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Formation of Optically Pure Cyclic Amines by Intramolecular Conjugate Displacement

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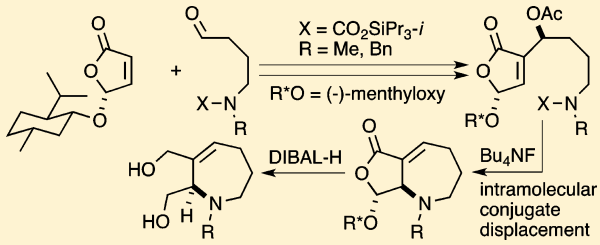
Supporting Information

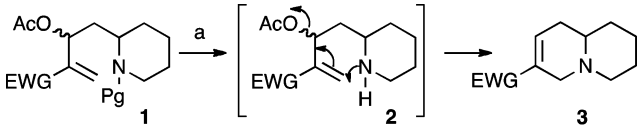
ABSTRACT: Intramolecular conjugate displacement (ICD) has been applied to the Morita–Baylis–Hillman adducts formed from (5*S*)-5-(*l*-menthyloxy)-2(5*H*)-furanone and aldehydes that carry a protected *β*- or *γ*-amino group. DIBAL-H reduction of the resulting ICD products releases optically pure six- or seven-membered cyclic amines having a stereogenic center *α* to nitrogen.



INTRODUCTION

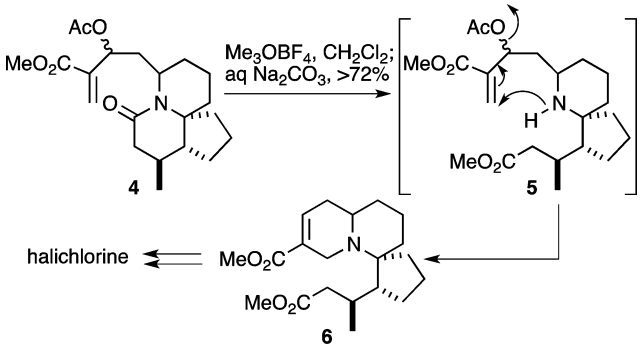
Intramolecular conjugate displacement (ICD), the transition-metal-free process summarized by Scheme 1, is a useful method for constructing bicyclic amines having nitrogen at a ring fusion[1] position; the procedure has been used as a key step (Scheme 2) in the total synthesis of the marine alkaloid halichlorine.[2] The method is also applicable to the formation of carbocycles, and an advanced example from this laboratory,[3] again not requiring the use of a transition metal,[4] is the conversion of **7** into **8** (eq 1), a substance that resembles the core structures of CP-225,917 and CP-263,114. We have now modified the ICD process in a way that leads to optically pure cyclic amines having a stereogenic center *α* to nitrogen. Existing methods for making cyclic amines with asymmetric centers *α* to nitrogen are often based on one or more of the following strategies:[5] ring-closing metathesis of olefinic pendants attached to an acyclic chiral amine;[5a−d] catalyzed asymmetric addition of diethylzinc to acyclic imines, followed by cyclization;[5e] Grignard addition to pyridinium salts having a chiral auxiliary on nitrogen;[5f−i] asymmetric hydrogenation of cyclic imines;[5j] asymmetric allylboration of cyclic imines;[5k] and Diels–Alder cycloaddition of imines bearing a chiral auxiliary on nitrogen.[5l]

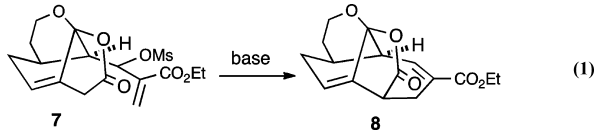
Scheme 1. Intramolecular Conjugate Displacement



Pg = protecting group, EWG = electron-withdrawing group, a = deprotection of nitrogen

Scheme 2. Intramolecular Conjugate Displacement Step in the Synthesis of Halichlorine





(1)

The principle of the new route (Scheme 3) is to attach to the acceptor double bond a removable chiral auxiliary R*, and for this purpose compounds of type **11** (*n* = 1, 2) were prepared by linking a lactone **9**, or a synthetic equivalent, with a variety of *N*-protected *β*-amino- or *γ*-aminoaldehydes (**10**, *n* = 1, 2) (Scheme 3). The resulting alcohols (**11**) are acetylated, and then one of the nitrogen protecting groups is removed so that the ICD (see arrows in structure **13**) can take place to afford the bicyclic lactone **14**. We anticipated[6] that the nitrogen would attack from the face opposite to the substituent R*O if steric factors were the determining influence; finally, reduction should serve to dismantle the lactone subunit, release the chiral auxiliary, and afford the optically pure functionalized amine **15**.

RESULTS AND DISCUSSION

A suitable starting lactone appeared to be the known menthol derivative **16**,[7] which is easily prepared in two steps from furfural by photooxygenation in methanol, followed by reaction

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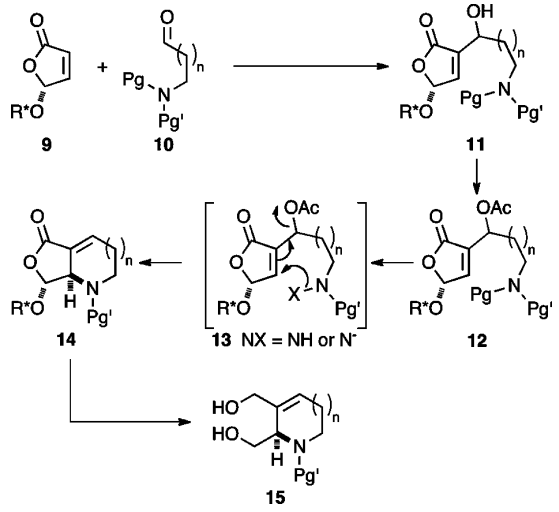
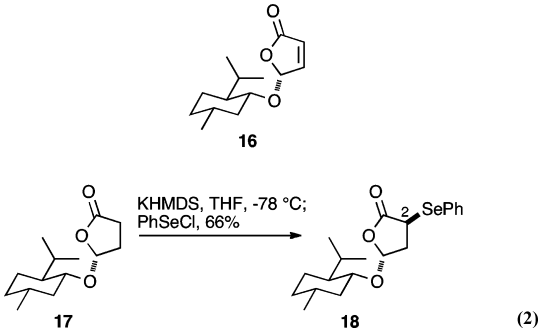
Scheme 3. Asymmetric Intramolecular Conjugate Displacement



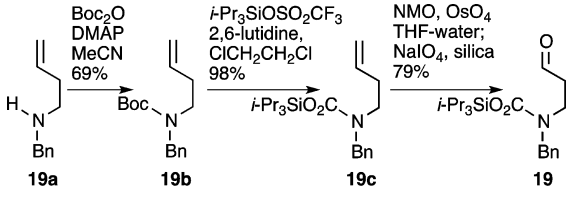
with (−)-menthol. Since the enantiomer of **16** is also readily available,[7a] both chiralities for **15** should also be accessible. As described below, lactone **16** was used for coupling with a number of aldehydes, either directly or after conversion to the selenide **18**, which was obtained by hydrogenation of **16**[8] [H_2 (50 psi), Pd/C, EtOAc, Et_3N, 100%], followed by deprotonation and selenation with PhSeCl (66%) (eq 2). The selenation



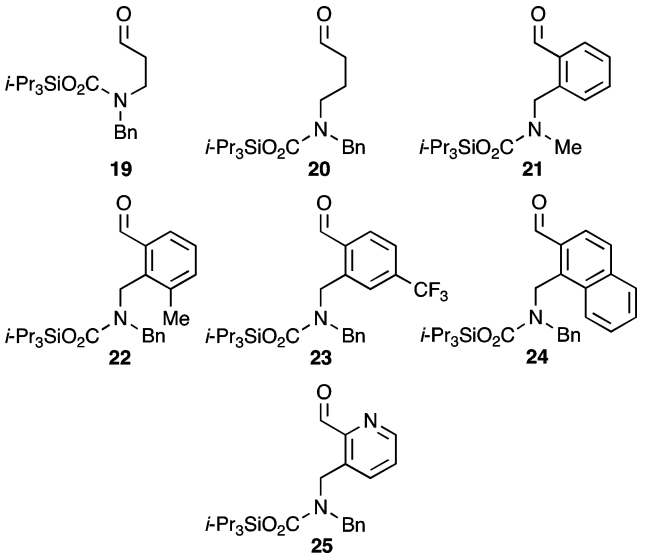
of **17** produced both C(2) epimers with the 2*S* isomer **18** being the major component.[9] The stereochemical assignment to **18** was made after deprotonation (LDA) and reprotonation (aqueous NH_4Cl) to give the crystalline 2*R* isomer, whose structure was determined by X-ray analysis.

Preparation of Amino Aldehydes. The aldehydes **19**−**25**, which were used for condensation with **16** and **18**,[9] were made by the methods summarized in Schemes 4−10. In a typical approach, the known *N*-benzyl amine **19a**[10] (Scheme 4) was protected as its *N*-Boc derivative **19b**,[10] and when this was treated with *i*-$Pr_3SiOSO_2CF_3$ in the presence of 2,6-lutidine, it was converted into the *O*-silyl carbamate **19c**.[11] Cleavage of the

Scheme 4. Preparation of Aldehyde 19

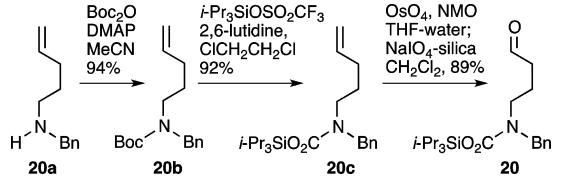


double bond was best done by the Lemieux−Johnson method, which gave a much higher yield (79%) than ozonolysis (32%), to afford the required aldehyde **19**. We later found that a two-step procedure (OsO_4, NMO, aqueous THF, followed by $NaIO_4$/silica gel[12]) allowed further improvement to 81%. The aldehyde should be used within a couple of days.



The next higher homologue (**20**) was prepared in a very similar way[13] (Scheme 5). Again, the final diol cleavage was

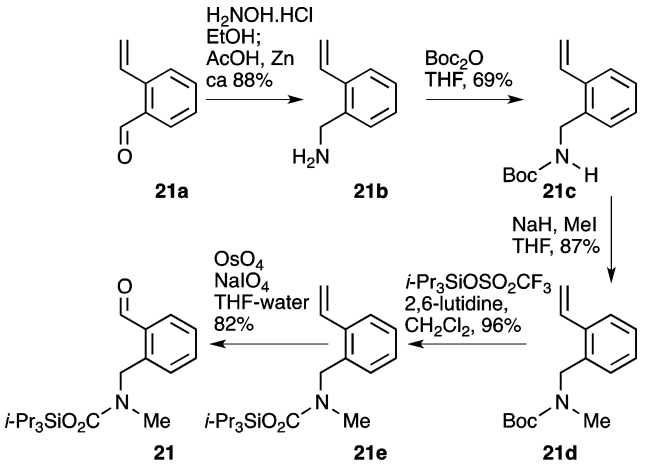
Scheme 5. Preparation of Aldehyde 20



best done using $NaIO_4$/silica gel;[12] by this method the yield in the last two steps was 89%, while ozonolysis (O_3, MeOH; Me_2S) gave 70%.

The preparation of **21** (Scheme 6) began with the known[14] conversion of *o*-vinylbenzaldehyde (**21a**) to the benzylamine **21b** and *N*-protection with Boc_2O (**21b** → **21c**[15]). *N*-

Scheme 6. Preparation of Aldehyde 21



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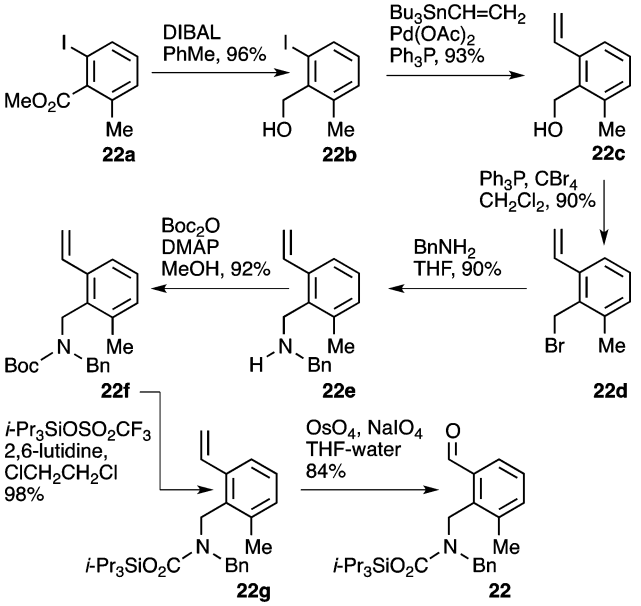
Methylation (NaH, MeI), treatment with *i*-$Pr_3SiOSO_2CF_3$, and double bond cleavage (Lemieux–Johnson) then gave **21**.

Compound **22**, a methyl-substituted version of **21**, was made by the route summarized in Scheme 7. The iodo ester **22a**,

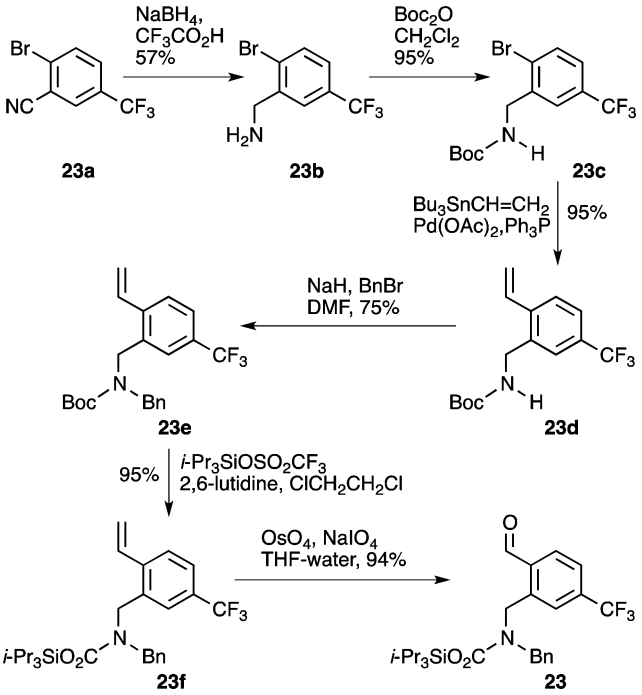
Scheme 7. Preparation of Aldehyde 22



which is readily available from 2-methylbenzoic acid,[16] was reduced (DIBAL-H) and subjected to Stille coupling with tributyl(vinyl)tin to give alcohol **22c**. Replacement of the hydroxyl by bromine and displacement with $BnNH_2$ produced the *N*-benzyl amine **22e**, which was protected (Boc_2O) and subjected to the same reactions as **21d**.

Aldehyde **23**, containing a trifluoromethyl substituent, was prepared (Scheme 8) from the commercial bromonitrile **23a**.

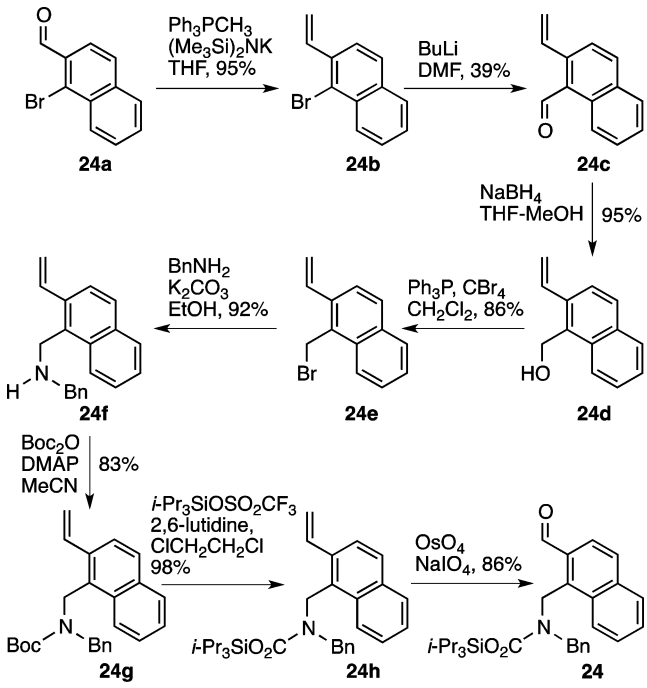
Scheme 8. Preparation of Aldehyde 23



Reduction of the nitrile group, using $NaBH_4/CF_3CO_2H$,[17] gave the substituted benzylamine **23b** (Scheme 8). This was protected as its carbamate (Boc_2O) and then subjected to a Stille coupling to install the vinyl group (**23b** → **23c** → **23d**). *N*-Benzylation,[18] conversion to the triisopropylsilyl carbamate **23f**, and double bond cleavage (OsO_4, $NaIO_4$) led to **23**. We had first carried out the Stille coupling *after* *N*-benzylation, but the route shown in Scheme 8 is better, as some of the intermediates are easier to purify.

The naphthalene aldehyde **24** was made (Scheme 9) starting from 1-bromonaphthalene-2-carbaldehyde (**24a**), which is

Scheme 9. Preparation of Aldehyde 24



readily available[19] from commercial 1-bromo-2-methylnaphthalene. Following reported procedures, Wittig reaction converted **24a** into the bromo olefin **24b**,[20] and the aldehyde **24c** was then obtained[20] by halogen/metal exchange and quenching with DMF. Simple reduction with $NaBH_4$ gave alcohol **24d**, which was converted into bromide **24e**. Reaction with $BnNH_2$ generated the secondary amine **24f**, and the remainder of the synthesis followed the pattern used for the other examples (**24f** → **24g** → **24h** → **24**). An attempt at reductive amination to convert **24c** directly into **24f** ($BnNH_2$, $MgSO_4$, CH_2Cl_2; $NaBH_4$, MeOH) gave a complex mixture.

The substituted pyridine aldehyde **25** was made (Scheme 10) starting from 2-bromopyridine, which was formylated by a literature procedure (Scheme 10)[21] and reductively aminated with $BnNH_2$, again following a reported method.[22] With **25c** in hand, we applied the operations used earlier to elaborate the compound into aldehyde **25** (Scheme 10).

