10–7.35 (m, 5 H), 5.38 (m, 1 H), 4.74–5.00 (m, 3 H), 3.07 (m, 1 H), 2.45 (dd, 1 H, *J* = 6, 15 Hz), 0.9–2.2 (m, 39 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.96, 152.70, 152.18, 147.27, 133.06, 127.98, 125.01, 124.88, 115.77, 110.47, 77.45, 52.96, 50.28, 41.36, 40.59, 39.04, 34.35, 31.22, 26.02, 21.66, 20.98, 18.72, 10.96. Anal. Calcd for $C_{33}H_{51}NO_3Si$: C, 73.69; H, 9.57; N, 2.60. Found: C, 73.57; H, 9.60; N, 2.66.

2(*R*)-Vinyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = vinyl, R* = 8-phenylmenthyl): viscous oil (6%); $[\alpha]^{25}$D +43.20° (*c* 1.2, $CHCl_3$); IR (film) 2940, 2860, 1715, 1660, 1570, 1360, 1295, 1250, 1115, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.1–7.32 (m, 6 H), 5.66 (m, 1 H), 4.62–5.17 (m, 4 H), 2.82 (dd, 1 H, *J* = 6, 15 Hz), 2.45 (dd, 1 H, *J* = 1.5, 15 Hz), 0.9–2.1 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.87, 151.20, 150.76, 146.76, 132.99, 127.95, 125.50, 125.27, 116.64, 110.11, 77.19, 54.06, 51.02, 42.24, 40.36, 39.72, 34.22, 31.88, 26.33, 21.72, 18.88, 18.81, 18.62, 11.15; HRMS exact mass calcd for $C_{33}H_{51}NO_3Si$ 537.3638 (M^+), found 537.3635.

2(*S*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-(4-phenoxyphenyl)menthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *o*-tolyl, R* = 8-(4-phenoxyphenyl)menthyl): white solid (71%); mp 57–8 °C; $[\alpha]^{25}$D +57.30° (*c* 0.45, $CHCl_3$); IR (KBr) 3060, 3030, 2960, 2920, 2860, 1720, 1660, 1580, 1490, 1300, 1240, 975, 755 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (s, 1 H), 6.7–7.34 (m, 13 H), 4.75 (m, 1 H), 4.40 (d, 1 H, *J* = 8 Hz), 3.02 (dd, 1 H, *J* = 8, 15 Hz), 2.33 (d, 1 H, *J* = 15 Hz), 2.16 (s, 3 H), 0.9–1.85 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.38, 157.03, 154.67, 152.18, 148.85, 147.24, 130.60, 129.73, 127.43, 126.56, 126.24, 123.72, 123.20, 118.74, 118.00, 110.41, 76.81, 52.48, 51.38, 40.85, 38.88, 34.13, 30.93, 30.48, 25.98, 21.66, 21.56, 21.40, 19.14, 18.88, 18.75, 11.12; HRMS exact mass calcd for $C_{44}H_{59}NO_4Si$ 693.4213 (M^+), found 693.4218.

2(*R*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-(4-phenoxyphenyl)menthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *o*-tolyl, R* = 8-(4-phenoxyphenyl)menthyl): white solid (7%); mp 56–7 °C; $[\alpha]^{25}$D –35.33° (*c* 0.29, $CHCl_3$); IR (KBr) 3060, 3030, 2940, 2920, 2860, 1720, 1660, 1570, 1485, 1295, 1240, 1110, 1020, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.9–7.4 (m, 14 H), 5.67 (d, 1 H, *J* = 8 Hz), 4.85 (m, 1 H), 3.13 (dd, 1 H, *J* = 8, 15 Hz), 2.50 (d, 1 H, *J* = 15 Hz), 2.38 (s, 3 H), 0.85–1.56 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.22, 152.93, 148.92, 139.84, 137.22, 133.80, 131.15, 129.60, 127.72, 126.82, 126.21, 122.78, 119.13, 118.49, 118.26, 77.13, 53.09, 51.02, 47.34, 42.24, 41.27, 39.52, 34.16, 31.28, 29.67, 26.89, 21.62, 19.00, 18.91, 18.78, 11.19; HRMS exact mass calcd for $C_{44}H_{59}NO_4Si$ 693.4213 (M^+), found 693.4211.

2(*S*)-(4-Methoxyphenyl)-1-[((1*R*,2*S*,5*R*)-8-(4-phenoxyphenyl)menthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *p*-MeOPh, R* = 8-(4-phenoxyphenyl)menthyl): white solid (85%); mp 53–4 °C; $[\alpha]^{25}$D +29.45° (*c* 0.36, $CHCl_3$); IR (KBr) 3040, 2950, 2860, 1715, 1660, 1570, 1510, 1380, 1295, 1240, 1175, 1120, 1020, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.95 (s, 1 H), 6.7–7.4 (m, 13 H), 4.79 (m, 1 H), 3.90 (d, 1 H, *J* = 6 Hz), 3.72 (s, 3 H), 2.87 (dd, 1 H, *J* = 6, 15 Hz), 2.48 (d, 1 H, *J* = 15 Hz), 0.8–2.00 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.77, 158.77, 157.03, 154.48, 152.41, 148.01, 147.53, 131.21, 129.66, 126.50, 126.40, 123.07, 118.58, 118.16, 113.74, 111.25, 77.55, 55.16, 54.45, 50.44, 42.88, 40.91, 38.75, 34.19, 31.09, 30.90, 26.08, 21.53, 18.78, 18.65, 11.02. Anal. Calcd for $C_{44}H_{59}NO_5Si$: C, 74.42; H, 8.38; N, 1.97. Found: C, 74.66; H, 8.34; N, 1.99.