Coupling of the Aldehydes with Chiral Auxiliaries. Our first attempt to couple aldehyde **19** with the optically pure lactone **16** involved addition of a mixture of the lactone and aldehyde to a solution of PhSeLi in THF, as this version of the Baylis–Hillman condensation had been reported[23] to work well (high yield and high diastereoselectivity) with **16** and a number of other aldehydes, such as PhCHO, *i*-PrCHO, *t*-BuCHO, and cinnamaldehyde. In the present case, however, the reaction did

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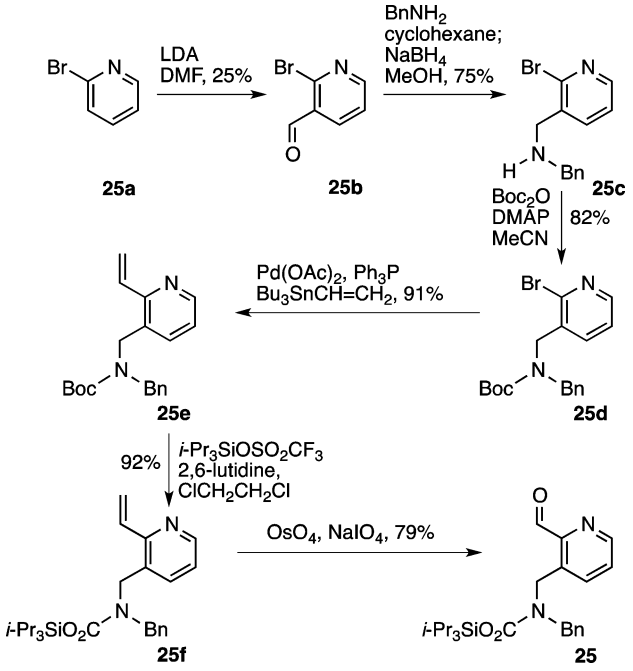
Scheme 10. Preparation of Aldehyde 25

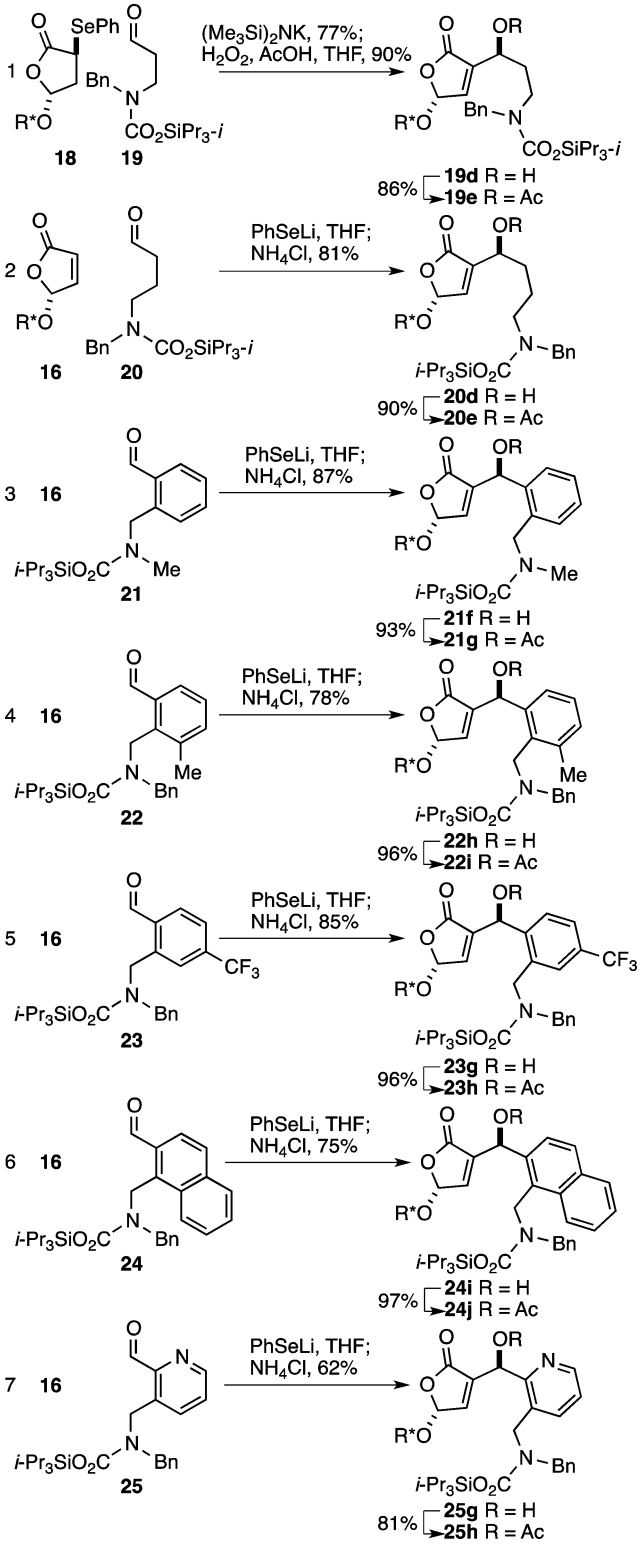


not work and we recovered both starting materials; therefore, we tried condensation with lactone **18**. Deprotonation of **18** with LDA or $(Me_3Si)_2NK$ and addition of aldehyde **19** gave the expected hydroxy selenide as an inconsequential mixture of diastereoisomers, the yield with $(Me_3Si)_2NK$ (75%) being higher than that with LDA (ca. 60%) (Table 1, entry 1). Oxidation with H_2O_2 generated the unsaturated alcohol **19d**, in accord with the normal regiochemical outcome for oxidation of *β*-hydroxy selenides,[24] and the alcohol **19d** was then acetylated, using AcCl (**19d** → **19e**) (Table 1, entry 1). As expected, the C(2) epimer of **18** behaved in the same way, as did mixtures of the two epimers.[9]

When we came to examine aldehyde **20**, we again tried the procedure using PhSeLi,[23] and in this case, the desired alcohol **20d** was formed in good yield (81%); the same method worked equally well for aldehydes **21**–**25**. The reactions with aldehydes **20**–**25** were conducted at −42 °C because, under these conditions, the required double bond was generated in situ without the need for an additional step (addition of BnBr[23]) to eliminate the PhSe group. We assume that for the products derived from **20**–**25** (i.e., for compounds **20d**, **21f**, **22h**, **23g**, **24i**, **25g**) the stereochemistry at the hydroxyl-bearing carbon of the isolated alcohols follows the uniform pattern observed for this type of Morita–Baylis–Hillman process.[23] We tried to obtain crystals of four of the alcohols (**19d**, **20d**, **24i**, **25g**), but were successful only with **19d**, and single crystal X-ray analysis of this compound established the indicated stereochemistry, which follows the same pattern observed previously,[23] even though the condensation method (via deprotonation of **18**) was different from that (via addition of PhSeNa to **16**) used for the other examples (entries 2–7).

The condensation method leading to the results shown in entries 2–7 is known[23,25] to give essentially (>99% de) a *single* isomer, but the ^{1}H NMR spectra of our alcohols and their acetates are complex, and we had to decide if rotamers or isomers were present. For some alcohols the ^{13}C NMR spectrum clearly corresponded to a single isomer (**19d**, **21f**, **22h**, **23g**, **24i**). In the case of acetate **20e**, where the ^{13}C NMR

Table 1. Condensation of Auxiliaries with Aldehydes[a]



[a]R*O = *l*-menthyloxy.

spectrum by itself did not distinguish between the presence of rotamers or isomers, we observed signal coalescence in the ^{1}H NMR spectrum run at 60 °C, indicating we were dealing with rotamers. Likewise, the ^{13}C and ^{1}H NMR spectra of alcohol **25g** showed several pairs of signals, but the ^{1}H NMR signals coalesced at (or below) 60 °C, establishing that the material consisted of rotamers.

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Intramolecular Conjugate Displacement. When acetate **19e** was treated with Bu_4NF in THF at room temperature, the silicon protecting group was removed and the bicyclic amine **19f** was isolated as a single stereoisomer (^1H and ^{13}C NMR) in 81% yield, after workup with aqueous NH_4Cl. The structure of **19f** was established by a number of NMR measurements, and we initially assumed that the stereochemistry would conform to the expectation summarized in Scheme 3 (see **14**, R*O and adjacent H *syn*). However, a crystalline sample was eventually obtained, and surprisingly, single crystal X-ray analysis showed that the R*O group and *nitrogen* were *syn*. The coupling constant $^3J_{7,7a}$ (see **19f**) was 5.5 Hz. Examination of the reaction mixture before flash chromatography revealed the presence of a minor isomer (10:1). This compound ($^3J_{7,7a}$ = 6 Hz) was isolated and, presumably, differs from **19f** only at C(7a), but we were unable to obtain it in crystalline form for rigorous stereochemical determination.

In the case of compound **20e** two products were always formed, and the optimum procedure involved running the reaction at room temperature for 1 h; under these conditions the product ratio was 1:31 ratio in favor of **20f** ($^3J_{8,8a}$ = 2.5 Hz) in a combined yield of 78%. The total product from several runs (at different temperatures) was pooled and subjected to preparative TLC so as to isolate the minor component, which proved to be the C(8a) isomer [COSY, ^1H NMR ($^3J_{8,8a}$ = 5.1 Hz) and ^{13}C NMR].

Acetate **21g**, derived from an aromatic aldehyde, cyclized efficiently (92%) at 0 °C, giving the ICD product (**21h**) as a single stereoisomer ($^3J_{6,7}$ = 3.2 Hz). The choice of 0 °C was arbitrarily made to illustrate the mildness of the conditions required for cyclization.

Acetate **22i** gave mainly **22j**, but the outcome was more complicated than for **21g**. When the ICD was conducted at −78 °C, the ^1H NMR spectrum of the isolated sample of **22j** ($^3J_{6,7}$ = 3.0 Hz) showed a small signal at δ 7.65. On the assumption that this represents the olefinic signal of a stereoisomer of **22j**, then the ratio of **22j** and its stereoisomer is 23:1 (combined yield 96%); when the reaction was done at 0 °C, this ratio was 9.6:1. When a small sample of the 23:1 mixture was subjected to preparative TLC (silica, 1:1 hexane/CH_2Cl_2), it was possible to isolate **22j** free of the minor component). We assume that the minor component (which we did not get pure by the preparative TLC) is the C(7) epimer of **22j**.

Acetate **23h**, in which the benzene ring carries a trifluoromethyl group, reacted smoothly with Bu_4NF in THF at 0 °C to give the expected heterocycle **23i** ($^3J_{6,7}$ = 3.5 Hz) in 91% yield. The reaction product is crystalline, and the structure and absolute stereochemistry were confirmed by single crystal X-ray diffraction.

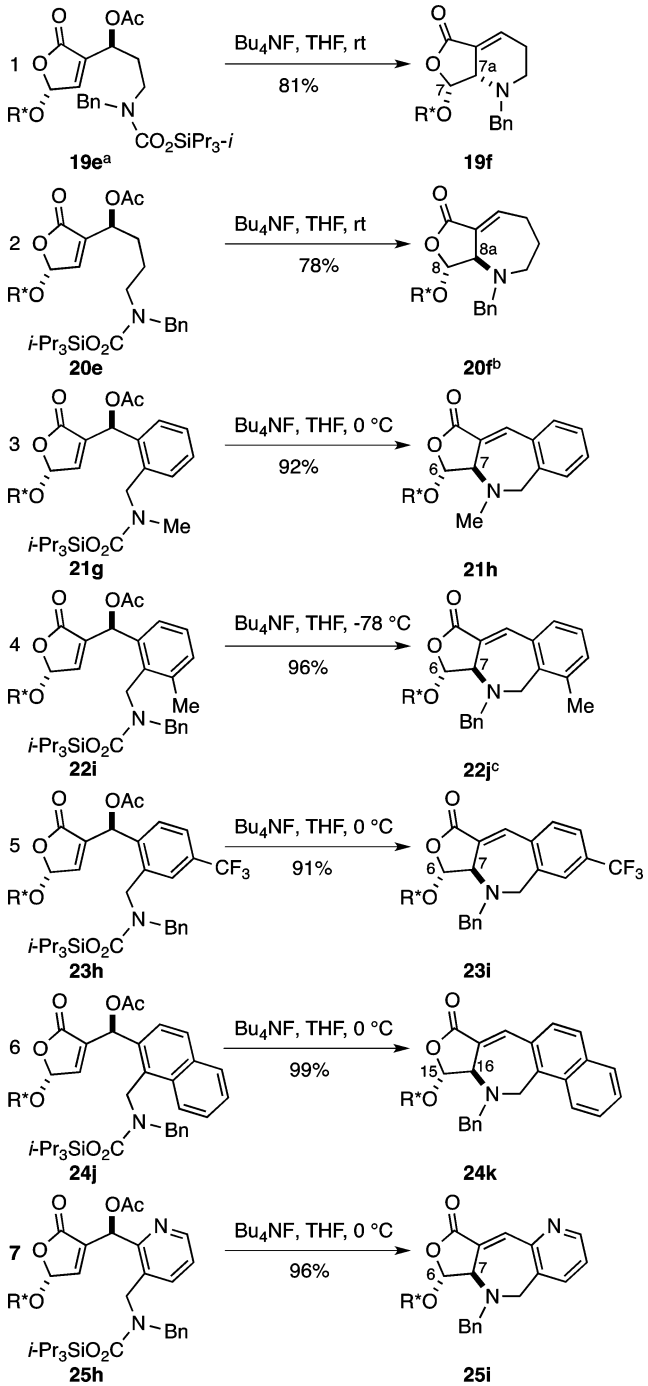
The naphthyl acetate **24j** also cyclized in very high yield (99%) to give **24k** ($^3J_{15,16}$ = 2.0 Hz) as a single stereoisomer. Its structure was confirmed by single crystal X-ray diffraction.

Acetate **25h** gave **25i** ($^3J_{6,7}$ = 3.5 Hz) as a single isomer.

The stereochemistry for the products of entries 2−4 and 7 in Table 2 was assigned by analogy to the firmly established results for **23i** and **24k** and the fact that all products, with the exception of **19f**, have appropriate ^3J values consistent with the indicated stereochemistry.

With the exception of example 1 of Table 2, all of the ICD products result from attack of nitrogen *anti* to the menthyloxy substituent and *syn* to the acetate leaving group. The formation of the six-membered ring shown in entry 1 is anomalous in this respect, and once the stereochemical assignment to **19f** had been established (by X-ray analysis), we were prompted to make a determined effort to obtain crystals of its precursor **19d**. These efforts were eventually successful, as indicated earlier, and we had expected that the stereochemistry of the hydroxyl-bearing carbon of **19d** would be opposite to that in the other examples, especially as **19d** had been prepared by a different route. Had that been the case, our results would suggest a general preference for attack *syn* to the leaving group and the stereochemistry of **19f** would then imply that such a

Table 2. Intramolecular Conjugate Displacements[a]



[a]R*O = *l*-menthyloxy. [b]Ratio of **20f** to C(8) epimer = 31:1; combined yield = 78%. [c]Ratio of **22j** to C(7) epimer = 23:1; Combined yield = 96%.

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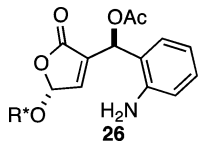
stereoelectronic effect was more powerful than steric factors.[26] In the event, X-ray analysis showed that the stereochemistry of **19d** conforms to the standard pattern, and we have not established the reason for the stereochemical outcome of the ICD process **19e** → **19f**.

In addition to the ICD substrates from aldehydes **19**-**25**, we also prepared (see Supporting Information for flowchart) amine **26**, but the yield in one step of the route (-NO_2 → -NH_2, using Zn, NH_4Cl[27]) was poor; and subsequent attempts at an ICD reaction were unsuccessful, as only an *O* → *N* acetyl transfer appeared to occur.



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Reduction of the Lactones. Each of the products produced by the ICD process was reduced with DIBAL-H in THF, and, with the exception of the pyridyl example **25i**, which gave a product containing slight impurities, yields were in the range of 75−90% (Table 3).

CONCLUSION

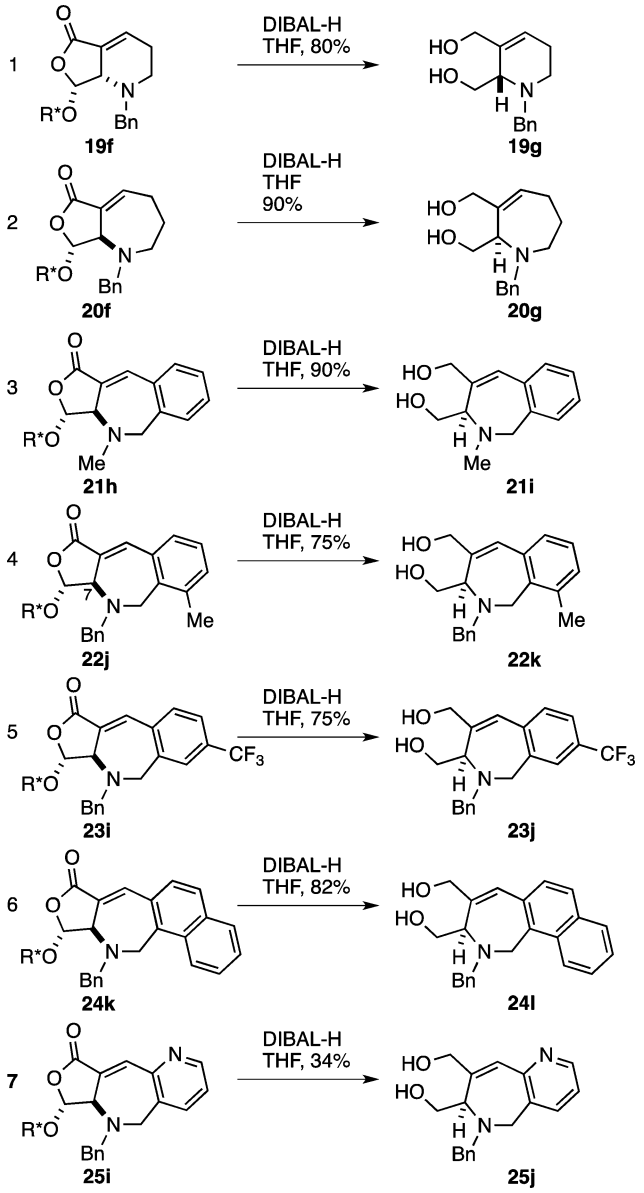
Our experiments show that intramolecular conjugate displacement, using the chiral auxiliaries **16** or **18**, leads to nitrogen heterocycles having a stereogenic center α to nitrogen. Six- and seven-membered rings can be formed, including those fused to aromatic rings. Removal of the auxiliary from the ICD products leads to optically pure amines; these carry functionality that is ready for further manipulations.

EXPERIMENTAL SECTION

General Procedures. Solvents used for chromatography were distilled before use. Commercial thin layer chromatography plates (silica gel, Merck 60F-254) were used. Silica gel for flash chromatography was Merck type 60 (230−400 mesh). Dry solvents were prepared under an inert atmosphere and transferred by syringe or cannula. The symbols s, d, t and q used for ^{13}C NMR spectra indicate zero, one, two, or three attached hydrogens, respectively, the assignments being made by from APT spectra. Solutions were evaporated under water pump vacuum, and the residue was then kept under oil pump vacuum.

(3*S*,5*R*)-5-{[(1*R*,2*S*,5*R*)-5-Methyl-2-(propan-2-yl)cyclohexyl]-oxy}-3-(phenylselanyl)oxolan-2-one (18). BuLi (2.5 M in hexane, 1.45 mL, 3.63 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of *i*-Pr_2NH (0.52 mL, 3.72 mmol) in THF (30 mL). After 30 min at −78 °C, **17**[8] (860.0 mg, 3.58 mmol) in THF (4 mL) was added dropwise, and stirring was continued for 70 min at −78 °C. PhSeCl (329.2 mg, 1.72 mmol) in THF (1 mL) was then added quickly to the reaction mixture by syringe. After 16 min, saturated aqueous NH_4Cl (20 mL) was added, and the mixture was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.8 × 14 cm), using 1:20 Et_2O/hexanes, gave **18** (451.0 mg, 66%) as a light yellow oil: $[\alpha]^{20}_D$ −93.54 (*c* 1.04, $CHCl_3$); FTIR ($CHCl_3$, cast) 3057, 2954, 2924, 2869, 1774, 1578, 1477, 1455, 1439 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75−1.05 (m, 12 H), 1.14−1.23 (m, 1 H), 1.26−1.40 (m, 1 H), 1.59−1.67 (m, 2 H), 1.95−2.07 (m, 2 H), 2.34−2.40 (m, 1 H), 2.46−2.52 (m, 1 H), 3.43−3.50 (m, 1 H), 4.09 (dd, *J* = 8.0, 8.4 Hz, 1 H), 5.45 (dd, *J* = 2.8, 5.6 Hz, 1 H), 7.30−7.40 (m, 3 H), 7.60−7.68 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.6 (q), 20.9 (q), 22.2 (q), 23.0 (t), 25.4 (d), 31.3 (d), 34.2 (t), 35.9 (d), 37.5 (t), 39.8 (t), 47.7 (d), 77.1 (d), 99.2 (d), 126.4 (s), 129.0 (d), 129.4 (d), 136.0 (d), 175.1 (s); exact mass (electrospray) *m*/*z* calcd for $C_{20}H_{28}NaO_3Se$ (M + Na) 419.1096, found 419.1093.

Table 3. Removal of Chiral Auxiliary



In some runs, a small amount (ca. 9%) of the C(2) epimer was also isolated: mp 105−108 °C; $[\alpha]^{20}_D$ −97.75 (*c* 1.04, $CHCl_3$); FTIR ($CHCl_3$, cast) 3073, 2991, 2947, 2917, 2866, 1779, 1745, 1577, 1478, 1452, 1439 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.80−1.07 (m, 12 H), 1.24−1.29 (m, 1 H), 1.37−1.44 (m, 1 H), 1.66−1.73 (m, 2 H), 2.09−2.14 (m, 1 H), 2.26−2.35 (m, 2 H), 2.89 (ddd, *J* = 5.5, 9.5, 14.5 Hz 1 H), 3.58 (dt, *J* = 4.0, 10.5 Hz, 1 H), 3.84 (dd, *J* = 4.0, 9.5 Hz, 1 H), 5.74 (dd, *J* = 2.0, 6.0 Hz, 1 H), 7.32−7.38 (m, 3 H), 7.72−7.75 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.5 (q), 21.1 (q), 22.3 (q), 22.8 (t), 25.1 (d), 31.4 (d), 34.3 (t), 35.2 (d), 37.2 (t), 39.6 (t), 47.7 (d), 99.0 (d), 128.5 (d), 129.1 (s), 129.3 (d), 134.8 (d), 176.0 (s); exact mass (electrospray) *m*/*z* calcd for $C_{20}H_{28}NaO_3Se$ (M + Na) 419.1097, found 419.1096.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-(but-3-en-1-yl)carbamate (19c). 2,6-Lutidine (0.12 mL, 1.03 mmol) and *i*-$Pr_3SiOSO_2CF_3$ (0.24 mL, 0.89 mmol) were added successively to a stirred solution of **19b**[10] (130.2 mg, 0.50 mmol) in $ClCH_2CH_2Cl$ (10 mL). After 15 min, the mixture was lowered into a preheated oil bath set at 96 °C, and stirring was continued for 18 h. The mixture was cooled, evaporated and diluted with Et_2O (10 mL). The solution was washed with saturated aqueous NH_4Cl and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 ×

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18 cm), using 1:20 *t*-BuOMe/hexanes, gave **19c** (177.1 mg, 98%) as a colorless oil: FTIR ($CHCl_3$, cast) 3066, 3031, 2945, 2893, 2868, 1681, 1642, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.06−1.14 (m, 18 H), 1.24−1.42 (m, 3 H), 2.25−2.33 (m, 2 H), 3.26 (t, J = 7.5 Hz, 1 H), 3.33 (t, J = 7.5 Hz, 1 H), 4.52 (s, 2 H), 4.99−5.07 (m, 2 H), 5.68−5.81 (m, 1 H), 7.22−7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.13 (d), 12.15 (d), 17.87 (q), 17.92 (q), 19.95 (q), 32.3 (t), 32.9 (t), 46.4 (t), 46.6 (t), 50.4 (t), 51.3 (t), 116.6 (s), 116.8 (s), 127.0 (d), 127.18 (d), 127.24 (d), 127.7 (d), 128.5 (d), 135.1 (d), 135.4 (d), 138.17 (s), 138.19 (s), 155.0 (s), 155.4 (s); exact mass (electrospray) m/z calcd for $C_{21}H_{35}NNaO_2Si$ (M + Na) 384.2329, found 384.2332.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-(3-oxopropyl)carbamate (19). *N*-Methyl-morpholine-*N*-oxide (1.39 g, 11.87 mmol), followed by OsO_4 (tiny crystal, catalytic), was added to a stirred solution of **19c** (1.07 g, 2.97 mmol) in THF (15 mL) and water (15 mL). The flask was stoppered and covered with Al foil, and the mixture was stirred for 3 h. The mixture was diluted with EtOAc and washed with water and brine. The organic extract was dried ($MgSO_4$) and evaporated. The residue was dissolved in CH_2Cl_2 (30 mL), and $NaIO_4/SiO_2$[12] (18%w/w, 12.71 g, 10.69 mmol) was then added with stirring. After 30 min, no starting material was left (TLC control, silica gel, 3:20 EtOAc/hexanes). The mixture was filtered through Celite and evaporated. Flash chromatography of the residue over silica gel (3.8 × 18 cm), using 3:20 EtOAc/hexanes, gave **19** (0.85 g, 79%) as a light yellow oil: FTIR ($CHCl_3$, cast) 3065, 2946, 2893, 2868, 2726, 1725, 1679, 1606, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.06−1.11 (m, 18 H), 1.26−1.40 (m, 3 H), 2.65 (dt, J = 1.0, 7.0 Hz) and 2.69 (dt, J = 1.5, 7.0 Hz, both signals together 2 H), 3.51−3.57 (m, 2 H), 4.52 and 4.54 (two s, 2 H), 7.23−7.35 (m, 5 H), 9.72−9.75 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.1 (d), 17.8 (q), 17.9 (q), 40.7 (t), 41.1 (t), 42.8 (t), 43.4 (t), 50.9 (t), 51.9 (t), 127.1 (d), 127.4 (d), 127.5 (d), 127.9 (d), 128.7 (d), 137.8 (s), 137.9 (s), 155.0 (s), 155.2 (s), 200.2 (d), 200.8 (d); exact mass (electrospray) m/z calcd for $C_{20}H_{34}NO_3Si$ (M + H) 364.2303, found 364.2307.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-{(3*S*)-3-hydroxy-3-[5-(5*R*)-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-3-(phenylselanyl)oxolan-3-yl]propyl}carbamate (pre-19d). Selenide **18** (91.7 mg, 0.23 mmol) in THF (0.5 mL) was added dropwise to a stirred and cooled (−78 °C) solution of $(Me_3Si)_2NK$ (0.5 M in PhMe, 0.48 mL, 0.24 mmol) in THF (4 mL). Stirring at −78 °C was continued for 70 min, and then **19** (88.9 mg, 0.25 mmol) in THF (0.5 mL) was added dropwise. Stirring at −78 °C was continued for 70 min. The mixture was quenched with saturated aqueous NH_4Cl (5 mL) and extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 3:25 EtOAc/hexanes, gave pre-**19d** (136.0 mg, 77%) as an oil: FTIR ($CHCl_3$, cast) 3386, 3061, 3031, 2950, 2927, 2868, 1772, 1677, 1650, 1607, 1579, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.72−1.14 (m, 30 H), 1.19−1.44 (m, 6 H), 1.55−1.69 (m, 2 H), 1.89−1.98 (m, 1 H), 2.04−2.17 (m, 1 H), 2.27−2.55 (m, 2 H), 2.82−3.03 (m, 1 H), 3.43−3.61 (m, 1 H), 3.66−3.87 (m, 3 H), 4.36−4.62 (m, 2 H), 5.64−5.73 (m, 1 H), 7.18−7.41 (m, 8 H), 7.55−7.77 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.0 (d), 12.1 (d), 12.2 (d), 15.5 (q), 17.80 (q), 17.82 (q), 18.0 (q), 21.1 (q), 22.2 (q), 22.3 (q), 22.8 (t), 24.9 (d), 29.6 (t), 31.4 (d), 34.3 (t), 34.4 (t), 35.5 (t), 39.6 (t), 42.3 (t), 47.7 (d), 47.8 (d), 50.3 (t), 50.4 (t), 68.0 (d), 77.1 (d), 97.7 (d), 126.5 (s), 127.0 (d), 127.5 (d), 128.6 (d), 128.7 (d), 128.98 (d), 129.03 (d), 129.20 (d), 129.24 (d), 134.8 (d), 137.27 (d), 137.30 (s), 137.9 (d), 156.7 (s), 176.7 (s); exact mass (electrospray) m/z calcd for $C_{40}H_{62}NO_6SeSi$ (M + H) 760.3506, found 760.3509.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-[(3*S*)-3-hydroxy-3-[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl)propyl]carbamate (19d). H_2O_2 (30%, 0.08 mL, 0.71 mmol) and AcOH (2 drops) were added to a stirred and cooled (0 °C) solution of pre-**19d** (82.4 mg, 0.11 mmol) in THF (2 mL). After 30 min, the ice bath was removed, and stirring was continued for 15 min. The mixture was neutralized with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 3:20 EtOAc/hexanes, gave **19d** (60.0 mg, 90%) as a colorless oil that became a solid after being covered with pentane and slow evaporation of the solvent: mp 103−105 °C; FTIR ($CHCl_3$, cast) 3416, 3089, 3065, 3031, 2950, 2927, 2868, 1769, 1677, 1652, 1587, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.79−1.13 (m, 30 H), 1.20−1.53 (m, 6 H), 1.64−1.68 (m, 2 H), 2.07−2.14 (m, 2 H), 2.19−2.23 (m, 1 H), 3.01−3.05 (m, 1 H), 3.63 (dt, J = 4.0, 10.4 Hz, 1 H), 3.86−3.93 (m, 1 H), 4.23 and 4.27 (two s, 1 H), 4.42−4.60 (m, 1 H), 4.80 and 4.84 (two s, 1 H), 4.97 and 4.98 (two s, 1 H), 5.99 (s, 1 H), 7.07 (s, 1 H), 7.23−7.36 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.0 (d), 15.8 (q), 17.8 (q), 20.8 (q), 22.2 (q), 23.2 (t), 25.3 (d), 31.5 (d), 33.8 (t), 34.2 (t), 40.5 (t), 42.2 (t), 47.7 (d), 50.7 (t), 63.5 (d), 79.1 (d), 99.3 (d), 127.1 (d), 127.5 (d), 128.7 (d), 137.1 (s), 140.2 (s), 143.5 (d), 157.0 (s), 170.2 (s); exact mass (electrospray) m/z calcd for $C_{34}H_{56}NO_6Si$ (M + H) 602.3871, found 602.3874. A sample was crystallized from petroleum ether (35−60 °C) for X-ray analysis.

(1*S*)-3-[Benzyl({[tris(propan-2-yl)silyl]oxy}carbonyl)amino]-1-[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]-oxy}-2-oxo-2,5-dihydrofuran-3-yl]propyl Acetate (19e). DMAP (4.7 mg, 0.039 mmol) was added to a stirred solution of **19d** (72.6 mg, 0.12 mmol) in CH_2Cl_2 (2 mL). The mixture was cooled to −78 °C, and AcCl (0.026 mL, 0.37 mmol) and pyridine (0.07 mL, 0.87 mmol) were added sequentially. The dry ice bath was replaced by an ice bath that was left in place but not recharged, and stirring was continued for 7.5 h. The mixture was quenched with hydrochloric acid (1 M, 2 mL) and water (4 mL), and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 3:20 EtOAc/hexanes, gave **19e** (66.9 mg, 86%) as a colorless oil: FTIR ($CHCl_3$, cast) 3089, 3066, 3031, 2949, 2868, 1771, 1679, 1606, 1587, 1559, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.79−1.12 (m, 29 H), 1.22−1.43 (m, 6 H), 1.64−1.69 (m, 2 H), 1.90−2.28 (m, 7 H), 3.20−3.46 (m, 2 H), 3.59−3.64 (m, 1 H), 4.41−4.57 (m, 2 H), 5.50−5.52 (m, 1 H), 5.96 (s, 1 H), 6.79 and 6.86 (two s, 1 H), 7.20−7.33 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.1 (d), 15.8 (q), 17.8 (q), 17.9 (q), 20.7 (q), 20.75 (q), 20.83 (q), 22.2 (q), 23.1 (t), 25.30 (d), 25.34 (d), 30.4 (t), 31.3 (t), 31.5 (d), 34.2 (t), 40.5 (t), 42.5 (t), 43.3(t), 47.7 (d), 50.4 (t), 50.8 (t), 66.4 (d), 66.9 (d), 79.3 (d), 79.5 (d), 98.88 (d), 98.91 (d), 127.1 (d), 127.3 (d), 127.4 (d), 127.9 (d), 128.6 (d), 136.6 (s), 137.7 (s), 137.8 (s), 143.83 (d), 143.85 (d), 144.37 (d), 144.39 (d), 154.9 (s), 155.2 (s), 168.5 (s), 168.8 (s), 169.5 (s), 169.8 (s); exact mass (electrospray) m/z calcd for $C_{36}H_{58}NO_7Si$ (M + H) 644.3977, found 644.3977.

(7*R*,7a*S*)-1-Benzyl-7-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)-cyclohexyl]oxy}-1*H*,2*H*,3*H*,5*H*,7*H*,7a*H*-furo[3,4-*b*]pyridin-5-one (19f). Bu_4NF (1.0 M in THF, 0.09 mL, 0.09 mmol) was added to a stirred solution of **19e** (39.0 mg, 0.059 mmol) in THF (4 mL). After 21 min, the mixture was quenched with saturated aqueous NH_4Cl (2 mL) and diluted with EtOAc (4 mL). The organic phase was washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.0 × 14 cm), using 3:20 EtOAc/hexanes, gave **19f** (28.7 mg, 81%) as white crystals: mp 123−124 °C; $[\alpha]^{20}_D$ −154.10 (*c* 1.07, $CHCl_3$); FTIR ($CHCl_3$, cast) 3062, 3029, 2954, 2922, 2869, 2804, 2759, 1774, 1694, 1636, 1603, 1495, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.81−0.90 (m, 10 H), 0.91−1.06 (m, 2 H), 1.37−1.44 (m, 2 H), 1.62−1.67 (m, 2 H), 2.00−2.07 (m, 2 H), 2.20−2.25 (m, 2 H), 2.44−2.52 (m, 1 H), 2.99 (dd, J = 6.5, 11.0 Hz, 1 H), 3.33 (d, J = 13.0 Hz, 1 H), 3.39−3.42 (m, 1 H), 3.61 (dt, J = 4.0, 11.0 Hz, 1 H), 3.99 (d, J = 13.0 Hz, 1 H), 5.78 (d, J = 5.5 Hz, 1 H), 6.90 (d, J = 3.0 Hz, 1 H), 7.27−7.36 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.5 (q), 20.8 (q), 22.2 (q), 23.1 (t), 25.1 (d), 26.4 (t), 31.5 (d), 34.3 (t), 39.8 (t), 47.4 (d), 47.7 (t), 59.1 (t), 62.2 (d), 77.1 (d), 99.0 (d), 127.2 (s), 127.6 (d), 128.4 (d), 129.7 (d), 135.8 (d), 136.5 (s), 167.8 (s); exact mass (electrospray) m/z calcd for $C_{24}H_{34}NO_3$ (M + H) 384.2533, found 384.2534.

In some experiments a small amount of the C(7a) epimer was isolated (10:1 ratio of major to minor products): $[\alpha]^{20}_D$ −116.93 (*c* 1.24, $CHCl_3$); FTIR ($CHCl_3$, cast) 2954, 2922, 2869, 2810, 1773,

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1692, 1495, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.81−1.10 (m, 12 H), 1.29−1.35 (m, 1 H), 1.36−1.44 (m, 1 H), 1.64−1.71 (m, 2 H), 2.12−2.19 (m, 2 H), 2.23−2.32 (m, 2 H), 2.35−2.42 (m, 1 H), 2.93 (dd, J = 6.5, 12.0 Hz, 1 H), 3.32 (d, J = 13.5 Hz, 1 H), 3.38−3.42 (m, 1 H), 3.69 (dt, J = 4.0, 11.0 Hz, 1 H), 4.24 (d, J = 14.0 Hz, 1 H), 5.59 (d, J = 6.0 Hz, 1 H), 6.86 (q, J = 3.5 Hz, 1 H), 7.30−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 16.0 (q), 20.9 (q), 22.2 (q), 23.2 (t), 25.5 (d), 26.5 (t), 31.4 (d), 34.3 (t), 39.7 (t), 47.8 (t), 47.9 (d), 59.2 (t), 65.4 (d), 78.5 (d), 104.0 (d), 127.3 (d), 128.4 (d), 129.2 (d), 129.4 (s), 135.1 (d), 137.5 (s), 166.1 (s); exact mass (electrospray) m/z calcd for $C_{24}H_{34}NO_3$ (M + H) 384.2533, found 384.2528.

[(2*R*)-1-Benzyl-2-(hydroxymethyl)-1,2,5,6-tetrahydropyridin-3-yl]methanol (19g). DIBAL-H (1.0 M in PhMe, 1.60 mL, 1.60 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **19f** (123.2 mg, 0.32 mmol) in THF (3 mL). Stirring at −78 °C was continued for 1 h, the cold bath was left in place but not recharged, and stirring was continued for 10 h. MeOH (0.5 mL) and a saturated aqueous solution of Rochelle's salt (ca. 5 mL) were then added sequentially. Stirring was continued for 2 h, and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 1:20 MeOH/EtOAc, gave **19g** (60.2 mg, 80%) as a light yellow oil: $[\alpha]^{20}_D$ −26.86 (c 1.13, $CHCl_3$); FTIR ($CHCl_3$, cast) 3360, 3085, 3062, 3028, 2923, 2873, 1592, 1495 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.88 (dd, J = 3.0, 18.0 Hz, 1 H), 2.26−2.32 (m, 1 H), 2.63 (ddd, J = 2.5, 5.0, 13.0 Hz, 1 H), 2.85−2.97 (m, 3 H), 3.21−3.23 (m, 1 H), 3.51 (dd, J = 8.5, 11.0 Hz, 1 H), 3.67−3.77 (m, 3 H), 4.00 (AB q, J = 12.5 Hz, $\Delta\nu_{AB}$ = 32.3 Hz, 2 H), 5.95 (s, 1 H), 7.25−7.33 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.7 (t), 42.0 (t), 57.5 (t), 60.3 (d), 61.3 (t), 65.3 (t), 124.6 (d), 127.3 (d), 128.5 (d), 129.0 (d), 135.7 (s), 138.7 (s); exact mass (electrospray) m/z calcd for $C_{14}H_{20}NO_2$ (M + H) 234.1489, found 234.1490.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-(pent-4-en-1-yl)carbamate (20c). 2,6-Lutidine (0.26 mL, 2.24 mmol) and i-$Pr_3SiOSO_2CF_3$ (0.60 mL, 2.23 mmol) were added successively to a stirred solution of **20b**[13] (0.60 g, 2.18 mmol) in $ClCH_2CH_2Cl$ (30 mL). After 15 min, the mixture was lowered into a preheated oil bath set at 96 °C, and stirring was continued for 12 h. The mixture was cooled, evaporated, and diluted with Et_2O (40 mL). The solution was washed with saturated aqueous NH_4Cl and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using 1:20 t-BuOMe/hexanes, gave **20c** (0.756 g, 92%) as a colorless oil: FTIR ($CHCl_3$, cast) 3066, 3031, 2945, 2867, 1680, 1642, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.06−1.14 (m, 18 H), 1.22−1.44 (m, 3 H), 1.58−1.70 (m, 2 H), 2.02 (quintet, J = 7.5 Hz, 2 H), 3.17−3.29 (m, 2 H), 4.51 (s, 2 H), 4.93−5.03 (m, 2 H), 5.69−5.86 (m, 1 H), 7.22−7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.15 (d), 12.17 (d), 17.9 (q), 18.0 (q), 26.9 (t), 27.5 (t), 31.0 (t), 31.1 (t), 46.6 (t), 46.7 (t), 50.4 (t), 51.1 (t), 114.9 (s), 115.0 (s), 127.0 (d), 127.16 (d), 127.21 (d), 127.7 (d), 128.49 (d), 128.50 (d), 137.7 (d), 138.0 (d), 138.2 (s), 138.3 (s), 155.0 (s), 155.5 (s); exact mass (electrospray) m/z calcd for $C_{22}H_{37}NNaO_2Si$ (M + Na) 398.2486, found 398.2488.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-(4-oxobutyl)carbamate (20). *N*-Methylmorpholine-*N*-oxide (590 mg, 5.04 mmol), followed by OsO_4 (1.0 M in PhMe, 0.1 mL, 0.1 mmol), was added to a stirred solution of **20c** (612.3 mg, 1.63 mmol) in THF (6 mL) and water (6 mL). The mixture was stirred for 45 min, during which time the solution turned dark brown. The mixture was diluted with EtOAc, washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was dissolved in CH_2Cl_2 (18 mL), and $NaIO_4/SiO_2$[12] (20.4% w/w, 6.616 g, 5.587 mmol) was then added with stirring. Stirring was continued for 20 min by which time all of the diol had reacted (TLC control, silica, 1:10 EtOAc/hexane). The mixture was filtered through Celite, using CH_2Cl_2 as a rinse, and the filtrate was evaporated. Flash chromatography of the residue over silica gel (2.8 × 15 cm), using 1:10 EtOAc/hexanes, gave **20** (550 mg, 89%) as an oil: FTIR ($CHCl_3$, cast) 3065, 2945, 2893, 2868, 2720, 1727, 1678, 1606, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.06−1.12 (m, 18 H), 1.26−1.42 (m, 3 H), 1.80−1.90 (m, 2 H), 2.39 (dt, J = 1.2, 7.2 Hz) and 2.44 (dt, J = 1.2, 7.2 Hz, both signals together 2 H), 3.24 (t, J = 7.6 Hz) and 3.28 (t, J = 7.6, both signals together 2 H), 4.51 (s, 2 H), 7.22−7.34 (m, 5 H), 9.71−9.74 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.1 (d), 17.85 (q), 17.91 (q), 20.1 (t), 20.7 (t), 40.9 (t), 41.1 (t), 46.0 (t), 46.1 (t), 50.2 (t), 51.0 (t), 127.0 (d), 127.3 (d), 127.4 (d), 127.8 (d), 128.6 (d), 137.9 (s), 138.0 (s), 155.2 (s), 155.4 (s), 201.0 (d), 201.6 (d); exact mass (electrospray) m/z calcd for $C_{21}H_{35}NNaO_3Si$ (M + Na) 400.2278, found 400.2281.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-{(4*S*)-4-hydroxy-4-[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]butyl}carbamate (20d). BuLi (2.5 M in hexane, 0.115 mL, 0.29 mmol) was added dropwise to a stirred and cooled (−20 °C) solution of PhSeSePh (88.9 mg, 0.28 mmol) in THF (1 mL). After 10 min, the mixture was cooled to −42 °C (dry ice/MeCN), and a mixture of **16** (62.0 mg, 0.26 mmol) and **20** (146.7 mg, 0.39 mmol) in THF (1.5 mL) was added dropwise. Stirring at −42 °C was continued for 9 h, and the mixture was quenched with saturated aqueous NH_4Cl (3 mL) and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.6 × 15 cm), using 1:5 EtOAc/hexanes, gave **20d** (130.6 mg, 81%) as a colorless oil: FTIR ($CHCl_3$, cast) 3440, 3089, 3065, 2948, 2868, 1767, 1673, 1559, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.79−1.12 (m, 29 H), 1.21−1.85 (m, 11 H), 2.07−2.14 (m, 2 H), 3.23−3.29 (m, 2 H), 3.42−3.49 (m, 1 H), 3.59−3.65 (m, 1 H), 3.96 (br s, 1 H), 4.41−4.57 (m, 3 H), 5.97 (s, 1 H), 6.83 and 6.93 (two s, 1 H), 7.21−7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.1 (d), 15.7 (q), 15.8 (q), 17.7 (q), 17.8 (q), 17.9 (q), 20.9 (q), 22.2 (q), 23.1 (t), 23.2 (t), 23.7 (t), 24.1 (t), 25.3 (d), 31.4 (t), 31.5 (d), 32.5 (t), 34.2 (t), 40.4 (t), 46.1 (t), 46.6 (t), 47.7 (d), 50.1 (t), 50.9 (t), 66.4 (d), 67.0 (d), 79.1 (d), 79.3 (d), 99.2 (d), 127.0 (d), 127.26 (d), 127.31 (d), 127.8 (d), 128.5 (d), 128.6 (d), 137.8 (s), 138.1 (s), 139.8 (s), 140.5 (s), 142.9 (d), 143.2 (d), 155.5 (s), 155.8 (s), 170.39 (s), 170.42 (s); exact mass (electrospray) m/z calcd for $C_{35}H_{57}NNaO_6Si$ (M + Na) 638.3847, found 638.3847.