2(*R*)-(4-Methoxyphenyl)-1-[((1*R*,2*S*,5*R*)-8-(4-phenoxyphenyl)menthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *p*-MeOPh, R* = 8-(4-phenoxyphenyl)menthyl): white solid (3%); mp 44–5 °C; $[\alpha]^{25}$D –10.29° (*c* 0.175, $CHCl_3$); IR (KBr) 2960, 2870, 1720, 1665, 1575, 1490, 1300, 1250, 1180, 1120, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.7–7.4 (m, 14 H), 5.49 (bd, 1 H, *J* = 6 Hz), 4.90 (m, 1 H), 3.73 (s, 3 H), 3.12 (dd, 1 H, *J* = 6, 15 Hz), 2.65 (dd, 1 H, *J* = 1.5, 15 Hz), 0.9–2.0 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.57, 158.94, 157.45, 154.29, 151.73, 147.70, 145.32, 130.92, 129.57, 126.92, 126.79, 122.78, 118.49, 118.26, 113.99, 77.16, 55.26, 55.19, 51.02, 42.93, 42.24, 39.49, 34.16, 31.32, 26.82, 21.66, 18.84, 18.72, 11.15. Anal. Calcd for $C_{44}H_{59}NO_5Si$: C, 74.42; H, 8.38; N, 1.97. Found: C, 74.60; H, 8.39; N, 1.94.

2(*S*)-Cyclohexyl-1-[((1*R*,2*S*,5*R*)-8-(4-phenoxyphenyl)menthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *c*-Hex, R* = 8-(4-phenoxyphenyl)menthyl): white solid (65%); mp 68–9 °C; $[\alpha]^{25}$D –22.58° (*c* 0.21, $CHCl_3$); IR (KBr) 2930, 2860, 1710, 1655, 1570, 1485, 1245, 1120, 1020, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.8 (s, 1 H), 6.9–7.4 (m, 9 H), 4.86 (m, 1 H), 0.9–2.85 (m, 51 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.35, 157.03, 154.41, 152.80, 148.14, 147.18, 129.63, 126.82, 126.17, 123.04, 118.23, 111.02, 77.84, 56.32, 50.38, 41.56, 39.10, 39.04, 38.88, 34.42, 31.35, 30.60, 29.64, 28.92, 26.37, 26.05, 25.92, 22.40, 21.69, 18.78, 18.72, 11.02. Anal. Calcd for $C_{43}H_{63}NO_4Si$: C, 75.28; H, 9.26; N, 2.04. Found: C, 75.41; H, 9.31; N, 2.06.

2(*R*)-Cyclohexyl-1-[((1*R*,2*S*,5*R*)-8-(4-phenoxyphenyl)menthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *c*-Hex, R* = 8-(4-phenoxyphenyl)menthyl): white solid (2%); mp 58–9 °C; $[\alpha]^{25}$D +41.50° (*c* 0.15, $CHCl_3$); IR (KBr) 2920, 2860, 1715, 1655, 1565, 1490, 1300, 1245, 1110, 1010 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.59 (s, 1 H), 6.89–7.33 (m, 9 H), 4.91 (m, 1 H), 4.21 (d, 1 H, *J* = 7 Hz), 2.73 (dd, 1 H, *J* = 7, 16 Hz), 2.55 (dd, 1 H, *J* = 1.5, 16 Hz), 0.9–2.0 (m, 49 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.19, 157.42, 154.35, 151.89, 147.24, 145.17, 129.57, 126.72, 122.78, 118.42, 118.36, 110.63, 77.10, 57.39, 51.09, 42.24, 39.52, 39.07, 38.46, 34.19, 31.32, 29.28, 29.18, 27.28, 26.86, 26.44, 26.11, 26.05, 25.92, 21.72, 18.81, 18.75, 11.12. Anal. Calcd for $C_{43}H_{63}NO_4Si$: C, 75.28; H, 9.26; N, 2.04. Found: C, 75.00; H, 9.33; N, 2.01.

2(*S*)-Vinyl-1-[((1*R*,2*S*,5*R*)-8-((4-phenoxyphenyl)menthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = vinyl, R* = 8-(4-phenoxyphenyl)menthyl): white solid (75%); mp 56–7 °C; $[\alpha]^{25}$D +24.76° (*c* 0.105, $CHCl_3$); IR (KBr) 2950, 2860, 1715, 1660, 1580, 1485, 1300, 1240, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77 (s, 1 H), 6.9–7.4 (m, 9 H), 5.47 (m, 1 H), 4.8–5.05 (m, 3 H), 3.45 (bs, 1 H), 2.66 (dd, 1 H, *J* = 7, 15 Hz), 2.28 (d, 1 H, *J* = 15 Hz), 0.8–2.2 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.99, 157.00, 154.44, 152.25, 147.18, 133.18, 129.66, 126.37, 123.17, 118.65, 118.07, 115.96, 110.79, 77.19, 53.51, 50.57, 41.56, 40.43, 38.81, 34.35, 31.28, 30.83, 26.21, 21.66, 18.78, 18.72, 10.99. Anal. Calcd for $C_{39}H_{55}NO_4Si$: C, 74.36; H, 8.80; N, 2.22. Found: C, 74.46; H, 8.87; N, 2.15.