(1*S*)-4-[Benzyl({[tris(propan-2-yl)silyl]oxy}carbonyl)amino]-1-[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]-oxy}-2-oxo-2,5-dihydrofuran-3-yl]butyl Acetate (20e). DMAP (3.4 mg, 0.028 mmol) was added to a stirred solution of **20d** (87.4 mg, 0.14 mmol) in CH_2Cl_2 (2.5 mL). The mixture was cooled to −78 °C, and AcCl (0.03 mL, 0.42 mmol) and pyridine (0.07 mL, 0.85 mmol) were added sequentially. The mixture was cooled in an ice bath that was left in place but not recharged, and stirring was continued for 7.5 h. The mixture was quenched with hydrochloric acid (1 M, 1 mL) and water (5 mL), and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 1:1 EtOAc/hexanes, gave **20e** (84.4 mg, 90%) as a colorless oil: FTIR ($CHCl_3$, cast) 3064, 3030, 2948, 2868, 1772, 1749, 1678, 1606, 1559, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.78−1.12 (m, 30 H), 1.23−1.44 (m, 5 H), 1.53−1.88 (m, 6 H), 2.06 and 2.07 (two s, 3 H), 2.09−2.12 (m, 2 H), 3.21 (t, J = 7.5 Hz) and 3.27 (t, J = 7.5 Hz, both signals together 2 H), 3.60−3.66 (m, 1 H), 4.44−4.52 (m, 2 H), 5.51−5.56 (m, 1 H), 5.96 (s, 1 H), 6.81 and 6.84 (two s, 1 H), 7.21−7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.1 (d), 15.8 (q), 15.9 (q), 17.87 (q), 17.94 (q), 20.7 (q), 20.82 (q), 20.84 (q), 20.9 (q), 22.2 (q), 23.16 (t), 23.18 (t), 23.4 (t), 24.0 (t), 25.4 (d), 30.2 (t), 30.4 (t), 31.5 (d), 34.2 (t), 40.5 (t), 46.1 (t), 46.5 (t), 47.7 (d), 50.2 (t), 51.0 (t), 68.19 (d), 68.24 (d), 79.3 (d), 79.5 (d), 98.85 (d), 98.90 (d), 127.0 (d), 127.2 (d), 127.3 (d), 127.8 (d), 128.53 (d), 128.54 (d), 137.0 (s), 138.0 (s), 138.1 (s), 143.9 (d), 144.1 (d), 155.0 (s), 155.4 (s), 168.76 (s), 168.82 (s), 169.6 (s), 169.8 (s); exact mass (electrospray) m/z calcd for $C_{37}H_{59}NNaO_7Si$ (M + Na) 680.3953, found 680.3955.

(8*R*,8a*R*)-1-Benzyl-8-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)-cyclohexyl]oxy}-1*H*,2*H*,3*H*,4*H*,6*H*,8*H*,8a*H*-furo[3,4-*b*]azepin-6-one (20f). Bu_3NF (1.0 M in THF, 0.059 mL, 0.059 mmol) was added to a stirred solution of **20e** (39.0 mg, 0.059 mmol) in THF (0.8 mL). After 2 min, the reaction mixture was quenched with saturated aqueous NH_4Cl (1 mL) and diluted with EtOAc (4 mL). The organic

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phase was washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.0 × 14 cm), using 3:25 EtOAc/hexanes, gave **20f** (18.3 mg, 78%) as a light yellow oil: FTIR ($CHCl_3$, cast) 3086, 3061, 3028, 2952, 2926, 2869, 1764, 1678, 1603, 1495, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) isomer mixture δ 0.78−1.05 (m, 12 H), 1.21−1.26 (m, 1 H), 1.31−1.39 (m, 1 H), 1.49−1.53 (m, 1 H), 1.61−1.67 (m, 2 H), 1.80−1.87 (m, 1 H), 2.06−2.14 (m, 2 H), 2.36−2.48 (m, 1 H), 2.52−2.58 (m, 1 H), 2.81−2.86 (m, 1 H), 3.08−3.12 (m, 1 H), 3.41−3.47 (m, 1 H), 3.55−3.67 (m, 1 H), 3.73−3.93 (m, 1 H), 4.09 (d, J = 2.5 Hz, 1 H), 5.54−5.69 (m, 1 H), 7.13−7.39 (m, 6 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.3 (q), 15.7 (q), 15.8 (q), 17.7 (q), 20.8 (t), 20.9 (q), 22.3 (q), 23.1 (t), 23.4 (t), 24.7 (t), 25.4 (d), 25.5 (d), 26.8 (t), 28.5 (t), 29.1 (t), 31.4 (d), 34.3 (t), 36.7 (t), 39.1 (t), 39.6 (t), 47.7 (d), 47.8 (d), 52.6 (t), 53.9 (t), 54.5 (t), 57.8 (t), 66.9 (d), 68.4 (d), 76.3 (d), 77.2 (d), 97.3 (d), 101.6 (d), 127.19 (d), 127.23 (d), 128.2 (d), 128.5 (d), 128.7 (s), 129.1 (d), 130.7 (s), 138.8 (s), 142.1 (d), 144.1 (d), 168.6 (s); exact mass (electrospray) m/z calcd for $C_{25}H_{36}NO_3$ (M + H) 398.2690, found 398.2687.

Data for the major isomer: $[\alpha]^{20}_D$ −94.57 (c 1.22, $CHCl_3$); FTIR ($CHCl_3$, cast) 3086, 3063, 3028, 2952, 2927, 2869, 1764, 1678, 1603, 1495, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.77−1.07 (m, 12 H), 1.25−1.30 (m, 1 H), 1.33−1.42 (m, 1 H), 1.51−1.58 (m, 1 H), 1.63−1.70 (m, 2 H), 1.83−1.90 (m, 1 H), 2.08−2.20 (m, 2 H), 2.44−2.51 (m, 1 H), 2.55−2.61 (m, 1 H), 2.83−2.89 (m, 1 H), 3.13 (ddd, J = 2.5, 5.5, 14.5 Hz, 1 H), 3.61 (dt, J = 4.0, 10.5 Hz, 1 H), 3.63 (AB q, J = 14.3 Hz, $\Delta\nu_{AB}$ = 143.0 Hz, 2 H), 4.12 (q, J = 2.5 Hz, 1 H), 5.57 (d, J = 2.5 Hz, 1 H), 7.27−7.30 (m, 2 H), 7.34−7.38 (m, 4 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.7 (q), 20.85 (t), 20.94 (q), 22.3 (q), 23.1 (t), 25.4 (d), 29.1 (t), 31.4 (d), 34.3 (t), 39.6 (t), 47.8 (d), 52.6 (t), 54.5 (t), 68.4 (d), 77.2 (d), 101.6 (d), 127.2 (d), 128.47 (d), 128.48 (d), 130.7 (s), 138.8 (s), 144.1 (d), 168.6 (s); exact mass (electrospray) m/z calcd for $C_{25}H_{36}NO_3$ (M + H) 398.2690, found 398.2691.

Data for the minor isomer: $[\alpha]^{20}_D$ −157.58 (c 0.99, $CHCl_3$); FTIR ($CHCl_3$, cast) 3061, 3026, 2952, 2923, 2868, 2801, 2732, 1770, 1684, 1630, 1494, 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.77−1.09 (m, 12 H), 1.33−1.46 (m, 2 H), 1.64−1.81 (m, 4 H), 2.08−2.13 (m, 2 H), 2.27−2.35 (m, 1 H), 2.42 (ddd, J = 2.5, 8.8, 13.8 Hz, 1 H), 2.49−2.55 (m, 1 H), 3.14 (ddd, J = 2.5, 7.6, 13.6 Hz, 1 H), 3.67 (dt, J = 4.0, 10.8 Hz, 1 H), 3.70 (AB q, J = 13.3 Hz, $\Delta\nu_{AB}$ = 246.4 Hz, 2 H), 3.90−3.93 (m, 1 H), 5.72 (d, J = 5.0 Hz, 1 H), 7.16−7.19 (m, 1 H), 7.28−7.31 (m, 1 H), 7.34−7.37 (m, 2 H), 7.41−7.43 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.8 (q), 20.8 (q), 23.4 (t), 25.5 (d), 26.8 (t), 28.5 (t), 31.4 (d), 34.3 (t), 39.1 (t), 47.7 (d), 53.9 (t), 57.8 (t), 66.9 (d), 76.7 (d), 97.3 (d), 127.2 (d), 128.2 (d), 128.7 (s), 129.1 (d), 138.8 (s), 142.1 (d), 169.4 (s); exact mass (electrospray) m/z calcd for $C_{25}H_{36}NO_3$ (M + H) 398.2690, found 398.2692.

[(2*R*)-1-Benzyl-3-(hydroxymethyl)-2,5,6,7-tetrahydro-1*H*-azepin-2-yl]methanol (20g). DIBAL-H (1.0 M in PhMe, 0.66 mL, 0.66 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **20f** (52.5 mg, 0.13 mmol) in THF (1.5 mL). Stirring at −78 °C was continued for 2 h, the cold bath was left in place but not recharged, and stirring was continued for 12 h. MeOH (0.3 mL) and a saturated aqueous solution of Rochelle's salt (ca. 5 mL) were then added sequentially. Stirring was continued for 3 h, and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 3:100 MeOH/EtOAc, gave **20g** (29.6 mg, 90%) as an oil: $[\alpha]^{20}_D$ −2.10 (c 1.00, $CHCl_3$); FTIR ($CHCl_3$, cast) 3363, 3086, 3061, 3028, 2926, 2848, 1559, 1522, 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.40−1.47 (m, 1 H), 1.74−1.86 (m, 2 H), 2.18−2.38 (m, 3 H), 2.97−3.03 (m, 1 H), 3.12−3.22 (m, 1 H), 3.46−3.57 (m, 2 H), 3.73−3.87 (m, 3 H), 3.93 (s, 2 H), 5.99 (t, J = 5.7 Hz, 1 H), 7.21−7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4 (t), 28.1 (t), 49.9 (t), 55.9 (t), 59.2 (t), 64.3 (d), 68.1 (t), 127.4 (d), 128.7 (d), 129.0 (d), 130.6 (d), 139.5 (s), 140.9 (s); exact mass (electrospray) m/z calcd for $C_{15}H_{22}NO_2$ (M + H) 248.1645, found 248.1648.

***tert*-Butyl *N*-[(2-Ethenylphenyl)methyl]-*N*-methylcarbamate (21d).** NaH (60% in oil, 60.0 mg, 1.50 mmol) was added to a stirred solution of **21c**[15] (153.3 mg, 0.66 mmol) in THF (6 mL). After 15 min, the mixture was cooled to 0 °C, and MeI (0.16 mL, 2.57 mmol) was added. The ice bath was left in place but not recharged, and stirring was continued for 18 h. Water (4 mL) was added to destroy the excess of NaH, and the mixture was extracted with Et_2O. The combined organic extracts were washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 1:20 EtOAc/hexanes, gave **21d** (140.6 mg, 87%) as a colorless oil: FTIR ($CHCl_3$, cast) 3064, 2976, 2931, 1696, 1628, 1603, 1572, 1481, 1453 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.49 (s, 9 H), 2.71 and 2.78 (two br s, 3 H), 4.54 (s, 2 H), 5.30 (d, J = 11.0 Hz, 1 H), 5.63 (d, J = 17.5 Hz, 1 H), 6.98 (br s, 1 H), 7.15−7.16 (m, 1 H), 7.23−7.29 (m, 2 H), 7.49−7.51 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.4 (q), 33.4 (q), 49.6 (t), 50.1 (t), 79.6 (s), 116.0 (s), 126.1 (d), 127.5 (d), 127.8 (d), 128.6 (d), 134.2 (d), 134.8 (s), 137.2 (s), 155.8 (s); exact mass (electrospray) m/z calcd for $C_{15}H_{21}NNaO_2$ (M + Na) 270.1465, found 270.1465.

Tris(propan-2-yl)silyl *N*-[(2-Ethenylphenyl)methyl]-*N*-methylcarbamate (21e). 2,6-Lutidine (0.10 mL, 0.86 mmol) and *i*-$Pr_3SiOSO_2CF_3$ (0.20 mL, 0.72 mmol) were added successively to a stirred solution of **21d** (123.6 mg, 0.50 mmol) in CH_2Cl_2 (5 mL), and stirring was continued for 9.5 h. The mixture was washed with saturated aqueous NH_4Cl and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 1:20 Et_2O/hexanes, gave **21e** (167.8 mg, 96%) as a colorless oil: FTIR ($CHCl_3$, cast) 3064, 2945, 2892, 2868, 1682, 1559, 1465, 1421 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.04−1.13 (m, 18 H), 1.28−1.40 (m, 3 H), 2.79 and 2.85 (two s, 3 H), 4.61 (s, 2 H), 5.30 (t, J = 10.4 Hz, 1 H), 5.64 (d, J = 17.2 Hz, 1 H), 6.94 (dd, J = 10.8, 17.2 Hz) and 7.01 (dd, J = 10.8, 17.2 Hz, both signals together 1 H), 7.16−7.20 (m, 1 H), 7.23−7.28 (m, 2 H), 7.49−7.53 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.1 (d), 17.86 (q), 17.90 (q), 33.7 (q), 34.0 (q), 50.0 (t), 50.9 (t), 116.1 (s), 116.5 (s), 126.0 (d), 126.2 (d), 127.3 (d), 127.5 (d), 127.68 (d), 127.72 (d), 127.9 (d), 128.8 (d), 133.7 (d), 134.1 (d), 134.4 (s), 134.5 (s), 136.7 (s), 137.3 (s), 155.0 (s), 155.1 (s); exact mass (electrospray) m/z calcd for $C_{20}H_{33}NNaO_2Si$ (M + Na) 370.2173, found 370.2172.

Tris(propan-2-yl)silyl *N*-[(2-Formylphenyl)methyl]-*N*-methylcarbamate (21). OsO_4 (1.0 M in PhMe, 0.05 mL, 0.05 mmol) was added to a stirred solution of **21e** (157.5 mg, 0.45 mmol) in THF (4 mL) and water (1.5 mL). The mixture was stirred for 7 min, during which time the solution turned dark brown. $NaIO_4$ (301.1 mg, 1.41 mmol) was then added slowly, and stirring was continued for 1.5 h. The mixture was filtered through Celite, using EtOAc as a rinse. The filtrate was washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 1:10 EtOAc/hexanes, gave **21** (129.3 mg, 82%) as a light yellow oil: FTIR ($CHCl_3$, cast) 3071, 2945, 2892, 2867, 2729, 1683, 1601, 1576, 1464 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.95−1.11 (m, 18 H), 1.19−1.35 (m, 3 H), 2.94 and 2.99 (two s, 3 H), 4.96 (s, 2 H), 7.35 (d, J = 7.5 Hz, 1 H), 7.46 (q, J = 8.0 Hz, 1 H), 7.58 (q, J = 7.5 Hz, 1 H), 7.84 (d, J = 7.5 Hz, 1 H) 10.14 and 10.20 (two s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.0 (d), 12.1 (d), 17.7 (q), 17.9 (q), 35.0 (q), 35.3 (q), 49.8 (t), 51.4 (t), 126.4 (d), 127.3 (d), 127.5 (d), 127.8 (d), 133.3 (s), 133.5 (d), 133.9 (d), 134.0 (d), 135.1 (d), 140.1 (s), 140.5 (s), 155.29 (s), 155.33 (s), 193.0 (d), 193.4 (d); exact mass (electrospray) m/z calcd for $C_{19}H_{31}NNaO_3Si$ (M + Na) 372.1965, found 372.1962.

Tris(propan-2-yl)silyl *N*-({2-[(*S*)-Hydroxy[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl)methyl]phenyl}methyl)-*N*-methylcarbamate (21f). BuLi (2.5 M in hexane, 0.22 mL, 0.55 mmol) was added dropwise to a stirred and cooled (−20 °C) solution of PhSeSePh (174.0 mg, 0.55 mmol) in THF (1.58 mL). After 10 min, a portion of the freshly prepared PhSeLi solution (0.6 mL) was added dropwise by syringe to a stirred and cooled (−42 °C) solution of **16** (42.6 mg, 0.18 mmol) and **21** (87.5 mg, 0.25 mmol) in THF (2 mL). Stirring at −42 °C (dry ice/MeCN) was continued for 9 h, and the mixture was quenched with saturated aqueous NH_4Cl (3 mL) and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$),

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and evaporated. Flash chromatography of the residue over silica gel (1.2 × 15 cm), using 1:5 EtOAc/hexanes, gave **21f** (91.2 mg, 87%) as a colorless oil: FTIR ($CHCl_3$, cast) 3410, 3068, 2949, 2869, 2726, 1771, 1660, 1606, 1465 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.76−1.75 (m, 38 H), 2.09 (s, 2 H), 2.87−3.23 (m, 3 H), 3.62 (dt, J = 4.0, 10.5 Hz, 1 H), 4.24−4.81 (m, 2 H), 5.78−6.01 (m, 2 H), 6.65−6.97 (m, 1 H), 7.25−7.42 (m, 4 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.0 (d), 15.9 (q), 17.8 (q), 20.8 (q), 22.2 (q), 23.3 (t), 25.4 (d), 31.5 (d), 35.6 (q), 40.3 (t), 47.7 (d), 49.5 (t), 65.8 (d), 79.2 (d), 99.3 (d), 127.7 (d), 127.8 (d), 128.4 (d), 128.6 (d), 135.4 (s), 137.9 (s), 139.4 (s), 144.6 (d), 155.6 (s), 170.0 (s); exact mass (electrospray) m/z calcd for $C_{33}H_{53}NNaO_6Si$ (M + Na) 610.3534, found 610.3527.

(*S*)-(2-{[Methyl({[tris(propan-2-yl)silyl]oxy}carbonyl)amino]-methyl}phenyl)-[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)-cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl Acetate (21g). DMAP (3.4 mg, 0.028 mmol) was added to a stirred solution of **21f** (199.5 mg, 0.34 mmol) in CH_2Cl_2 (9 mL). The mixture was cooled to 0 °C, and AcCl (0.09 mL, 1.24 mmol) and pyridine (0.19 mL, 2.35 mmol) were added sequentially. The ice bath was left in place but not recharged, and stirring was continued for 5.5 h. The mixture was quenched with hydrochloric acid (1 M, 3 mL) and water (6 mL), and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 3:20 EtOAc/hexanes, gave **21g** (199.3 mg, 93%) as a colorless oil: FTIR ($CHCl_3$, cast) 3069, 2949, 2928, 2895, 2868, 2725, 1775, 1749, 1680, 1606, 1583, 1553, 1465 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.74−1.43 (m, 35 H), 1.63−1.68 (m, 2 H), 2.01−2.10 (m, 5 H), 2.90 and 2.92 (two s, 3 H), 3.59−3.65 (m, 1 H), 4.71 and 4.79 (two s, 2 H), 6.01 (d, J = 6.0 Hz, 1 H), 6.73 and 6.78 (two s, 1 H), 6.89 (s, 1 H), 7.20−7.39 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.0 (d), 12.1 (d), 15.8 (q), 17.8 (q), 17.9 (q), 20.8 (q), 22.2 (q), 23.18 (t), 23.20 (t), 25.30 (d), 25.34 (d), 31.4 (d), 34.2 (t), 34.57 (q), 34.61 (q), 40.4 (t), 47.7 (d), 48.7 (t), 49.9 (t), 65.9 (d), 66.7 (d), 79.3 (d), 79.4 (d), 98.8 (d), 98.9 (d), 126.1 (d), 127.4 (d), 127.5 (d), 127.6 (d), 127.9 (d), 128.1 (d), 129.2 (d), 133.7 (s), 134.2 (s), 135.8 (s), 135.9 (s), 136.6 (s), 136.9 (s), 144.9 (d), 145.5 (d), 155.4 (s), 155.6 (s), 168.30 (s), 168.35 (s), 169.1 (s), 169.2 (s); exact mass (electrospray) m/z calcd for $C_{35}H_{55}NNaO_7Si$ (M + Na) 652.3640, found 652.3632.

(6*R*,7*R*)-8-Methyl-6-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)-cyclohexyl]oxy}-5-oxa-8-azatricyclo[8.4.0.0^{3,7}]tetradeca-1-(14),2,10,12-tetraen-4-one (21h). Bu_3NF (1.0 M in THF, 0.317 mL, 0.317 mmol) was added to a stirred and cooled (0 °C) solution of **21g** (199.3 mg, 0.317 mmol) in THF (4 mL). After 15 min, the mixture was quenched with saturated aqueous NH_4Cl (4 mL) and diluted with EtOAc (4 mL). The organic phase was washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.4 × 14 cm), using 1:5 EtOAc/hexanes, gave **21h** (108.1 mg, 92%) as a light yellow oil: $[\alpha]^{20}_D$ 119.87 (c 1.12, $CHCl_3$); FTIR ($CHCl_3$, cast) 3064, 3017, 2953, 2924, 2870, 2852, 2794, 1763, 1657, 1600, 1568, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.77−1.06 (m, 12 H), 1.17−1.26 (m, 1 H), 1.35−1.44 (m, 1 H), 1.61−1.69 (m, 2 H), 2.06−2.18 (m, 2 H), 2.44 (s, 3 H), 3.21 (t, J = 3.2 Hz, 1 H), 3.61 (dt, J = 4, 10.4 Hz, 1 H), 3.80 (AB q, J = 15.2 Hz, $\Delta\nu_{AB}$ = 116.8 Hz, 2 H), 5.57 (d, J = 3.2 Hz, 1 H), 7.28−7.43 (m, 4 H), 7.73 (d, J = 2.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7 (q), 20.9 (q), 22.3 (q), 23.1 (t), 25.3 (d), 31.4 (d), 34.3 (t), 39.7 (t), 40.8 (q), 47.7 (d), 59.1 (t), 68.6 (d), 77.7 (d), 103.5 (d), 127.8 (d), 129.4 (d), 129.6 (s), 130.7 (d), 131.3 (d), 135.6 (s), 139.2 (s), 139.4 (d), 168.5 (s); exact mass (electrospray) m/z calcd for $C_{23}H_{32}NO_3$ (M + H) 370.2377, found 370.2379.

[(3*R*)-3-(Hydroxymethyl)-2-methyl-2,3-dihydro-1*H*-2-benzazepin-4-yl]methanol (21i). DIBAL-H (1.0 M in PhMe, 1.46 mL, 1.46 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **21h** (108.1 mg, 0.29 mmol) in THF (3 mL). Stirring at −78 °C was continued for 1 h, the cold bath was left in place but not recharged, and stirring was continued for 6.5 h. MeOH (0.5 mL) and a saturated aqueous solution of Rochelle's salt (ca. 6 mL) were then added sequentially. Stirring was continued for 12 h, and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 1:20 MeOH/EtOAc, gave **21i** (58.0 mg, 90%) as a white solid: $[\alpha]^{20}_D$ 59.87 (c 1.18, $CHCl_3$); FTIR ($CHCl_3$, cast) 3349, 3059, 3018, 2928, 2878, 1665, 1600, 1577, 1559, 1541, 1491 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.29 (s, 3 H), 3.16 (s, 2 H), 3.43 (t, J = 10.0 Hz, 1 H), 3.51 (dd, J = 5.0, 9.5 Hz, 1 H), 3.78 (dd, J = 5.0, 10.0 Hz, 1 H), 3.89 (AB q, J = 15.0 Hz, $\Delta\nu_{AB}$ = 229.78 Hz, 2 H), 4.19 (AB q, J = 13.0 Hz, $\Delta\nu_{AB}$ = 28.58 Hz, 2 H), 6.63 (s, 1 H), 7.16−7.26 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4 (t), 41.5 (q), 54.1 (t), 62.2 (t), 67.3 (d), 67.4 (t), 127.27 (d), 127.30 (d), 128.8 (d), 129.2 (d), 131.0 (d), 135.3 (s), 137.9 (s), 140.8 (s); exact mass (electrospray) m/z calcd for $C_{13}H_{18}NO_2$ (M + H) 220.1332, found 220.1332.

(2-Iodo-6-methylphenyl)methanol (22b). DIBAL-H (1.0 M in PhMe, 4.0 mL, 4.0 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **22a**[16] (440.9 mg, 1.60 mmol) in PhMe (5 mL). Stirring at −78 °C was continued for 2.25 h, the cooling bath was removed, and stirring was continued for 15 min. The mixture was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$) and evaporated to give **22b** as a white solid (96%): FTIR ($CHCl_3$, cast) 3280, 3053, 3009, 2967, 2934, 2732, 2618, 1588, 1555, 1480, 1445 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.77−1.80 (m, 1 H), 2.50 (s, 3 H), 4.84 (d, J = 6.5 Hz, 2 H), 6.88 (t, J = 7.5 Hz, 1 H), 7.17 (d, J = 7.5 Hz, 1 H), 7.70 (d, J = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.5 (q), 67.1 (t), 101.7 (s), 129.9 (d), 131.0 (d), 137.6 (d), 139.2 (s), 140.5 (s); HRMS (EI) m/z calcd for C_8H_9IO 247.9698, found 247.9700.

(2-Ethenyl-6-methylphenyl)methanol (22c). Ph_3P (135.0 mg, 0.51 mmol) was added to a stirred solution of $Pd(OAc)_2$ (27.6 mg, 0.12 mmol) in PhMe (2.5 mL). The mixture turned yellow after several minutes. Alcohol **22b** (297.6 mg, 1.20 mmol) and then a solution of tributyl(vinyl)tin (456.6 mg, 1.44 mmol) in PhMe (1.0 mL) were added, the latter by syringe. The solution was purged with a stream of Ar for 10 min and then heated to 110−120 °C for 15 h, during which time the solution turned black. The mixture was cooled and filtered through Celite, using MeOH as a rinse. Evaporation of the filtrate and flash chromatography of the red residue over silica gel (2.8 × 14 cm), using 1:5 Et_2O/hexanes, gave **22c** (165.9 mg, 93%): FTIR ($CHCl_3$, cast) 3256, 3085, 3070, 3027, 2958, 2933, 2720, 2591, 1626, 1591, 1581, 1497, 1470 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.49 (t, J = 5.5 Hz, 1 H), 2.47 (s, 3 H), 4.80 (d, J = 5.5 Hz, 2 H), 5.39 (dd, J = 1.5, 11.0 Hz, 1 H), 5.69 (dd, J = 1.5, 17.0 Hz, 1 H), 7.15−7.25 (m, 3 H), 7.39 (d, J = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.5 (q), 58.9 (t), 117.1 (t), 124.4 (d), 128.3 (d), 130.1 (d), 134.8 (d), 135.4 (s), 137.4 (s), 138.2 (s); HRMS (EI) m/z calcd for $C_{10}H_{12}O$ 148.0888, found 148.0886.

2-(Bromomethyl)-1-ethenyl-3-methylbenzene (22d). Ph_3P (394.6 mg, 1.49) was added to a stirred and cooled (0 °C) mixture of **22c** (183.7 mg, 1.24 mmol) and CBr_4 (479.6 mg, 1.49 mmol) in CH_2Cl_2 (6 mL). Stirring at 0 °C was continued for 50 min, at which point no starting material remained (TLC, silica, 1:20 EtOAc/hexane). Evaporation of the mixture and flash chromatography of the residue over silica gel (2.8 × 14 cm), using hexanes, gave **22d** (236.0 mg, 90%) as a white solid: FTIR ($CHCl_3$, cast) 3085, 3067, 3028, 3008, 2978, 2950, 2912, 2868, 1628, 1581, 1472, 1462 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.47 (s, 3 H), 4.65 (s, 2 H), 5.48 (dd, J = 1.0, 11.0 Hz, 1 H), 5.75 (dd, J = 1.0, 17.0 Hz, 1 H), 7.12−7.18 (m, 2 H), 7.24 (t, J = 7.5 Hz, 1 H), 7.37 (d, J = 7.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.2 (q), 28.8 (t), 117.6 (t), 124.7 (d), 128.8 (d), 130.2 (d), 132.8 (s), 134.2 (d), 137.5 (s), 138.2 (s); HRMS (EI) m/z calcd for $C_{10}H_{11}Br$ 212.0024, found 212.0021.

Benzyl[(2-ethenyl-6-methylphenyl)methyl]amine (22e). $BnNH_2$ (0.2 mL, 1.79 mmol) was added to a stirred solution of **22d** (127.9 mg, 0.61 mmol) in THF (3 mL), and stirring was continued for 12 h. The mixture was diluted with EtOAc and washed twice with aqueous NaOH (1 N) and then with brine. The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.4 × 14 cm), using 3:20 EtOAc/hexanes, gave **22e** (130.0 mg, 90%) as a yellow oil: FTIR ($CHCl_3$,

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cast) 3323, 3084, 3063, 3027, 2976, 2950, 2915, 2859, 1626, 1604, 1582, 1495, 1453 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.35 (s, 1 H), 2.37 (s, 3 H), 3.83 (s, 2 H), 3.90 (s, 2 H), 5.31 (dd, J = 1.5, 11.0 Hz, 1 H), 5.66 (dd, J = 1.5, 17.0 Hz, 1 H), 7.06 (dd, J = 11.0, 17.0 Hz, 1 H), 7.12 (d, J = 7.5 Hz, 1 H), 7.17 (t, J = 7.5 Hz, 1 H), 7.27−7.31 (m, 1 H), 7.35−7.41 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.5 (q), 46.7 (t), 54.1 (t), 116.2 (t), 124.0 (d), 127.0 (d), 127.3 (d), 128.2 (d), 128.3 (d), 130.0 (d), 135.2 (d), 135.7 (s), 137.2 (s), 137.9 (s), 140.5 (s); exact mass (electrospray) m/z calcd for $C_{17}H_{20}N$ (M + H) 238.1590, found 238.1591.

***tert*-Butyl *N*-Benzyl-*N*-[(2-ethenyl-6-methylphenyl)methyl]-carbamate (22f).** DMAP (126.7 mg, 1.03 mmol) and Boc_2O (226.3 mg, 1.03 mmol) were added successively to a stirred solution of **22e** (137.5 mg, 0.50 mmol) in MeCN (6 mL), and stirring was continued for 37 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (1.8 × 14 cm), using 1:20 Et_2O/hexanes, gave **22f** (158.9 mg, 92%) as a colorless oil: FTIR ($CHCl_3$, cast) 3087, 3065, 3030, 3006, 2976, 2930, 1693, 1626, 1605, 1581, 1540, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.53 (s, 9 H), 2.13 (s, 3 H), 4.15 (s, 2 H), 4.72 (s, 2 H), 5.20 (dd, J = 1.5, 11.0 Hz, 1 H), 5.55 (d, J = 17.5 Hz, 1 H), 6.87 (br s, 1 H), 7.06−7.09 (m, 3 H), 7.19−7.36 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.8 (q), 28.5 (q), 42.8 (t), 47.4 (t), 80.0 (s), 116.0 (t), 124.6 (d), 126.8 (d), 127.0 (d), 127.8 (d), 128.4 (d), 130.1 (d), 132.3 (s), 135.5 (d), 138.2 (s), 139.2 (s), 155.8 (s); exact mass (electrospray) m/z calcd for $C_{22}H_{27}NNaO_2$ (M + Na) 360.1934, found 360.1937.

[Tris(propan-2-yl)silyl *N*-Benzyl-*N*-[(2-ethenyl-6-methylphenyl)methyl]carbamate (22g). 2,6-Lutidine (0.10 mL, 0.86 mmol) and i-$Pr_3SiOSO_2CF_3$ (0.21 mL, 0.76 mmol) were added successively to a stirred solution of **22f** (147.1 mg, 0.44 mmol) in $ClCH_2CH_2Cl$ (5 mL). The mixture was lowered into a preheated oil bath set at 96 °C, and stirring was continued for 4 h. The mixture was cooled, evaporated, and diluted with Et_2O (10 mL). The solution was washed with saturated aqueous NH_4Cl and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using 1:25 Et_2O/hexanes, gave **22g** (186.6 mg, 98%) as a colorless oil: FTIR ($CHCl_3$, cast) 3087, 3065, 3030, 2945, 2893, 2867, 1677, 1606, 1581, 1550, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.07−1.20 (m, 18 H), 1.31−1.48 (m, 3 H), 2.05 and 2.08 (two s, 3 H), 4.19 (s, 2 H), 4.74 and 4.78 (two s, 2 H), 5.15 (d, J = 11.0 Hz, 1 H), 5.50−5.57 (m, 1 H), 6.78 (dd, J = 11.0, 17.0 Hz) and 6.85 (dd, J = 11.0, 17.5 Hz, both signals together 1 H), 7.01−7.06 (m, 3 H), 7.17−7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.17 (d), 12.23 (d), 17.9 (q), 18.0 (q), 19.7 (q), 19.8 (q), 43.2 (t), 44.1 (t), 47.1 (t), 47.9 (t), 116.1 (t), 116.4 (t), 124.3 (d), 124.7 (d), 126.5 (d), 126.9 (d), 127.4 (d), 127.8 (d), 127.9 (d), 128.3 (d), 128.4 (d), 130.1 (d), 130.2 (d), 131.4 (s), 132.0 (s), 135.0 (d), 135.2 (d), 137.9 (s), 138.0 (s), 138.1 (s), 138.4 (s), 139.1 (s), 139.2 (s), 155.1 (s), 155.3 (s); exact mass (electrospray) m/z calcd for $C_{27}H_{40}NO_2Si$ (M + H) 438.2823, found 438.2820.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-[(2-formyl-6-methylphenyl)methyl]carbamate (22). OsO_4 (1.0 M in PhMe, 0.05 mL, 0.05 mmol) was added to a stirred solution of **22g** (184.4 mg, 0.42 mmol) in THF (3 mL) and water (1 mL). The mixture was stirred for 8 min, during which time the solution turned dark brown. $NaIO_4$ (280.0 mg, 1.31 mmol) was then added slowly, and stirring was continued for 50 min. The mixture was then filtered through Celite, using EtOAc as a rinse. The filtrate was washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 1:20 EtOAc/hexanes, gave **22** (155.3 mg, 84%) as a light yellow oil: FTIR ($CHCl_3$, cast) 3066, 3031, 2946, 2892, 2867, 2728, 1676, 1591, 1552, 1496, 1465 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.09−1.20 (m, 18 H), 1.30−1.50 (m, 3 H), 2.24 (s, 3 H), 4.26 (s, 2 H), 5.10 (s, 2 H), 6.97−7.03 (m, 2 H), 7.24−7.29 (m, 3 H), 7.34−7.39 (m, 2 H), 7.71 (d, J = 7.0 Hz, 1 H), 9.94 and 10.07 (two s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.1 (d), 17.9 (q), 18.0 (q), 19.3 (q), 41.4 (t), 42.2 (t), 47.8 (t), 48.5 (t), 126.6 (d), 127.2 (d), 127.4 (d), 127.9 (d), 128.1 (d), 128.6 (d), 135.98 (d), 136.02 (s), 136.8 (s), 137.5 (s), 139.7 (s), 155.1 (s), 155.3 (s), 191.5 (s), 192.2 (s); exact mass (electrospray) m/z calcd for $C_{26}H_{38}NO_3Si$ (M + H) 440.2615, found 440.2615.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-({2-[(*S*)-hydroxy[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl]-6-methylphenyl}-methyl)-carbamate (22h). BuLi (2.5 M in hexane, 0.28 mL, 0.70 mmol) was added dropwise to a stirred and cooled (−20 °C) solution of PhSeSePh (220.6 mg, 0.70 mmol) in THF (1.72 mL). After 10 min, a portion of the freshly prepared PhSeLi solution (1.0 mL) was added dropwise by syringe to a stirred and cooled (−42 °C) solution of **16** (75.0 mg, 0.32 mmol) and **22h** (190.1 mg, 0.43 mmol) in THF (4 mL). Stirring was continued for 10 h at −42 °C (dry ice/MeCN), and the mixture was quenched with saturated aqueous NH_4Cl (3 mL) and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 15 cm), using 3:20 EtOAc/hexanes, gave **22h** (167.4 mg, 78%) as a colorless oil: FTIR ($CHCl_3$, cast) 3431, 3066, 3032, 2951, 2927, 2868, 1773, 1674, 1607, 1552, 1496, 1462 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.79−1.46 (m, 35 H), 1.64−1.72 (m, 2 H), 2.06−2.14 (m, 2 H), 2.25−2.27 (m, 3 H), 3.43−3.63 (m, 2 H), 4.37−4.90 (m, 4 H), 5.43−5.66 (m, 1 H), 5.97 (s, 1 H), 6.62−6.90 (m, 1 H), 7.10−7.51 (m, 8 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.1 (d), 15.8 (q), 15.9 (q), 17.9 (q), 20.1 (q), 20.2 (q), 20.8 (q), 20.9 (q), 22.2 (q), 23.1 (t), 23.3 (t), 25.2 (d), 25.4 (d), 31.5 (d), 34.2 (t), 40.3 (t), 40.5 (t), 43.7 (t), 44.0 (t), 47.7 (d), 47.8 (d), 65.4 (d), 65.6 (d), 78.9 (d), 79.3 (d), 99.1 (d), 99.2 (d), 125.1 (d), 125.2 (d), 126.5 (d), 126.6 (d), 127.2 (d), 128.2 (d), 128.7 (d), 130.9 (d), 131.0 (d), 137.9 (s), 138.6 (s), 138.7 (s), 139.6 (s), 139.8 (s), 140.0 (s), 144.3 (d), 155.5 (s), 169.8 (s); exact mass (electrospray) m/z calcd for $C_{40}H_{60}NO_6Si$ (M + H) 678.4184, found 678.4185.