2(*R*)-Vinyl-1-[((1*R*,2*S*,5*R*)-8-(4-phenoxyphenyl)menthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = vinyl, R* = 8-(4-phenoxyphenyl)menthyl): white solid (5%); mp 51–2 °C; $[\alpha]^{27}$D +91.25° (*c* 0.08, $CHCl_3$); IR (KBr) 2950, 2860, 1720, 1660, 1570, 1490, 1300, 1245, 1085, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.54 (bs, 1 H), 6.89–7.33 (m, 9 H), 5.7 (m, 1 H), 4.88–5.19 (m, 4 H), 2.90 (dd, 1 H, *J* = 7, 15 Hz), 2.48 (dd, 1 H, *J* = 1.5, 15 Hz), 0.8–2.0 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.90, 157.48, 154.35, 151.34, 146.69, 145.40, 133.06, 129.60, 126.79, 122.81, 118.52, 118.29, 116.64, 110.40, 77.20, 54.19, 51.09, 42.24, 40.49, 39.52, 34.22, 31.35, 26.82, 21.72, 18.84, 18.78, 11.12; HRMS exact mass calcd for $C_{39}H_{55}NO_4Si$ 629.3900 (M^+), found 629.3901.

2(*S*)-Phenyl-1-[(1*R*,2*S*,5*R*)-menthoxycarbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = Ph, R* = menthyl): viscous oil (87%, de 44%); $[\alpha]^{27}$D –47.53° (*c* 0.89, $CHCl_3$); IR ($CHCl_3$) 2980, 2885, 1715, 1655, 1575, 1300, 1245, 1115, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (s, 1 H), 7.14–7.3 (m, 5 H), 5.63 (d, 1 H, *J* = 7 Hz), 4.67 (m, 1 H), 3.14 (dd, 1 H, *J* = 7, 16 Hz), 2.76 (dd, 1 H, *J* = 1.5, 16 Hz), 0.77–1.94 (m, 39 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.35, 152.64, 148.08, 138.74, 128.66, 127.69, 125.53, 111.51, 78.10, 55.68, 47.18, 42.72, 40.52, 33.93, 31.28, 26.66, 23.40, 21.85, 20.69, 18.75, 18.65, 16.42, 11.12. Anal. Calcd for $C_{31}H_{49}NO_3Si$: C, 72.75; H, 9.65; N, 2.74. Found: C, 72.72; H, 9.69; N, 2.67.

2(*R*)-Phenyl-1-[(1*R*,2*S*,5*R*)-menthoxycarbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = Ph, R* = menthyl): viscous oil (87%, de 44%); $[\alpha]^{27}$D –46.94° (*c* 0.98, $CHCl_3$); IR ($CHCl_3$) 2960, 2860, 1710, 1655, 1570, 1300, 1240, 1110, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14 (s, 1 H), 7.12–7.3 (m, 5 H), 5.63 (d, 1 H, *J* = 7 Hz), 4.58 (m, 1 H), 3.16 (dd, 1 H, *J* = 7, 15 Hz), 2.7 (d, 1 H, *J* = 15 Hz), 2.14 (d, 1 H, *J* = 11 Hz), 0.50–1.63 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.25, 152.76, 148.34, 139.13, 129.73, 127.69, 125.33, 111.44, 78.07, 55.90, 46.95, 42.98, 42.88, 40.94, 34.00, 31.35, 22.85, 21.91, 20.65, 18.81, 18.68, 15.65, 11.09. Anal. Calcd for $C_{31}H_{49}NO_3Si$: C, 72.75; H, 9.65; N, 2.74. Found: C, 72.85; H, 9.71; N, 2.72.

2(*R*)-(2-Methylpropyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *i*-Bu, R* = 8-phenylmenthyl): white solid (86%); mp 141–3 °C; $[\alpha]^{23}$D –60.29° (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) 2965, 2870, 1705, 1650, 1570, 1465, 1385, 1315, 1260, 1120, 1015, 975, 880, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.72 (s, 1 H), 7.10–7.60 (m, 5 H), 4.85–5.10 (m, 1 H), 2.80–3.10 (m, 1 H), 0.85–2.50 (m, 49 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.03, 152.21, 147.46, 128.08, 125.37, 125.07, 110.11, 50.54, 50.08, 41.78, 40.29,

39.20, 34.45, 31.34, 30.80, 26.24, 24.04, 23.66, 21.88, 21.69, 19.03, 18.84, 18.77, 11.08. Anal. Calcd for $C_{35}H_{57}NO_3Si$: C, 74.02; H, 10.12; N, 2.47. Found: C, 73.89; H, 10.16; N, 2.42.