(*S*)-(2-{[Benzyl({[tris(propan-2-yl)silyl]oxy}carbonyl)amino]-methyl}-3-methylphenyl)[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl Acetate (22i). DMAP (2.2 mg, 0.018 mmol) was added to a stirred solution of **22h** (62.2 mg, 0.092 mmol) in CH_2Cl_2 (1.5 mL). The mixture was then cooled to 0 °C, and AcCl (0.03 mL, 0.41 mmol) and pyridine (0.05 mL, 0.62 mmol) were added sequentially. The ice bath was left in place but not recharged, and stirring was continued for 40 min. The mixture was quenched with hydrochloric acid (1 M, 2 mL) and water (3 mL), and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 1:10 EtOAc/hexanes, gave **22i** (64.0 mg, 96%) as a colorless oil: FTIR ($CHCl_3$, cast) 3066, 3032, 2950, 2868, 1778, 1753, 1676, 1606, 1555, 1496, 1459 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.80−1.46 (m, 35 H), 1.64−1.72 (m, 2 H), 2.02−2.18 (m, 8 H), 3.54−3.72 (m, 1 H), 4.14−4.44 (m, 2 H), 4.77−4.94 (m, 2 H), 5.77 and 5.94 (two s, 1 H), 6.70−6.85 (m, 2 H), 7.03−7.29 (m, 8 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.1 (d), 15.9 (q), 17.8 (q), 18.0 (q), 20.0 (q), 20.7 (q), 20.80 (q), 20.85 (q), 22.2 (q), 23.3 (t), 25.5 (d), 31.5 (d), 34.2 (t), 40.5 (t), 43.5 (t), 47.7 (d), 48.2 (t), 67.5 (d), 79.3 (d), 98.6 (d), 125.7 (d), 125.9 (d), 126.1 (d), 126.7 (d), 127.1 (d), 128.1 (d), 128.4 (d), 131.4 (d), 131.6 (d), 132.8 (s), 133.1 (s), 136.0 (s), 136.3 (s), 136.7 (s), 136.9 (s), 137.1 (s), 137.9 (s), 138.2 (s), 139.5 (s), 139.6 (s), 145.8 (d), 155.4 (s), 168.0 (s), 169.0 (s), 169.1 (s); exact mass (electrospray) m/z calcd for $C_{42}H_{61}NNaO_7Si$ (M + Na) 742.4110, found 742.4106.

(6*R*,7*R*)-8-Benzyl-11-methyl-6-{[(1*S*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-5-oxa-8-azatricyclo[8.4.0.0^{3,7}]-tetradeca-1(14),2,10,12-tetraen-4-one (22j). Bu_3NF (1.0 M in THF, 0.0385 mL, 0.0385 mmol) was added to a stirred and cooled (−78 °C) solution of **22i** (27.7 mg, 0.0385 mmol) in THF (0.8 mL). After 15 min, the mixture was quenched with saturated aqueous NH_4Cl (3 mL) and diluted with EtOAc (4 mL). The organic phase was washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.0 × 14 cm), using 1:20 EtOAc/hexanes, gave **22j** (17.0 mg, 96%) as a foam: $[\alpha]^{20}_D$ 97.44 (c 1.07, $CHCl_3$); FTIR ($CHCl_3$, cast) 3063, 3028, 2954, 2924, 2869, 1763, 1661, 1586, 1495, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.76−1.06 (m, 12 H), 1.14−1.20 (m, 1 H), 1.34−1.40 (m, 1 H), 1.59−1.67 (m, 2 H), 2.02−2.12 (m, 2 H), 2.21 (s, 3 H), 3.40 (t, J = 3.0 Hz, 1

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H), 3.61 (dt, J = 4.0, 10.5 Hz, 1 H), 3.76 (AB q, J = 15.0 Hz, $\Delta\nu_{AB}$ = 104.9 Hz, 2 H), 3.82 (AB q, J = 15.0 Hz, $\Delta\nu_{AB}$ = 41.4 Hz, 2 H), 5.65 (d, J = 3.0 Hz, 1 H), 7.15−7.48 (m, 8 H), 7.82 (d, J = 2.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.7 (q), 20.1 (q), 20.9 (q), 22.2 (q), 23.1 (t), 25.3 (d), 31.3 (d), 34.3 (t), 39.6 (t), 47.7 (d), 49.1 (t), 56.6 (t), 67.6 (d), 77.3 (d), 103.9 (d), 127.3 (d), 127.4 (d), 128.2 (d), 128.5 (d), 128.9 (d), 129.3 (s), 131.5 (d), 137.0 (s), 138.1 (s), 138.2 (s), 139.0 (s), 140.4 (d), 168.7 (s); exact mass (electrospray) m/z calcd for $C_{30}H_{38}NO_3$ (M + H) 460.2846, found 460.2846.

[(3-*R*)-2-Benzyl-3-(hydroxymethyl)-9-methyl-2,3-dihydro-1*H*-2-benzazepin-4-yl]methanol (22k). DIBAL-H (1.0 M in PhMe, 0.38 mL, 0.38 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **22j** (35.2 mg, 0.077 mmol) in THF (1 mL). Stirring at −78 °C was continued for 2 h, the cold bath was left in place but not recharged, and stirring was continued for 5 h. MeOH (0.3 mL) and a saturated aqueous solution of Rochelle's salt (ca. 3 mL) were then added sequentially. Stirring was continued for 1.2 h, and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 1:1 EtOAc/hexanes, gave **22k** (17.7 mg, 75%) as a light yellow solid: $[\alpha]^{20}_D$ 21.97 (c 0.83, $CHCl_3$); FTIR ($CHCl_3$, cast) 3384, 3062, 3028, 2922, 2858, 1733, 1671, 1585, 1495, 1454 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.93 (s, 3 H), 3.43 (t, J = 9.5 Hz, 1 H), 3.61 (s, 2 H), 3.72 (dd, J = 5.5, 9.5 Hz, 1 H), 3.77 (dd, J = 5.5, 10 Hz, 1 H), 3.87 (s, 2 H), 4.25 (AB q, J = 13.0 Hz, $\Delta\nu_{AB}$ = 30.3 Hz, 2 H), 6.71 (s, 1 H), 7.03 (dd, J = 1.5, 7.0 Hz, 1 H), 7.13−7.22 (m, 4 H), 7.26−7.35 (m, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.7 (q), 46.2 (t), 58.1 (t), 62.6 (t), 66.1 (d), 67.6 (t), 126.8 (d), 127.4 (d), 128.5 (d), 129.0 (d), 129.3 (d), 129.67 (d), 129.70 (d), 135.9 (s), 136.0 (s), 136.8 (s), 138.5 (s), 140.6 (s); exact mass (electrospray) m/z calcd for $C_{20}H_{24}NO_2$ (M + H) 310.1802, found 310.1803.

***tert*-Butyl *N*-{[2-Bromo-5-(trifluoromethyl)phenyl]methyl}-carbamate (23c).** Boc_2O (157.7 mg, 0.72 mmol) in CH_2Cl_2 (2 mL) was added to a stirred solution of **23b**[17] (181.9 mg, 0.72 mmol) in CH_2Cl_2 (5 mL). Stirring was continued for 14 h, and the solvent was evaporated. Flash chromatography of the residue over silica gel (2.8 × 14 cm), using 1:20 EtOAc/hexanes, gave **23c** (242.1 mg, 95%) as a white solid: FTIR ($CHCl_3$, cast) 3296, 3062, 2986, 2936, 2817, 1678, 1646, 1603, 1582, 1518, 1475 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.48 (s, 9 H), 4.43 (d, J = 6.0 Hz, 2 H), 5.16 (s, 1 H), 7.40 (d, J = 7.5 Hz, 1 H), 7.62 (s, 1 H), 7.67 (d, J = 8.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.3 (q), 44.6 (t), 80.1 (s), 123.8 ($\mathbf{C}F_3$, $^1J_{CF}$ = 272 Hz), 125.4 ($\mathbf{C}CCF_3$, $^3J_{CF}$ = 3.6 Hz), 125.7 (d), 127.0 (s), 130.1 ($\mathbf{C}CF_3$, $^2J_{CF}$ = 33.1 Hz), 133.3 (d), 139.2 (s), 155.8 (s); exact mass (electrospray) m/z calcd for $C_{13}H_{15}BrF_3NNaO_2$ (M + Na) 376.0130, found 376.0127.

***tert*-Butyl *N*-{[2-Ethenyl-5-(trifluoromethyl)phenyl]methyl}-carbamate (23d).** Ph_3P (110.0 mg, 0.42 mmol) was added to a stirred solution of $Pd(OAc)_2$ (22.0 mg, 0.096 mmol) in PhMe (5 mL). The color of the mixture turned yellow after several minutes. Bromide **23c** (340.8 mg, 0.96 mmol) and tributyl(vinyl)tin (351.0 mg, 1.11 mmol) were then added sequentially. The solution was purged with a stream of Ar for 5 min and then heated (Ar atmosphere) to 110−120 °C for 19 h, during which time the mixture turned black. The mixture was cooled and filtered through Celite, using MeOH as a rinse. Evaporation of the filtrate and flash chromatography of the residue over silica gel (2.8 × 14 cm), using 1:20 EtOAc/hexanes, gave **23d** (275.8 mg, 95%) as a light yellow solid: FTIR ($CHCl_3$, cast) 3342, 2980, 2934, 1696, 1619, 1514, 1456 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.48 (s, 9 H), 4.44 (d, J = 4.0 Hz, 2 H), 4.87 (s, 1 H), 5.48 (d, J = 11.0 Hz, 1 H), 5.48 (d, J = 17.0 Hz, 1 H), 6.99 (dd, J = 11.0, 17.0 Hz, 1 H), 7.52−7.54 (m, 2 H), 7.60 (d, J = 7.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.3 (q), 42.2 (t), 79.9 (s), 118.8 (t), 120.8 (s), 123.0 (s), 124.49 (d), 124.52 (d), 125.1 (d), 125.16 (d), 125.19 (s), 126.6 (d), 127.3 (s), 129.8 ($\mathbf{C}CF_3$, $^2J_{CF}$ = 32 Hz), 132.8 (d), 136.4 (s), 140.2 (s), 155.6 (s); exact mass (electrospray) m/z calcd for $C_{15}H_{18}F_3NNaO_2$ (M + Na) 324.1182, found 324.1183.

***tert*-Butyl *N*-Benzyl-*N*-{[2-ethenyl-5-(trifluoromethyl)-phenyl]methyl}carbamate (23e).** A solution of **23d** (275.8 mg, 0.92 mmol) in DMF (2 mL) was added dropwise to a stirred suspension of NaH (60% in oil, 47.0 mg, 1.18 mmol) in DMF (7 mL). Stirring was continued for 30 min, and then BnBr (0.24 mL, 1.38 mmol) was added. Stirring was continued for 19.5 h, and the mixture was quenched with hydrochloric acid (1 N) and extracted with Et_2O. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 × 14 cm), using 1:50 EtOAc/hexanes, gave **23e** (268.7 mg, 75%) as a colorless oil: FTIR ($CHCl_3$, cast) 3089, 3066, 3032, 2978, 2931, 1696, 1620, 1573, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.50 (s, 9 H), 4.31−4.55 (m, 4 H), 5.39 (dd, J = 1.0, 11.0 Hz, 1 H), 5.68 (dd, J = 1.0, 17.5 Hz, 1 H), 6.90 (br s, 1 H), 7.17 (br s, 2 H), 7.25−7.38 (m, 4 H), 7.50 (d, J = 8.5 Hz, 1 H), 7.56 (d, J = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.3 (q), 46.8 (t), 49.4 (t), 80.5 (s), 118.4 (t), 120.9 (s), 123.1 (s), 124.3 (d), 125.2 (s), 126.6 (d), 127.4 (d), 128.6 (d), 129.7 ($\mathbf{C}CF_3$, $^2J_{CF}$ = 33.1 Hz), 133.1 (d), 135.5 (s), 137.6 (s), 140.7 (s), 155.7 (s); exact mass (electrospray) m/z calcd for $C_{22}H_{24}F_3NNaO_2$ (M + Na) 414.1651, found 414.1654.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-{[2-ethenyl-5-(trifluoromethyl)phenyl]methyl}carbamate (23f). 2,6-Lutidine (0.14 mL, 1.20 mmol) and *i*-$Pr_3SiOSO_2CF_3$ (0.30 mL, 1.11 mmol) were added successively to a stirred solution of **23e** (236.9 mg, 0.61 mmol) in $ClCH_2CH_2Cl$ (6 mL). The mixture was lowered into a preheated oil bath set at 96 °C, and stirring was continued for 4 h. The mixture was cooled, evaporated and diluted with Et_2O (10 mL). The solution was washed with saturated aqueous NH_4Cl and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using 1:50 EtOAc/hexanes, gave **23f** (282.0 mg, 95%) as a colorless oil: FTIR ($CHCl_3$, cast) 3089, 3065, 3032, 2947, 2893, 2868, 1681, 1620, 1574, 1549, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.09−1.16 (m, 18 H), 1.34−1.44 (m, 3 H), 4.44−4.64 (m, 4 H), 5.42 (d, J = 11.0 Hz, 1 H), 5.70−5.76 (m, 1 H), 6.84 (dd, J = 11.0, 17.5 Hz) and 6.97 (dd, J = 11.0, 17.0 Hz, both signals together 1 H), 7.21 (d, J = 7.5 Hz, 1 H), 7.27−7.38 (m, 4 H), 7.43 (d, J = 12.0 Hz, 1 H), 7.54 (d, J = 7.5 Hz, 1 H), 7.58−7.63 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) (because of the presence of rotamers, the signal splitting by fluorine is ignored) δ 12.08 (d), 12.15 (d), 17.8 (q), 17.9 (q), 47.0 (t), 47.7 (t), 50.0 (t), 118.6 (t), 118.9 (t), 120.9 (s), 123.0 (s), 123.89 (d), 123.92 (d), 124.2 (d), 124.3 (d), 124.4 (d), 124.5 (d), 125.21 (d), 125.24 (d), 126.6 (d), 126.7 (d), 127.3 (d), 127.5 (d), 127.55 (d), 127.64 (d), 127.8 (d), 128.0 (d), 128.4 (d), 128.7 (d), 129.3 (s), 129.5 (s), 129.6 (s), 129.8 (s), 129.9 (s), 130.07 (s), 130.12 (s), 130.3 (s), 132.6 (d), 133.0 (d), 135.2 (s), 135.4 (s), 137.2 (s), 137.4 (s), 140.1 (s), 140.7 (s), 155.2 (s), 155.4 (s); exact mass (electrospray) m/z calcd for $C_{27}H_{36}F_3NNaO_2Si$ (M + Na) 514.2360, found 514.2359.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-{[2-formyl-5-(trifluoromethyl)phenyl]methyl}carbamate (23). OsO_4 (1.0 M in PhMe, 0.05 mL, 0.05 mmol) was added to a stirred solution of **23f** (273.1 mg, 0.56 mmol) in THF (4.5 mL) and water (1.5 mL). The mixture was stirred for 8 min, during which time the solution turned dark brown. $NaIO_4$ (369.0 mg, 1.72 mmol) was then added slowly and stirring was continued for 1 h. The mixture was filtered through Celite, using EtOAc as a rinse. The filtrate was washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 × 14 cm), using 1:20 EtOAc/hexanes, gave **23** (257.1 mg, 94%) as a light yellow oil: FTIR ($CHCl_3$, cast) 3089, 3066, 3032, 2947, 2893, 2869, 2740, 1703, 1681, 1583, 1553, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.99−1.14 (m, 18 H), 1.25−1.42 (m, 3 H), 4.57 and 4.62 (two s, 2 H), 4.97 and 5.01 (two s, 2 H), 7.22−7.35 (m, 5 H), 7.63 (s, 1 H), 7.71 (t, J = 8.0 Hz, 1 H), 7.95 (d, J = 8.0 Hz, 1 H), 10.17 and 10.22 (two s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) (because of the presence of rotamers, the signal splitting by fluorine is ignored) δ 12.0 (d), 12.1 (d), 17.7 (q), 17.8 (q), 47.47 (t), 47.54 (t), 51.4 (t), 51.6 (t), 120.0 (s), 120.1 (s), 122.2 (s), 122.3 (s), 123.97 (d), 123.99 (d), 124.18 (d), 124.21 (d), 124.3 (d), 124.4 (d), 124.5 (s), 124.79 (d), 124.81 (d), 126.6 (s), 126.7 (s), 127.3 (d), 127.6 (d), 127.7 (d), 128.0 (d), 128.4 (d), 128.7 (d), 128.8 (d), 133.4 (d), 134.6 (d), 134.8 (s), 134.9 (s), 135.0 (s), 135.2 (s), 135.3 (s), 135.4 (s),

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135.5 (s), 136.1 (s), 137.0 (s), 137.2 (s), 141.2 (s), 141.9 (s), 155.3 (s), 155.4 (s), 191.8 (d), 192.0 (d); exact mass (electrospray) m/z calcd for $C_{26}H_{34}F_3NNaO_3Si$ (M + Na) 516.2152, found 516.2151.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-({2-[(*S*)-hydroxy[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl]-5-(trifluoromethyl)phenyl}methyl)carbamate (23g). BuLi (2.5 M in hexane, 0.24 mL, 0.60 mmol) was added dropwise to a stirred and cooled (−20 °C) solution of PhSeSePh (189.1 mg, 0.60 mmol) in THF (0.96 mL). After 10 min, a portion of the freshly prepared PhSeLi solution (0.8 mL) was added dropwise by syringe to a stirred and cooled (−42 °C) solution of **16** (92.0 mg, 0.39 mmol) and **23** (257.1 mg, 0.52 mmol) in THF (4.5 mL). Stirring was continued for 8 h at −42 °C (dry ice/MeCN), and the mixture was quenched with saturated aqueous NH_4Cl (4 mL) and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 × 15 cm), using 1:5 EtOAc/hexanes, gave **23g** (240.4 mg, 85%) as a colorless oil: FTIR ($CHCl_3$, cast) 3421, 3089, 3066, 3033, 2951, 2929, 2869, 1770, 1680, 1655, 1587, 1556, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.79−1.09 (m, 29 H), 1.22−1.47 (m, 5 H), 1.65−1.73 (m, 2 H), 2.11 (br s, 2 H), 3.32 (br s, 1 H), 3.60−3.68 (m, 1 H), 4.32−4.78 (m, 5 H), 5.67−6.02 (m, 2 H), 6.54 and 6.98 (two s, 1 H), 7.27−7.53 (m, 8 H); ^{13}C NMR ($CDCl_3$, 125 MHz) (because of the presence of rotamers, the signal splitting by fluorine is ignored) δ 12.0 (d), 16.0 (q), 17.8 (q), 20.8 (q), 22.2 (q), 23.3 (t), 25.5 (d), 31.5 (d), 34.2 (t), 40.4 (t), 47.0 (t), 47.7 (d), 52.2 (t), 65.4 (d), 79.5 (d), 99.5 (d), 120.6 (s), 122.8 (s), 124.5 (d), 124.90 (d), 124.94 (s), 125.0 (d), 127.1 (s), 127.5 (d), 127.8 (d), 128.1 (d), 128.9 (d), 130.6 (s), 130.8 (s), 131.1 (s), 136.6 (s), 137.1 (s), 138.6 (s), 141.6 (s), 144.5 (d), 145.0 (d), 155.6 (s), 169.9 (s); exact mass (electrospray) m/z calcd for $C_{40}H_{56}F_3NNaO_6Si$ (M + Na) 754.3721, found 754.3717.

(*S*)-(2-{[Benzyl({[tris(propan-2-yl)silyl]oxy}carbonyl)amino]methyl}-4-(trifluoromethyl)phenyl)[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl Acetate (23h). DMAP (3.5 mg, 0.031 mmol) was added to a stirred solution of **23g** (240.0 mg, 0.33 mmol) in CH_2Cl_2 (4 mL). The mixture was then cooled to 0 °C, and AcCl (0.11 mL, 1.52 mmol) and pyridine (0.19 mL, 2.35 mmol) were added sequentially. The ice bath was left in place but not recharged, and stirring was continued for 50 min. The mixture was quenched with hydrochloric acid (1 M, 3 mL) and water (3 mL), and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 × 14 cm), using 1:10 EtOAc/hexanes, gave **23h** (243.7 mg, 96%) as a colorless oil: FTIR ($CHCl_3$, cast) 3033, 2951, 2869, 1775, 1680, 1623, 1496, 1466 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.74−1.13 (m, 30 H), 1.20−1.42 (m, 5 H), 1.62−1.70 (m, 2 H), 2.00−2.09 (m, 5 H), 3.57−3.64 (m, 1 H), 4.46−4.58 (m, 2 H), 4.69−4.84 (m, 2 H), 5.97 (d, J = 10.0 Hz, 1 H), 6.60 and 6.69 (two s, 1 H), 6.85 and 6.91 (two s, 1 H), 7.22−7.35 (m, 5 H), 7.44−7.53 (m, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) (because of the presence of rotamers, the signal splitting by fluorine is ignored) δ 12.0 (d), 12.1 (d), 15.8 (q), 17.7 (q), 17.8 (q), 20.57 (q), 20.62 (q), 20.8 (q), 22.2 (q), 23.2 (t), 24.7 (t), 25.4 (d), 31.5 (d), 34.2 (t), 36.6 (t), 40.4 (t), 46.6 (t), 47.5 (t), 47.7 (d), 50.8 (t), 51.0 (t), 65.2 (d), 66.1 (d), 79.5 (d), 79.6 (d), 98.9 (d), 99.0 (d), 122.65 (s), 122.70 (s), 123.1 (d), 124.2 (d), 124.3 (d), 124.8 (s), 124.9 (s), 127.0 (s), 127.48 (d), 127.54 (d), 128.2 (d), 128.4 (d), 128.6 (d), 128.7 (d), 130.82 (s), 130.85 (s), 131.08 (s), 131.11 (s), 131.3 (s), 131.4 (s), 131.60 (s), 131.63 (s), 135.7 (s), 136.1 (s), 137.0 (s), 137.2 (s), 137.3 (s), 137.38 (s), 137.43 (s), 137.6 (s), 138.1 (s), 145.2 (d), 145.9 (d), 155.5 (s), 155.6 (s), 168.0 (s), 168.8 (s), 169.0 (s); exact mass (electrospray) m/z calcd for $C_{42}H_{58}F_3NNaO_7Si$ (M + Na) 796.3827, found 796.3825.

(6*R*,7*R*)-8-Benzyl-6-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)-cyclohexyl]oxy}-12-(trifluoromethyl)-5-oxa-8-azatricyclo-[8.4.0.0^{3,7}]tetradeca-1(14),2,10,12-tetraen-4-one (23i). Bu_3NF (1.0 M in THF, 0.076 mL, 0.076 mmol) was added to a stirred and cooled (0 °C) solution of **23h** (58.9 mg, 0.076 mmol) in THF (1 mL). After 10 min, the mixture was quenched with saturated aqueous NH_4Cl (3 mL) and diluted with EtOAc (4 mL). The organic phase was washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.0 × 14 cm), using 1:20 EtOAc/hexanes, gave **23i** (35.6 mg, 91%) as a white solid: mp 136−140 °C; $[\alpha]^{20}_D$ 159.11 (c 1.47, $CHCl_3$); FTIR ($CHCl_3$, cast) 3087, 3064, 3029, 2955, 2925, 2870, 1764, 1666, 1617, 1496, 1455 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.79−1.06 (m, 12 H), 1.16−1.22 (m, 1 H), 1.34−1.43 (m, 1 H), 1.61−1.69 (m, 2 H), 2.07−2.13 (m, 2 H), 3.52 (t, J = 3.5 Hz, 1 H), 3.61 (dt, J = 4.5, 11.0 Hz,1 H), 3.72 (AB q, J = 15 Hz, $\Delta\nu_{AB}$ = 67.3 Hz, 2 H), 3.74 (AB q, J = 13.8 Hz, $\Delta\nu_{AB}$ = 27.5 Hz, 2 H), 5.69 (d, J = 3.5 Hz, 1 H), 7.32−7.42 (m, 6 H), 7.56 (d, J = 8.0 Hz, 1 H), 7.65 (dd, J = 1.5, 8.0 Hz, 1 H), 7.76 (d, J = 3.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.8 (q), 20.9 (q), 22.2 (q), 23.1 (t), 25.3 (d), 31.4 (d), 34.3 (t), 39.9 (t), 47.7 (d), 53.3 (t), 57.1 (t), 68.2 (d), 78.1 (d), 104.1 (d), 120.4 (s), 122.6 (s), 124.8 (J_{CF} = 4.1 Hz), 126.9 (s), 127.4 (J_{CF} = 3.6 Hz), 127.67 (d), 127.73 (d), 128.5 (d), 128.6 (d), 128.7 (d), 128.8 (d), 130.7 (**C**CF_3, $^2J_{CF}$ = 32.7 Hz), 131.4 (d), 132.8 (s), 137.3 (d), 138.1 (s), 139.4 (s), 140.2 (s), 167.9 (s); exact mass (electrospray) m/z calcd for $C_{30}H_{35}F_3NO_3$ (M + H) 514.2564, found 514.2567.

[(3*R*)-2-Benzyl-3-(hydroxymethyl)-8-(trifluoromethyl)-2,3-dihydro-1*H*-2-benzaze-pin-4-yl]methanol (23j). DIBAL-H (1.0 M in PhMe, 0.11 mL, 0.11 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **23i** (11.3 mg, 0.022 mmol) in THF (0.6 mL). Stirring at −78 °C was continued for 1 h, the cold bath was left in place but not recharged, and stirring was continued for 7 h. MeOH (0.1 mL) and a saturated aqueous solution of Rochelle's salt (ca. 3 mL) were then added sequentially. Stirring was continued overnight, and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (0.6 × 8 cm), using 2:1 EtOAc/hexanes, gave **23j** (6.0 mg, 75%) as a light yellow solid: $[\alpha]^{20}_D$ 65.42 (c 1.35, $CHCl_3$); FTIR ($CHCl_3$, cast) 3375, 3087, 3064, 3030, 2922, 2855, 1650, 1616, 1495, 1455 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.50−3.58 (m, 3 H), 3.72−3.77 (m, 2 H), 3.87 (dd, J = 5.5, 11.0 Hz, 1 H), 4.20 (d, J = 15.5 Hz, 1 H), 4.24 (AB q, J = 13.5 Hz, $\Delta\nu_{AB}$ = 20.6 Hz, 2 H), 6.76 (s, 1 H), 7.15−7.22 (m, 3 H), 7.28−7.35 (m, 3 H), 7.42 (d, J = 8.0 Hz, 1 H), 7.55 (d, J = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 56.1 (t), 57.2 (t), 62.4 (t), 65.9 (d), 67.0 (t), 120.8 (s), 122.9 (s), 124.2 (J_{CF} = 3.9 Hz), 125.1 (s), 126.4 (J_{CF} = 3.6 Hz), 127.4 (d), 127.7 (d), 128.5 (d), 128.6 (d), 128.7 (s), 129.0 (s), 129.1 (d), 131.6 (d), 137.8 (s), 138.6 (s), 138.7 (s), 144.2 (s); exact mass (electrospray) m/z calcd for $C_{20}H_{21}F_3NO_2$ (M + H) 364.1519, found 364.1514.

(2-Ethenylnaphthalen-1-yl)methanol (24d). $NaBH_4$ (138.5 mg, 3.65 mmol) was added to a solution of **24c**[20] (132.7 mg, 0.73 mmol) in THF (2 mL) and EtOH (2 mL) at room temperature. The mixture was stirred for 30 min and quenched with cold water. The pH was adjusted to 5−6, and the solution was stirred for 15 min. The mixture was extracted with Et_2O, and the combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.4 × 14 cm), using 3:10 EtOAc/hexanes, gave **24d** (127.7 mg, 95%) as a white solid: FTIR ($CHCl_3$, cast) 3396, 3082, 3057, 2993, 2948, 2911, 1620, 1596, 1513, 1497 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.71 (s, 1 H), 5.19 (s, 2 H), 5.50 (dd, J = 1.0, 11.0 Hz, 1 H), 5.81 (dd, J = 1.0, 17.5 Hz, 1 H), 7.33 (dd, J = 11.0, 17.5 Hz, 1 H), 7.46−7.50 (m, 1 H), 7.54−7.75 (m, 1 H), 7.65 (d, J = 8.5 Hz, 1 H), 7.79 (d, J = 9.0 Hz, 1 H), 7.83 (d, J = 9.0 Hz, 1 H), 8.23 (d, J = 8.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 58.1 (t), 118.1 (t), 124.4 (d), 124.5 (d), 126.1 (d), 127.2 (d), 128.8 (d), 129.2 (d), 132.5 (s), 132.6 (s), 133.7 (s), 134.7 (d), 135.1 (s); HRMS (EI) m/z calcd for $C_{13}H_{12}O$ 184.0888, found 184.0885.

1-(Bromomethyl)-2-ethenylnaphthalene (24e). Ph_3P (156.2 mg, 0.59 mmol) and CBr_4 (195.7 mg, 0.59 mmol) were added successively to a stirred and cooled (0 °C) solution of **24d** (90.4 mg, 0.49 mmol) in CH_2Cl_2 (2.5 mL). After 1 h at 0 °C, the solvent was evaporated. Flash chromatography of the residue over silica gel (1.4 × 14 cm), using 1:50 EtOAc/hexanes, gave **24e** (104.5 mg, 86%) as a white solid: FTIR ($CHCl_3$, cast) 3085, 3057, 3020, 1618, 1595, 1564, 1512, 1470 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.07 (s, 2 H), 5.60 (dd, J = 1.0, 11.0 Hz, 1 H), 5.89 (dd, J = 1.0, 17.5 Hz, 1 H), 7.27 (dd, J

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= 11.0, 17.5 Hz, 1 H), 7.49−7.52 (m, 1 H), 7.60−7.63 (m, 2 H), 7.81 (d, J = 8.5 Hz, 1 H), 7.84 (d, J = 8.5 Hz, 1 H), 8.15 (d, J = 8.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 27.3 (t), 118.4 (t), 123.6 (d), 124.2 (d), 126.0 (d), 127.0 (d), 128.6 (d), 129.4 (s), 129.5 (d), 131.4 (s), 133.4 (s), 134.0 (d), 135.0 (s); HRMS (EI) m/z calcd for $C_{13}H_{11}Br$ 246.0044, found 246.0046.

Benzyl[(2-ethenylnaphthalen-1-yl)methyl]amine (24f). A solution of **24e** (147.3 mg, 0.60 mmol) and $BnNH_2$ (0.2 mL, 1.79 mmol) in THF (1.5 mL) was stirred at room temperature for 22 h and then diluted with EtOAc. The mixture was washed twice with aqueous NaOH (1 M) and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 1:5 EtOAc/hexanes, gave **24f** (149.1 mg, 92%) as a yellow oil: FTIR ($CHCl_3$, cast) 3324, 3084, 3061, 3026, 2917, 2850, 1665, 1622, 1597, 1564, 1511, 1495 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.57 (s, 1 H), 3.98 (s, 2 H), 4.26 (s, 2 H), 5.43 (dd, J = 1.0, 11.0 Hz, 1 H), 5.80 (dd, J = 1.0, 17.5 Hz, 1 H), 7.22 (dd, J = 11.0, 17.0 Hz, 1 H), 7.29−7.32 (m, 1 H), 7.36−7.52 (m, 6 H), 7.66 (d, J = 8.5 Hz, 1 H), 7.75 (d, J = 9.0 Hz, 1 H), 7.81 (d, J = 8.0 Hz, 1 H), 8.06 (d, J = 8.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 45.3 (t), 54.2 (t), 116.9 (t), 123.9 (d), 124.3 (d), 125.6 (d), 126.6 (d), 127.1 (d), 128.0 (d), 128.35 (d), 128.43 (d), 128.5 (d), 132.6 (s), 132.7 (s), 133.5 (s), 134.4 (s), 134.8 (d), 140.4 (s); exact mass (electrospray) m/z calcd for $C_{20}H_{20}N$ (M + H) 274.1590, found 274.1591.

***tert*-Butyl *N*-Benzyl-*N*-[(2-ethenylnaphthalen-1-yl)methyl]carbamate (24g).** DMAP (155.0 mg, 1.26 mmol) and Boc_2O (222.0 mg, 1.01 mmol) were added successively to a stirred solution of **24f** (137.5 mg, 0.50 mmol) in MeCN (5 mL). Stirring was continued for 24 h, and the solvent was evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 1:20 Et_2O/hexanes, gave **24g** (155.6 mg, 83%) as a colorless oil: FTIR ($CHCl_3$, cast) 3087, 3062, 3031, 3007, 2975, 2931, 1689, 1622, 1605, 1511, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.40−1.80 (m, 9 H), 4.15 (s, 2 H), 5.19 (s, 2 H), 5.31 (d, J = 11.0 Hz, 1 H), 5.71 (d, J = 17.0 Hz, 1 H), 7.04 (d, J = 7.0 Hz, 3 H), 7.20−7.30 (m, 3 H), 7.48−7.54 (m, 2 H), 7.64 (d, J = 8.5 Hz, 1 H), 7.80 (d, J = 9.0 Hz, 1 H), 7.82−7.86 (m, 1 H), 8.20 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.5 (q), 41.5 (t), 47.6 (t), 80.2 (s), 117.3 (t), 124.0 (d), 124.8 (d), 125.8 (d), 126.7 (d), 126.8 (d), 126.9 (d), 127.0 (d), 128.3 (d), 128.5 (d), 128.7 (d), 132.9 (s), 133.4 (s), 134.8 (d), 136.2 (s), 138.5 (s), 155.9 (s); exact mass (electrospray) m/z calcd for $C_{25}H_{27}NNaO_2$ (M + Na) 396.1934, found 396.1937.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-[(2-ethenylnaphthalen-1-yl)methyl]carbamate (24h). 2,6-Lutidine (0.036 mL, 0.31 mmol) and i-$Pr_3SiOSO_2CF_3$ (0.075 mL, 0.27 mmol) were added successively to a stirred solution of **24g** (57.1 mg, 0.15 mmol) in $ClCH_2CH_2Cl$ (2 mL) and stirring was continued for 24 h. The mixture was washed with saturated aqueous NH_4Cl and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 1:25 Et_2O/hexanes, gave **24h** (71.0 mg, 98%) as a colorless oil: FTIR ($CHCl_3$, cast) 3087, 3063, 3033, 2945, 2892, 2867, 1674, 1623, 1606, 1560, 1511, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.11−1.30 (m, 18 H), 1.36−1.56 (m, 3 H), 4.22 (s, 2 H), 5.23−5.29 (m, 3 H), 5.66−5.72 (m, 1 H), 6.86−7.07 (m, 3 H), 7.21−7.29 (m, 3 H), 7.42−7.51 (m, 2 H), 7.62−7.65 (m, 1 H), 7.79−7.85 (m, 2 H), 8.11−8.23 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.2 (d), 12.3 (d), 17.9 (q), 18.1 (q), 42.0 (t), 43.0 (t), 47.4 (t), 48.2 (t), 117.4 (t), 123.9 (d), 124.1 (d), 124.3 (d), 125.0 (d), 125.8 (d), 125.9 (d), 126.5 (d), 126.6 (d), 126.8 (d), 127.3 (d), 128.2 (d), 128.3 (d), 128.4 (d), 128.5 (d), 128.7 (d), 128.8 (d), 129.3 (s), 132.8 (s), 132.9 (s), 133.3 (s), 134.5 (d), 134.6 (d), 136.2 (s), 137.9 (s), 138.0 (s), 155.2 (s), 155.4 (s); exact mass (electrospray) m/z calcd for $C_{30}H_{40}NO_2Si$ (M + H) 474.2823, found 474.2821.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-[(2-formylnaphthalen-1-yl)methyl]carbamate (24). OsO_4 (1.0 M in PhMe, 0.05 mL, 0.05 mmol) was added to a stirred solution of **24g** (224.5 mg, 0.48 mmol) in THF (4 mL) and water (1.3 mL). The mixture was stirred for 7 min, during which time the solution turned dark brown. $NaIO_4$ (315.0 mg, 1.47 mmol) was then added slowly, and stirring was continued for 1.5 h. The mixture was filtered through Celite, using EtOAc as a rinse, and the filtrate was washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 1:20 EtOAc/hexanes, gave **24** (193.7 mg, 86%) as a light yellow oil: FTIR ($CHCl_3$, cast) 3287, 3064, 2945, 2892, 2867, 1675, 1623, 1599, 1549, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.10−1.29 (m, 18 H), 1.37−1.57 (m, 3 H), 4.21−4.24 (m, 2 H), 5.55 (s, 2 H), 6.94−7.01 (m, 2 H), 7.23−7.29 (m, 3 H), 7.58 (t, J = 7.5 Hz, 1 H), 7.65−7.67 (m, 1 H), 7.90−7.95 (m, 3 H), 8.34−8.43 (m, 1 H), 9.98 and 10.11 (two s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.2 (d), 12.3 (d), 17.7 (q), 17.9 (q), 18.1 (q), 39.7 (t), 40.7 (t), 47.7 (t), 48.6 (t), 123.4 (d), 123.57 (d), 123.64 (d), 125.3 (d), 126.0 (d), 126.6 (d), 127.2 (d), 127.4 (d), 127.5 (d), 128.7 (d), 128.8 (d), 128.9 (d), 129.3 (d), 129.39 (d), 129.42 (d), 132.4 (s), 133.3 (s), 133.5 (s), 136.1 (s), 136.6 (s), 137.0 (s), 137.1 (s), 137.2 (s), 155.1 (s), 155.3 (s), 190.4 (d), 190.9 (d); exact mass (electrospray) m/z calcd for $C_{29}H_{38}NO_3Si$ (M + H) 476.2615, found 476.2612.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-({2-[(*S*)-hydroxy[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl]naphthalen-1-yl}methyl)carbamate (24i). BuLi (2.5 M in hexane, 0.37 mL, 0.87 mmol) was added dropwise to a stirred and cooled (−20 °C) solution of PhSeSePh (274.0 mg, 0.87 mmol) in THF (2.03 mL). After 10 min, a portion of the freshly prepared PhSeLi solution (0.8 mL) was added dropwise by syringe to a stirred and cooled (−42 °C) solution of **16** (64.8 mg, 0.27 mmol) and **24** (168.1 mg, 0.35 mmol) in THF (3 mL). Stirring was continued for 9 h at −42 °C (dry ice/MeCN), and the mixture was quenched with saturated aqueous NH_4Cl (3 mL) and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 15 cm), using 3:20 EtOAc/hexanes, gave **24i** (145.0 mg, 75%) as a colorless oil: FTIR ($CHCl_3$, cast) 3434, 3061, 3033, 2950, 2928, 2868, 2726, 1770, 1671, 1605, 1553, 1513, 1496, 1461 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.77−1.68 (m, 37 H), 2.02−2.16 (m, 2 H), 3.21 (s, 1 H), 3.58−3.67 (m, 1 H), 4.09 (d, J = 16.5 Hz, 1 H), 4.61−4.78 (m, 1 H), 4.90−5.10 (m, 1 H), 5.39−5.48 (m, 1 H), 5.71 (s, 1 H), 5.94 (s, 1 H), 6.68 (s, 1 H), 6.99−7.17 (m, 2 H), 7.28−7.34 (m, 3 H), 7.50−7.54 (m, 3 H), 7.84−7.86 (m, 2 H), 8.21 (d, J = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.2 (d), 15.8 (q), 17.9 (q), 20.8 (q), 22.2 (q), 23.3 (t), 25.3 (d), 31.5 (d), 34.2 (t), 40.4 (t), 42.1 (t), 47.6 (d), 48.9 (t), 65.6 (d), 79.4 (d), 99.3 (d), 124.1 (d), 125.1 (d), 126.3 (d), 126.4 (d), 126.9 (d), 127.3 (d), 128.5 (d), 128.7 (d), 129.4 (d), 129.8 (s), 132.5 (s), 133.5 (s), 137.3 (s), 137.7 (s), 139.5 (s), 144.4 (d), 155.5 (s), 169.9 (s); exact mass (electrospray) m/z calcd for $C_{43}H_{59}NNaO_6Si$ (M + Na) 736.4004, found 736.4002.

(*S*)-(1-{[Benzyl({[tris(propan-2-yl)silyl]oxy}carbonyl)amino]methyl}naphthalen-2-yl)[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl Acetate (24j). DMAP (2.8 mg, 0.023 mmol) was added to a stirred solution of **24i** (129.8 mg, 0.18 mmol) in CH_2Cl_2 (2.5 mL). The mixture was then cooled to 0 °C, and AcCl (0.06 mL, 0.83 mmol) and pyridine (0.11 mL, 1.36 mmol) were added sequentially. The ice bath was left in place but not recharged, and stirring was continued for 1 h. The mixture was quenched with hydrochloric acid (1 M, 3 mL) and water (4 mL), and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.4 × 14 cm), using 3:25 EtOAc/hexanes, gave **24j** (133.0 mg, 97%) as a colorless oil: FTIR ($CHCl_3$, cast) 3063, 3033, 2949, 2868, 2726, 1775, 1751, 1672, 1605, 1558, 1513, 1496, 1459 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.76−1.56 (m, 35 H), 1.66−1.70 (m, 2 H), 2.03−2.13 (m, 5 H), 3.64 (dt, J = 4.0, 10.5 Hz, 1 H), 4.27−4.41 (m, 2 H), 5.31−5.49 (m, 2 H), 5.96 (s, 1 H), 6.76−6.92 (m, 2 H), 7.04 (d, J = 7.0 Hz, 2 H), 7.10−7.22 (m, 3 H), 7.46−7.54 (m, 3 H), 7.83 (d, J = 9.0 Hz, 2 H), 8.21 and 8.30 (two d, J = 8.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.2 (d), 12.3 (d), 15.9 (q), 17.8 (q), 18.1 (q), 20.7 (q), 20.9 (q), 22.2 (q), 23.3 (t), 25.4 (d), 31.5 (d), 34.2 (t), 40.5 (t), 42.8 (t), 47.7 (d), 48.4 (t), 67.4 (d), 79.4 (d), 98.7 (d), 124.2 (d), 125.6 (d), 125.9 (d), 126.6 (d), 126.7 (d), 127.0 (d), 128.3 (d), 128.4 (d), 129.3 (d), 131.6 (s), 132.8 (s), 133.6 (s), 133.7 (s), 136.8 (s),

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137.8 (s), 145.9 (d), 155.6 (s), 168.0 (s), 169.1 (s); exact mass (electrospray) m/z calcd for $C_{45}H_{61}NNaO_7Si$ (M + Na) 778.4110, found 778.4103.