2(*S*)-(2-Methylpropyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = *i*-Bu, R* = 8-phenylmenthyl): viscous oil (3%); $[\alpha]^{23}D$ +72.2° (*c* 0.72, $CHCl_3$); IR ($CHCl_3$) 2975, 2875, 1707, 1652, 1578, 1465, 1360, 1310, 1260, 1112, 1018, 880, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.00–7.50 (m, 6 H), 4.90–5.07 (m, 1 H), 4.46 (br s, 1 H), 2.68 (dd, 1 H, *J* = 6.0, 14.7 Hz), 2.35 (d, 1 H, *J* = 14.7 Hz), 0.85–2.10 (m, 47 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.77, 150.76, 127.95, 125.72, 125.24, 54.13, 51.25, 51.06, 50.99, 42.30, 39.84, 39.75, 38.97, 38.62, 34.22, 31.38, 26.70, 26.60, 25.66, 24.27, 23.56, 23.30, 21.72, 21.43, 18.91, 14.13, 11.22. Anal. Calcd for $C_{35}H_{57}NO_3Si$: C, 74.02; H, 10.12; N, 2.47. Found: C, 74.12; H, 10.17; N, 2.44.

2(*S*)-(1-Hexynyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = 1-hexynyl, R* = 8-phenylmenthyl): white solid (74%); mp 75–7 °C; $[\alpha]^{23}D$ +62.3° (*c* 0.41, $CHCl_3$); IR ($CHCl_3$) 2690, 2860, 1710, 1658, 1572, 1385, 1305, 1242, 973, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.64 (s, 1 H), 7.05–7.45 (m, 5 H), 4.80–5.05 (m, 1 H), 3.34 (br s, 1 H), 0.80–2.45 (m, 49 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.44, 152.54, 151.80, 146.76, 128.11, 127.92, 125.01, 124.85, 110.67, 83.82, 77.49, 76.00, 50.34, 44.01, 42.14, 41.52, 39.07, 34.35, 31.22, 30.96, 30.25, 26.02, 21.62, 21.59, 21.04, 18.68, 17.94, 13.42, 10.99. Anal. Calcd for $C_{37}H_{57}NO_3Si$: C, 75.07; H, 9.71; N, 2.37. Found: C, 74.86; H, 9.75; N, 2.31.

2(*R*)-(1-Hexynyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (4f, R = 1-hexynyl, R* = 8-phenylmenthyl): viscous oil (2%); $[\alpha]^{23}D$ +62.5° (*c* 0.37, $CHCl_3$); IR ($CHCl_3$) 2960, 2860, 1710, 1655, 1570, 1452, 1318, 1295, 1250, 1110, 1020, 880, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.00–7.55 (m, 6 H), 4.78–5.00 (m, 1 H), 3.50 (br s, 1 H), 0.85–2.50 (m, 49 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.02, 152.00, 150.01, 145.99, 128.24, 127.51, 125.22, 124.11, 111.11, 84.00, 78.01, 77.19, 51.05, 44.51, 42.14, 41.07, 39.11, 34.21, 31.99, 30.02, 30.00, 25.11, 21.77, 21.32, 21.00, 17.99, 17.50, 14.02, 11.05. Anal. Calcd for $C_{37}H_{57}NO_3Si$: C, 75.07; H, 9.71; N, 2.37. Found: C, 75.04; H, 9.73; N, 2.32.

2(*R*)-*n*-Propyl-1-[(((1*R*,2*S*)-2-(1-methyl-1-phenylethyl)cyclohexyl)-oxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = *n*-propyl, R* = (−)-TCC): white solid (95%); mp 124–4.5 °C; $[\alpha]^{25}D$ −63.6° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2940, 2860, 1700, 1656, 1650, 1450, 1380, 1320, 1250, 1110, 1010, 870 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.72 (s, 1 H), 7.40–7.09 (m, 5 H), 4.93–4.80 (m, 1 H), 2.75 (bs, 1 H), 2.42–2.19 (m, 1 H), 2.12–1.90 (m, 2 H), 1.85–0.75 (m, 42 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.95, 152.54, 152.26, 147.46, 128.04, 125.08, 110.09, 77.97, 51.25, 51.02, 40.33, 39.41, 33.49, 32.85, 30.79, 26.81, 25.85, 24.64, 21.64, 18.84, 18.78, 18.65, 13.88, 11.11. Anal. Calcd for $C_{33}H_{53}NO_3Si$: C, 73.42; H, 9.89; N, 2.60. Found: C, 73.32; H, 9.86; N, 2.51.

2(*R*)-Phenyl-1-[(((1*S*,2*R*)-2-(1-methyl-1-phenylethyl)cyclohexyl)-oxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (3f, R = phenyl, R* = (+)-TCC): white solid (88%); mp 154 °C; $[\alpha]^{24}D$ −9.5° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) 3048, 2943, 2861, 1719, 1661, 1584, 1496, 1448, 1402, 1326, 1255, 1120, 1014 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.98 (s, 1 H), 6.80–7.45 (m, 10 H), 4.65–4.85 (m, 1 H), 3.50–3.70 (br d, 1 H, *J* = 6 Hz), 2.60–2.80 (dd, 1 H, *J* = 6.6, 15 Hz), 2.20–2.40 (d, 1 H, *J* = 15 Hz), 0.95–2.15 (m, 36 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.38, 153.00, 152.33, 148.28, 139.31, 128.38, 128.11, 127.36, 125.23, 124.99, 111.25, 77.99, 54.69, 50.96, 42.92, 39.36, 32.70, 31.06, 26.61, 25.70, 24.46, 21.02, 18.82, 18.71, 11.13. Anal. Calcd for $C_{36}H_{51}NO_3Si$: C, 75.34; H, 8.96; N, 2.44. Found: C, 75.06; H, 8.98; N, 2.42.

2(*S*)2-Phenyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(trimethylsilyl)-2,3-dihydro-4-pyridone (3b, R = Ph, R* = 8-phenylmenthyl): white solid (82%); mp 97–8 °C; $[\alpha]^{23}D$ +77.5° (*c* 1.11, $CHCl_3$); IR ($CHCl_3$) 2954, 2925, 1719, 1657, 1580, 1497, 1456, 1389, 1357, 1324, 1302, 1246, 1184, 1124, 1027, 980, 961, 929, 872, 840, 766 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.92 (s, 1 H), 6.70–7.50 (m, 10 H), 4.70–4.85 (m, 1 H), 3.40–3.45 (m, 1 H), 2.60–2.80 (m, 1 H), 2.15–2.35 (m, 1 H), 0.65–2.10 (m, 17 H), 0.11 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.00, 153.00, 152.00, 147.09, 140.02, 128.30, 127.68, 125.59, 125.02, 124.82, 116.01, 77.44, 54,72, 50.20, 42.52, 40.66, 39.01, 34.49, 31.20, 31.00, 25.91, 21.44, 20,73, −1.50. Anal. Calcd for $C_{31}H_{41}NO_3Si$: C, 73.91; H, 8.20; N, 2.78. Found: C, 74.12; H, 7.93; N, 2.76.

2(*S*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(tri-*n*-propylsilyl)-2,3-dihydro-4-pyridone (3c, R = *o*-tolyl, R* = 8-phenylmenthyl): white solid (63%); mp 93–4 °C; $[\alpha]^{26}D$ +37.85° (*c* 1.2, $CHCl_3$); IR (KBr) 3050, 3020, 2960, 2920, 2870, 1715, 1655, 1570, 1325, 1295, 1240, 1125, 960, 765 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.0 (s, 1 H), 6.8–7.36 (m, 9 H), 4.78 (m, 1 H), 4.08 (d, 1 H, *J* = 8 Hz), 2.72 (dd, 1 H, *J* = 8, 15 Hz), 0.63–2.2 (m, 42 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 194.96, 152.76, 152.28, 148.24, 138.00, 133.35, 130.54, 128.05, 127.31, 126.04, 125.24, 124.85, 123.78, 112.70, 77.16, 52.15, 51.12, 40.75, 40.56, 39.17, 34.09, 30.90, 30.64, 25.89, 21.40, 20.98, 19.23, 18.42, 17.45, 14.61. Anal. Calcd for $C_{38}H_{55}NO_3Si$: C, 75.82; H, 9.21; N, 2.33. Found: C, 75.58; H, 9.15; N, 2.23.

2(*R*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(tri-*n*-propylsilyl)-2,3-dihydro-4-pyridone (4c, R = *o*-tolyl, R* = 8-phenylmenthyl): white solid (25%); mp 45–6 °C; $[\alpha]^{26}D$ +23.18° (*c* 0.17, $CHCl_3$); IR (KBr) 3020, 2950, 2920, 2860, 1715, 1655, 1570, 1355, 1295, 1250, 1110, 1020, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.8–7.3 (m, 10 H), 5.67 (d, 1 H, *J* = 9 Hz), 4.89 (m, 1 H), 3.01 (dd, 1 H, *J* = 9, 15 Hz), 2.39 (s, 3 H), 0.6–1.4 (m, 38 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 194.90, 151.21, 147.95, 137.32, 133.90, 131.09, 127.89, 127.63, 126.14, 125.27, 125.17, 123.82, 112.4, 77.16, 52.87, 51.02, 42.20, 41.01, 39.59, 34.19, 31.28, 26.53, 21.62, 19.00, 18.52, 17.55, 14.87; HRMS exact mass calcd for $C_{38}H_{55}NO_3Si$ 601.3951 (M^+), found 601.3951.

2(*S*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisobutylsilyl)-2,3-dihydro-4-pyridone (3d, R = *o*-tolyl, R* = 8-phenylmenthyl): white solid (65%); mp 103–4 °C; $[\alpha]^{26}D$ +44.08° (*c* 0.89, $CHCl_3$); IR (KBr) 3060, 3030, 2950, 2920, 2860, 1710, 1660, 1570, 1325, 1295, 1240, 980, 960, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.99 (s, 1 H), 6.7–7.4 (m, 9 H), 4.76 (m, 1 H), 4.06 (d, 1 H, *J* = 9 Hz), 2.66 (dd, 1 H, *J* = 9, 16 Hz), 2.15 (d, 1 H, *J* = 16 Hz), 2.1 (s, 3 H), 0.6–2 (m, 44 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 194.93, 152.73, 152.18, 147.72, 138.16, 133.28, 130.50, 128.02, 127.31, 125.95, 125.24, 124.85, 123.75, 113.77, 76.74, 51.99, 51.19, 40.78, 40.65, 39.13, 34.09, 30.86, 26.60, 26.37, 26.08, 25.82, 24.82, 23.08, 21.36, 20.72, 19.14; HRMS exact mass calcd for $C_{41}H_{61}NO_3Si$ 643.4421 (M^+), found 643.4423.

2(*R*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisobutylsilyl)-2,3-dihydro-4-pyridone (4d, R = *o*-tolyl, R* = 8-phenylmenthyl): viscous oil (24%); $[\alpha]^{25}D$ −32.50° (*c* 0.40, $CHCl_3$); IR (KBr) 2950, 2920, 2860, 1720, 1660, 1575, 1460, 1295, 1250, 1115, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.8–7.4 (m, 10 H), 5.69 (d, 1 H, *J* = 8 Hz), 4.8 (m, 1 H), 2.98 (dd, 1 H, *J* = 8, 15 Hz), 2.48 (d, 1 H, *J* = 15 Hz), 2.38 (s, 3 H), 0.7–1.9 (m, 44 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 194.83, 150.72, 147.56, 137.42, 133.86, 131.12, 128.40, 127.92, 127.69, 126.11, 125.75, 125.37, 113.73, 78.16, 54.16, 53.03, 50.93, 45.34, 42.14, 41.30, 39.81, 34.84, 34.22, 26.79, 26.24, 24.79, 23.53, 21.66, 18.97; HRMS exact mass calcd for $C_{41}H_{61}NO_3Si$ 643.4421 (M^+), found 643.4420.

2(*S*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triphenylsilyl)-2,3-dihydro-4-pyridone (3e, R = *o*-tolyl, R* = 8-phenylmenthyl): white solid (50%); mp 199–200 °C; $[\alpha]_D^{25}$ +39.07° (*c* 0.18, $CHCl_3$); IR (KBr) 3040, 2920, 1720, 1660, 1570, 1290, 1240, 1100, 695 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.04 (s, 1 H), 6.9–7.6 (m, 24 H), 4.7 (m, 1 H), 4.12 (m, 1 H), 0.61–2.83 (m, 22 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 194.51, 152.83, 152.60, 151.08, 137.45, 136.13, 133.86, 130.83, 129.44, 128.08, 127.76, 127.56, 126.11, 125.24, 125.08, 124.85, 123.78, 110.34, 52.67, 30.86, 30.60, 25.89, 21.36, 20.98, 19.26. Anal. Calcd for $C_{47}H_{49}NO_3Si$: C, 80.19; H, 7.11; N, 1.99. Found: C, 80.04; H, 7.07; N, 1.99.

2(*R*)-(2-Methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triphenylsilyl)-2,3-dihydro-4-pyridone (4e, R = *o*-tolyl, R* = 8-phenylmenthyl): white solid (35%); mp 93–4 °C; $[\alpha]^{25}D$ +9.03° (*c* 0.165, $CHCl_3$); IR (KBr) 3050, 2960, 2920, 1720, 1655, 1570, 1295, 1245, 1105, 1015, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.9–7.6 (m, 25 H), 5.62 (d, 1 H, *J* = 8 Hz), 4.73 (m, 1 H), 3.05–3.13 (dd, 1 H, *J* = 8, 15 Hz), 2.57 (d, 1 H, *J* = 15 Hz), 2.38 (s, 3 H), 0.78–1.71 (m, 17 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 194.25, 152.99, 150.96, 150.57, 137.03, 136.16, 134.06, 133.96, 131.28, 129.44, 127.85, 127.76, 126.27, 125.01, 124.95, 123.62, 109.21, 77.19, 52.96, 50.86, 42.07, 41.17, 39.30, 34.29, 31.09, 26.86, 26.18, 21.66, 19.01. Anal. Calcd for $C_{47}H_{49}NO_3Si$: C, 80.19; H, 7.11; N, 1.99. Found: C, 80.13; H, 7.08; N, 1.97.

General Procedure for the Preparation of Racemic 2,3-Dihydropyridones. To a stirred solution of a 3-(trialkylsilyl)-4-methoxypyridine (1 mmol) in 10 mL of THF at −23 °C was added dropwise benzyl or phenyl chloroformate (1 mmol), and stirring was continued for 30 min. A THF solution of the Grignard reagent (1.2 mmol) was added dropwise, and stirring was continued for 30 min. The cooling bath was removed, and the reaction mixture was allowed to come to room temperature over 30 min. The reaction mixture was quenched with 10% HCl (10 mL), and stirring was continued for 30 min. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 10 mL). The

combined organic layers were washed with water (2 × 5 mL) and brine (5 mL). After drying over $MgSO_4$, the solvent was removed in vacuo to give the crude product. Purification was done by radial PLC (silica gel, EtOAC/hexanes, 1:9).

Spectral data for these compounds are given in the supplementary material.

General Procedure for the Cleavage of the *N*-Carbamate Groups. Method A. A solution of the compound in ethanol was hydrogenated over 5% Pd/C under a balloon pressure of H_2 for 1 h. The reaction mixture was filtered through Celite, and the solvent was removed in vacuo to give the crude product. Recrystallization from hexanes or MeOH provided the pure product.

Method B. To a solution of the compound (1 mmol) in methanol was added NaOMe/MeOH (1.3 mL, 4.23 M solution). The reaction mixture was refluxed for 6–12 h under argon. After cooling, the solvent was removed in vacuo. A minimum amount of water was added to dissolve the salts, and the mixture was extracted with ether (4 × 10 mL). The organic layers were combined, washed with brine, and dried over $MgSO_4$. Removal of the solvent gave the crude product, which was purified by radial PLC (silica gel, EtOAc/hexanes,1:9).

Spectral data for these compounds are given in the supplementary material.

Preparation of a 1:1 Mixture of Diastereomeric 2,3-Dihydropyridones. To a stirred solution of the 2-substituted 5-(trialkylsilyl)-2,3-dihydro-4-pyridone (0.5 mmol) in THF (5 mL) at −78 °C was added *n*-BuLi (0.5 mmol in hexanes) dropwise. After 10 min, the chiral chloroformate (0.5 mL, 1 M solution in toluene) was added dropwise. Stirring was continued for 30 min at −78 °C. The cooling bath was removed, and the reaction mixture was allowed to come to room temperature over 30 min. Water (10 mL) was added, and the mixture was extracted with ether (3 × 10 mL). The combined organic extracts were washed with water (2 × 5 mL) and brine (1 × 5 mL). After drying over MgSO4, the solvent was concentrated to give a 1:1 mixture of chiral dihydropyridones, which were used as such for HPLC analysis.

General Procedure for the Removal of the 1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl] Group Using NaOMe. 2(*R*)-(2-Methylpropyl)-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (6f, R = *i*-Bu). To a solution of **3f** (R = *i*-Bu, R* = 8-phenylmenthyl) (0.170 g, 0.30 mmol) in 5 mL of MeOH was added 0.25 mL of a 4.37 M solution (1.09 mmol) of NaOMe in MeOH. The mixture was refluxed for 12 h and cooled to room temperature, and the solvent was removed in vacuo. The residue was partitioned between 10 mL of Et_2O and 10 mL of H_2O. The layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with 10 mL of brine, dried over $MgSO_4$, and filtered, and the solvent was removed in vacuo to give the crude product. Radial PLC (SiO_2, 10% EtOAc/hexane) gave the chiral auxiliary as a mixture of (−)-8-phenylmenthol and its methyl carbonate. Further elution afforded 0.068 g (92%) of the product as white crystals: mp 150–2 °C; $[\alpha]^{23}D$ +216.6° (*c* 1.34, $CHCl_3$); IR ($CHCl_3$) 3440, 2965, 2870, 1625, 1570, 1480, 1465, 1360, 1320, 1155, 905, 880 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.17 (d, 1 H, *J* = 6.6 Hz), 5.64 (br s, 1 H), 3.64–3.75 (m, 1 H), 2.44 (dd, 1 H, *J* = 5.5, 15.4 Hz), 2.31 (dd, 1 H, *J* = 12.5, 15.4 Hz), 1.64–1.73 (m, 1 H), 1.49–1.59 (m, 1 H), 1.36–1.46 (m, 1 H), 1.25 (sept, 3 H, *J* = 7.3 Hz), 1.03 (d, 18 H, *J* = 7.3 Hz), 0.94 (d, 6 H, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.70, 157.26, 97.29, 50.34, 42.98, 42.85, 24.08, 22.56, 22.46, 18.81, 11.15. Anal. Calcd for $C_{18}H_{35}NOSi$: C, 69.84; H, 11.40; N, 4.52. Found: C, 69.95; H, 11.37; N, 4.56.

The mixture of (−)-8-phenylmenthol and its methyl carbonate was treated with K_2CO_3 in aqueous MeOH at room temperature for 2 h to give 0.066 g (95%) of (−)-8-phenylmenthol, judged to be >98% pure by ^1H NMR.

General Procedure for the Desilylation Using HBr/HOAc. 2(*S*)-Phenyl-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-2,3-dihydro-4-pyridone (7, R = Ph, R* = 8-Phenylmenthyl). To a solution of **3f** (R = Ph, R* = 8-phenylmenthyl) (0.148 g, 0.290 mmol) in 5 mL of CH_2Cl_2 cooled to 0 °C was added 0.63 mL (2.95 mmol) of 30% HBr in HOAc. The reaction mixture was stirred at 0 °C for 5 min and at room temperature for 2 h. The reaction was quenched by the addition of 3 mL of water, the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were washed with 5 mL of brine, dried over $MgSO_4$, and filtered, and the solvent was removed in vacuo to give the crude product. Radial PLC (SiO_2, 15% EtOAc/hexane) gave 0.107 g (85%) of pure product as white crystals: mp 180–180.5 °C; $[\alpha]^{23}D$ +80.0° (*c* 1.36, $CHCl_3$); IR ($CHCl_3$) 3241, 3095, 3061, 3032, 2951, 2924, 2867, 1722, 1667, 1609, 1497, 1456, 1413, 1382, 1367, 1334, 1297, 1285, 1262, 1207, 1161, 1121, 1109, 1053, 1011, 977, 957, 937, 842, 796, 769, 744 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.85–8.05 (m, 1 H), 6.70–7.55 (m, 10 H), 5.50–5.90 (m, 1 H), 5.15–5.40 (m, 1 H), 4.65–4.95 (m, 1 H), 3.40–3.70 (m, 1 H), 2.50–3.05 (m, 1 H), 0.50–2.40 (m, 17 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 191.90, 142.75, 128.30, 128.08, 127.62, 127.50, 127.40, 125.20, 125.07, 124.82, 124.62, 106.82, 54.61, 50.02, 40.75, 40.65, 38.87, 34.16, 31.12, 30.96, 25.85, 21.46, 20.81. Anal. Calcd for $C_{28}H_{33}NO_3Si$: C, 77.93; H, 7.71; N, 3.24. Found: C, 77.85; H, 7.65; N, 3.23.

Preparation of 2(*S*)-(2-Methylphenyl)-2,3-dihydro-4-pyridone (8, R = *o*-tolyl). A General Method to Remove the Chiral Auxiliary and Trialkylsilyl Group via a One-Pot Reaction. To a stirred solution of (*S*)-(2-methylphenyl)-1-[((1*R*,2*S*,5*R*)-8-phenylmenthoxy)carbonyl]-5-(triisopropylsilyl)-2,3-dihydro-4-pyridone (0.082 g, 0.132 mmol) in methanol (10 mL) was added NaOMe/MeOH (0.3 mL, 4.37 M solution). The reaction mixture was refluxed for 8 h and cooled to room temperature, and oxalic acid (0.65 g, 5.22 mmol) was added. After stirring for 2 h, methanol was removed under vacuo, and the residue was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (5 mL) and dried over $MgSO_4$. Removal of the solvent under vacuo and purification by radial PLC (SiO_2, EtOAc/hexanes, 1:1) gave pure 2(*S*)-(2-methylphenyl)-2,3-dihydro-4-pyridone (0.027 g, 88%) as a white solid: mp 126–7 °C; $[\alpha]^{25}D$ +41.0° (*c* 0.22, $CHCl_3$); IR (KBr) 3420, 3005, 1630, 1590, 1485, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.1–7.6 (m, 5 H), 5.4 (bs, 1 H), 5.2 (d, 1 H, *J* = 9 Hz), 5.0 (dd, 1 H, *J* = 3, 15 Hz), 2.61 (t, 1 H, *J* = 15 Hz), 2.46 (dd, 1 H, *J* = 3, 15 Hz), 2.34 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 192.34, 151.57, 137.97, 135.03, 130.92, 128.08, 126.72, 125.69, 99.39, 54.77, 43.24, 28.94; HRMS exact mass calcd for $C_{12}H_{13}NO$ 187.0997 (M^+), found 187.0996. The first fraction contained the methyl carbonate of (−)-8-phenylmenthol, which was hydrolyzed with aqueous saturated K_2CO_3 solution and purified by radial PLC (SiO_2, EtOAc/hexanes, 1:4) to give pure (−)-8-phenylmenthol (0.034 g, 87%).

2(*S*)-Phenyl-2,3-dihydro-4-pyridone (8, R = Ph): white solid (85%); mp 102.5–103.5 °C; $[\alpha]^{23}D$ +332.3° (*c* 2.42, EtOH); IR ($CHCl_3$) 3440, 3280, 3010, 1650, 1630, 1590, 1580, 1490, 1450, 1395, 1320, 1165, 945, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.22–7.40 (m, 6 H), 5.92 (br s, 1 H), 5.00 (d, 1 H, *J* = 6.6 Hz), 4.68 (dd, 1 H, *J* = 4.8, 14.7 Hz), 2.62 (d, 1 H, *J* = 14.7 Hz), 2.40 (dd, 1 H, *J* = 4.8, 14.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 192.28, 151.76, 139.81, 128.82, 128.27, 126.46, 98.78, 58.07, 44.17. Anal. Calcd for $C_{11}H_{11}NO$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.00; H, 6.35; N, 7.87.

2(*S*)-Cyclohexyl-2,3-dihydro-4-pyridone (8, R = *c*-Hex): white solid (81%); mp 108–9 °C; $[\alpha]^{25}D$ +220.17° (*c* 1.195, $CHCl_3$); IR (KBr) 3280, 2920, 2840, 1610, 1560, 1550, 1245, 1210, 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.21 (d, 1 H, *J* = 6 Hz), 5.53 (s, 1 H), 4.97 (d, 1 H, *J* = 6 Hz), 3.45 (m, 1 H), 2.4 (m, 1 H), 1.5–1.9 (m, 5 H), 1.0–1.4 (m, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 193.44, 151.60, 98.45, 58.07, 40.85, 39.01, 28.83, 28.50, 26.15, 25.95; HRMS exact mass calcd for $C_{11}H_{17}NO$ 179.1310 (M^+), found 179.1310.

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Supplementary Material Available: Physical properties and spectroscopic data for **5a**, **5b**, and **6** with various R groups (26 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.