(15*R*,16*R*)-17-Benzyl-15-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-14-oxa-17-azatetracyclo[8.8.0.0^{2,7}.0^{12,16}]-octadeca-1,3,5,7,9,11-hexaen-13-one (24k). Bu_3NF (1.0 M in THF, 0.16 mL, 0.16 mmol) was added to a stirred and cooled (0 °C) solution of **24j** (120.0 mg, 0.16 mmol) in THF (2 mL). After 10 min, the mixture was quenched with saturated aqueous NH_4Cl (3 mL) and diluted with EtOAc (4 mL). The organic phase was washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 3:50 EtOAc/hexanes, gave **24k** (78.3 mg, 99%) as a light yellow solid: mp 183−184 °C; $[\alpha]^{20}_D$ 54.89 (c 0.98, $CHCl_3$); FTIR ($CHCl_3$, cast) 3057, 3026, 2954, 2924, 2869, 1763, 1658, 1618, 1596, 1559, 1511, 1495, 1454 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.74−1.17 (m, 13 H), 1.32−1.43 (m, 1 H), 1.61−1.67 (m, 2 H), 2.05−2.15 (m, 2 H), 3.20 (t, J = 2.0 Hz, 1 H), 3.64 (dt, J = 4.0, 10.5 Hz, 1 H), 3.84 (AB q, J = 15.0 Hz, $\Delta\nu_{AB}$ = 19.4 Hz, 2 H), 4.08 (AB q, J = 15.0 Hz, $\Delta\nu_{AB}$ = 276.1 Hz, 2 H), 5.73 (d, J = 2.0 Hz, 1 H), 7.41 (t, J = 7.0 Hz, 1 H), 7.48−7.59 (m, 7 H), 7.81 (d, J = 8.5 Hz, 1 H), 7.90 (t, J = 7.0 Hz, 2 H), 8.02 (d, J = 2.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.7 (q), 20.9 (q), 22.2 (q), 23.1 (t), 25.3 (d), 31.4 (d), 34.3 (t), 39.6 (t), 46.9 (t), 47.7 (d), 57.7 (t), 67.3 (d), 77.2 (d), 124.4 (d), 126.5 (d), 126.9 (d), 127.0 (d), 127.6 (d), 128.2 (d), 128.5 (d), 128.66 (d), 128.71 (d), 130.9 (s), 133.4 (s), 133.5 (s), 135.3 (s), 137.8 (s), 138.9 (s), 140.8 (d), 168.7 (s); exact mass (electrospray) m/z calcd for $C_{33}H_{38}NO_3$ (M + H) 496.2846, found 496.2843.

[(3*R*)-2-Benzyl-3-(hydroxymethyl)-1*H*,2*H*,3*H*-naphtho[1,2-*c*]-azepin-4-yl]methanol (24l). DIBAL-H (1.0 M in PhMe, 0.79 mL, 0.79 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **24k** (78.3 mg, 0.16 mmol) in THF (2 mL). Stirring at −78 °C was continued for 1 h, the cold bath was left in place but not recharged, and stirring was continued overnight. MeOH (0.3 mL) and a saturated aqueous solution of Rochelle's salt (ca. 5 mL) were then added sequentially. Stirring was continued for 2.5 h, and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 1:20 MeOH/Et_2O, gave **24l** (45.0 mg, 82%) as a white solid: $[\alpha]^{20}_D$ −26.39 (c 0.91, $CHCl_3$); FTIR ($CHCl_3$, cast) 3367, 3079, 3063, 3024, 2983, 2964, 2946, 2918, 2894, 2874, 2843, 1598, 1511, 1493, 1453 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.05 (br s, 2 H), 3.36 (t, J = 9.5 Hz, 1 H), 3.65−3.75 (m, 4 H), 4.26−4.39 (m, 4 H), 6.89 (s, 1 H), 7.20−7.22 (m, 2 H), 7.29−7.31 (m, 3 H), 7.37−7.39 (m, 2 H), 7.44−7.47 (m, 1 H), 7.71 (d, J = 8.5 Hz, 1 H), 7.77 (d, J = 8.5 Hz, 1 H), 7.83 (dd, J = 1.3, 8.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 46.3 (t), 59.1 (t), 62.9 (t), 65.8 (d), 67.6 (t), 123.4 (d), 125.7 (d), 126.4 (d), 127.4 (d), 127.5 (d), 128.3 (d), 128.49 (d), 128.53 (d), 129.1 (d), 129.7 (d), 132.1 (s), 132.7 (s), 133.5 (s), 133.7 (s), 138.7 (s), 142.5 (s); exact mass (electrospray) m/z calcd for $C_{23}H_{24}NO_2$ (M + H) 346.1802, found 346.1801.

***tert*-Butyl *N*-Benzyl-*N*-[(2-bromopyridin-3-yl)methyl]-carbamate (25d).** DMAP (54.6 mg, 0.44 mmol) and then a solution of Boc_2O (97.6 mg, 0.44 mmol) in MeCN (0.5 mL) were added successively to a stirred solution of **25c**[22] (61.4 mg, 0.22 mmol) in MeCN (2.5 mL), and stirring was continued for 30 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (1.2 × 14 cm), using 1:5 EtOAc/hexanes, gave **25d** (70.4 mg, 84%) as a colorless oil: FTIR ($CHCl_3$, cast) 3031, 2976, 2930, 1697, 1605, 1578, 1561, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.43 and 1.51 (two br s, 9 H), 4.41−4.53 (m, 4 H), 7.22−7.35 (m, 6 H), 7.43 and 7.54 (two s, 1 H), 8.26 (dd, J = 1.5, 4.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.4 (q), 49.1 (t), 49.4 (t), 50.5 (t), 50.9 (t), 80.7 (s), 123.0 (d), 127.6 (d), 128.1 (d), 128.7 (d), 134.6 (s), 134.7 (s), 135.9 (d), 136.9 (d), 137.4 (s), 137.5 (s), 142.4 (s), 142.8 (s), 148.5 (d), 155.8 (s); exact mass (electrospray) m/z calcd for $C_{18}H_{22}BrN_2O_2$ (M + H) 377.0859, found 377.0860.

***tert*-Butyl *N*-Benzyl-*N*-[(2-ethenylpyridin-3-yl)methyl]-carbamate (25e).** Ph_3P (79.0 mg, 0.30 mmol) was added to a stirred solution of $Pd(OAc)_2$ (15.7 mg, 0.071 mmol) in PhMe (4 mL). The color of the mixture turned yellow after several minutes. Bromide **25d** (258.9 mg, 0.69 mmol) and tributyl(vinyl)tin (261.3 mg, 0.82 mmol) were then added sequentially. The solution was purged with a stream of Ar for 10 min and then heated (Ar atmosphere) to 110−120 °C for 18 h, during which time the solution turned black. The mixture was cooled and filtered through Celite, using MeOH as a rinse. Evaporation of the filtrate and flash chromatography of the red residue over silica gel (2.8 × 14 cm), using 1:5 EtOAc/hexanes, gave **25e** (203.9 mg, 91%) as a light yellow oil: FTIR ($CHCl_3$, cast) 3088, 3063, 3027, 2976, 2928, 2873, 1695, 1605, 1584, 1561, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.48 (s, 9 H), 4.29−4.53 (m, 4 H), 5.47 (dd, J = 2.0, 10.5 Hz, 1 H), 6.35 (dd, J = 2.0, 17.0 Hz, 1 H), 6.93 (br s, 1 H), 7.12−7.22 (m, 3 H), 7.24−7.33 (m, 3 H), 7.42 (d, J = 7.5 Hz, 1 H), 8.50 (dd, J = 1.5, 4.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.4 (q), 45.8 (t), 49.3 (t), 80.5 (s), 120.2 (t), 122.4 (d), 127.4 (d), 128.6 (d), 130.0 (s), 132.3 (d), 137.5 (s), 148.4 (d), 155.7 (s); exact mass (electrospray) m/z calcd for $C_{20}H_{25}N_2O_2$ (M + H) 325.1911, found 325.1911.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-[(2-ethenylpyridin-3-yl)-methyl]carbamate (25f). 2,6-Lutidine (0.15 mL, 1.29 mmol) and i-$Pr_3SiOSO_2CF_3$ (0.31 mL, 1.13 mmol) were added successively to a stirred solution of **25e** (193.9 mg, 0.60 mmol) in $ClCH_2CH_2Cl$ (6.5 mL). After 15 min, the mixture was lowered into a preheated oil bath set at 96 °C, and stirring was continued for 4 h. The mixture was cooled, evaporated, and diluted with Et_2O (10 mL). The solution was washed with saturated aqueous NH_4Cl and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using 1:5 t-BuOMe/hexanes, gave **25f** (232.8 mg, 92%) as a colorless oil: FTIR ($CHCl_3$, cast) 3063, 3028, 2945, 2892, 2867, 2726, 1680, 1606, 1584, 1561, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.05 (d, J = 7.5 Hz) and 1.09 (d, J = 7.5 Hz, both signals together 18 H), 1.29−1.39 (m, 3 H), 4.36−4.59 (m, 4 H), 5.47 (dd, J = 2.0, 11.0 Hz, 1 H), 6.33−6.40 (m, 1 H), 6.85 (dd, J = 10.5, 17.0 Hz) and 6.99 (dd, J = 11.0, 17.0 Hz, both signals together 1 H), 7.11−7.17 (m, 2 H), 7.21−7.34 (m, 4 H), 7.41−7.45 (m, 1 H), 8.49−8.52 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.05 (d), 12.11 (d), 17.8 (q), 17.9 (q), 46.1 (t), 46.7 (t), 49.6 (t), 49.7 (t), 120.4 (t), 120.5 (t), 122.4 (d), 122.5 (d), 127.1 (d), 127.4 (d), 127.5 (d), 128.0 (d), 128.7 (d), 129.6 (s), 129.7 (s), 131.8 (d), 132.4 (d), 135.0 (d), 136.9 (d), 137.1 (s), 137.3 (s), 148.2 (d), 148.5 (d), 153.0 (s), 153.8 (s), 155.2 (s), 155.3 (s); exact mass (electrospray) m/z calcd for $C_{25}H_{37}N_2O_2Si$ (M + H) 425.2619, found 425.2621.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-[(2-formylpyridin-3-yl)-methyl]carbamate (25). OsO_4 (1.0 M in PhMe, 0.1 mL, 0.1 mmol) was added to a stirred solution of **25f** (216.0 mg, 0.51 mmol) in THF (4.5 mL) and water (1.5 mL). The mixture was stirred for 7 min, during which time the solution turned dark brown. $NaIO_4$ (338.0 mg, 1.58 mmol) was then added slowly, and stirring was continued for 2 h. The mixture was filtered through Celite, using EtOAc as a rinse. The filtrate was washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.8 × 14 cm), using 3:20 EtOAc/hexanes, gave **25** (156.3 mg, 79%) as a light yellow oil: FTIR ($CHCl_3$, cast) 3063, 3028, 2945, 2892, 2867, 2726, 1680, 1606, 1584, 1561, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.98 (d, J = 7.5 Hz) and 1.11 (d, J = 7.5 Hz, both signals together 18 H), 1.21−1.40 (m, 3 H), 4.52 and 4.59 (two s, 2 H), 4.95 and 5.02 (two s, 2 H), 7.20−7.34 (m, 5 H), 7.44−7.48 (m, 1 H), 7.73 (d, J = 7.5 Hz) and 7.78 (d, J = 7.5 Hz, both signals together 1 H), 8.70 (t, J = 6.0 Hz, 1 H), 10.11 and 10.14 (two s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.0 (d), 12.1 (d), 17.7 (q), 17.9 (q), 46.6 (t), 47.5 (t), 51.5 (t), 52.0 (t), 126.91 (d), 126.95 (d), 127.3 (d), 127.5 (d), 127.7 (d), 128.0 (d), 128.6 (d), 128.7 (d), 134.7 (d), 135.6 (d), 136.2 (s), 136.7 (s), 137.19 (s), 137.23 (s), 148.2 (d), 148.3 (d), 149.1 (s), 149.4 (s), 155.5 (s), 155.6 (s), 195.5 (d), 195.6 (d); exact mass (electrospray) m/z calcd for $C_{24}H_{35}N_2O_3Si$ (M + H) 427.2411, found 427.2410.

Tris(propan-2-yl)silyl *N*-Benzyl-*N*-({2-[(*R*)-hydroxy[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl]pyridin-3-yl}methyl)carbamate (25g). BuLi (2.5 M in hexane, 0.21 mL, 0.525 mmol) was added

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dropwise to a stirred and cooled (−20 °C) solution of PhSeSePh (167.2 mg, 0.525 mmol) in THF (0.99 mL). After 10 min, a portion of the freshly prepared PhSeLi solution (0.4 mL) was added dropwise by syringe to a stirred and cooled (−42 °C) solution of **16** (40.5 mg, 0.17 mmol) and **25** (108.8 mg, 0.255 mmol) in THF (1.7 mL). Stirring was continued for 9 h at −42 °C (dry ice/MeCN). The mixture was quenched with saturated aqueous NH_4Cl (3 mL) and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.4 × 15 cm), using 3:10 EtOAc/hexanes, gave **25g** (70.0 mg, 62%) as a colorless oil: FTIR ($CHCl_3$, cast) 3412, 3089, 3064, 3031, 2949, 2928, 2868, 1770, 1680, 1606, 1579, 1496, 1465 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.75−1.44 (m, 34 H), 1.67 (t, J = 12.5 Hz, 2 H), 2.02−2.12 (m, 2 H), 3.60 (dt, J = 4.0, 10.5 Hz, 1 H), 4.38−4.65 (m, 4 H), 4.72−4.92 (m, 1 H), 5.49−5.66 (m, 1 H), 5.94 (s, 1 H), 6.80 and 6.89 (two s, 1 H), 7.21−7.37 (m, 6 H), 7.54−7.59 (m, 1 H), 8.49 (d, J = 4.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.0 (d), 12.1 (d), 15.78 (q), 15.83 (q), 17.9 (q), 20.9 (q), 22.2 (q), 23.1 (t), 23.2 (t), 25.3 (d), 31.5 (d), 34.2 (t), 40.6 (t), 45.6 (t), 46.2 (t), 47.7 (d), 50.7 (t), 51.1 (t), 64.3 (d), 64.9 (d), 79.0 (d), 79.4 (d), 99.19 (d), 99.24 (d), 123.4 (d), 127.2 (d), 127.3 (d), 127.7 (d), 128.1 (d), 128.2 (d), 128.75 (d), 128.78 (d), 130.8 (s), 130.9 (s), 135.1 (d), 136.5 (d), 137.0 (s), 137.2 (s), 139.0 (s), 139.2 (s), 145.1 (d), 145.3 (d), 147.2 (d), 147.4 (d), 154.7 (s), 155.3 (s), 155.5 (s), 155.6 (s), 169.5 (s); exact mass (electrospray) m/z calcd for $C_{38}H_{57}N_2O_6Si$ (M + H) 665.3980, found 665.3977.

(*R*)-(3-{[Benzyl({[tris(propan-2-yl)silyl]oxy}carbonyl)amino]-methyl}pyridin-2-yl)[(5*R*)-5-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}-2-oxo-2,5-dihydrofuran-3-yl]methyl Acetate (25h). DMAP (4.0 mg, 0.032 mmol) was added to a stirred solution of **25g** (65.8 mg, 0.099 mmol) in CH_2Cl_2 (1.5 mL). The mixture was then cooled to 0 °C, and AcCl (0.032 mL, 0.44 mmol) and pyridine (0.06 mL, 0.74 mmol) were added sequentially. The ice bath was left in place but not recharged, and stirring was continued for 40 min. The mixture was quenched with hydrochloric acid (1 M, 1 mL) and water (3 mL), and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 3:10 EtOAc/hexanes, gave **25h** (57.0 mg, 81%) as a colorless oil: FTIR ($CHCl_3$, cast) 3064, 3032, 2949, 2868, 1771, 1749, 1681, 1576, 1496, 1466 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.73−1.40 (m, 33 H), 1.57−1.68 (m, 2 H), 2.04−2.10 (m, 5 H), 2.16−2.17 (m, 2 H), 3.61 (dt, J = 4.5, 10.5 Hz, 1 H), 4.45−4.55 (m, 2 H), 4.72−4.86 (m, 2 H), 6.02 (d, J = 5.0 Hz, 1 H), 6.54 and 6.65 (two s, 1 H), 7.00 (d, J = 14.5 Hz, 1 H), 7.21−7.34 (m, 6 H), 7.52 (d, J = 8.0 Hz) and 7.56 (d, J = 8.0 Hz, both signals together 1 H), 8.49 (d, J = 5.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.0 (d), 12.1 (d), 15.9 (q), 17.8 (q), 17.9 (q), 20.6 (q), 20.7 (q), 20.9 (q), 22.2 (q), 23.2 (t), 25.26 (d), 25.29 (d), 31.5 (d), 34.2 (t), 40.60 (t), 40.64 (t), 45.8 (t), 46.6 (t), 47.7 (d), 50.7 (t), 50.8 (t), 66.0 (d), 66.8 (d), 78.9 (d), 79.1 (d), 99.45 (d), 99.51 (d), 123.7 (d), 123.8 (d), 127.46 (d), 127.54 (d), 127.6 (d), 128.4 (d), 128.66 (d), 128.70 (d), 132.4 (s), 134.3 (d), 135.3 (s), 135.5 (s), 135.8 (d), 137.3 (s), 137.4 (s), 146.2 (d), 146.3 (d), 148.2 (d), 148.3 (d), 152.1 (s), 152.7 (s), 155.57 (s), 155.63 (s), 168.87 (s), 168.88 (s), 169.46 (s), 169.53 (s); exact mass (electrospray) m/z calcd for $C_{40}H_{58}N_2NaO_7Si$ (M + Na) 729.3905, found 729.3897.

(6*R*,7*R*)-8-Benzyl-6-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)-cyclohexyl]oxy}-5-oxa-8,14-diazatricyclo[8.4.0.0^{3,7}]tetradeca-1(14),2,10,12-tetraen-4-one (25i). Bu_3NF (1.0 M in THF, 0.058 mL, 0.058 mmol) was added to a stirred and cooled (0 °C) solution of **25h** (41.2 mg, 0.058 mmol) in THF (1 mL). After 10 min, the mixture was quenched with saturated aqueous NH_4Cl (2 mL) and diluted with EtOAc (4 mL). The organic phase was washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.2 × 14 cm), using 2:5 EtOAc/hexanes, gave **25i** (25.1 mg, 96%) as a light yellow solid: $[\alpha]^{20}_D$ 125.75 (c 1.22, $CHCl_3$); FTIR ($CHCl_3$, cast) 3029, 2954, 2925, 2869, 1764, 1670, 1604, 1566, 1496, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.78−1.05 (m, 12 H), 1.13−1.22 (m, 1 H), 1.34−1.43 (m, 1 H), 1.60−1.68 (m, 2 H), 2.06−2.13 (m, 2 H), 3.53 (t, J = 3.5 Hz, 1 H), 3.57−3.77 (m, 5 H), 5.68 (d, J = 3.5 Hz, 1 H), 7.21 (dd, J = 5.0, 8.0 Hz, 1 H), 7.29−7.44 (m, 6 H), 7.85 (d, J = 3.0 Hz, 1 H), 8.67 (dd, J = 1.5, 4.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.7 (q), 20.9 (q), 22.2 (q), 23.1 (t), 25.3 (d), 31.3 (d), 34.3 (t), 39.8 (t), 47.7 (d), 52.3 (t), 56.9 (t), 68.2 (d), 77.9 (d), 103.7 (d), 122.8 (d), 127.7 (d), 128.7 (d), 128.8 (d), 133.3 (s), 135.7 (s), 138.1 (d), 138.2 (s), 139.2 (d), 149.2 (d), 155.0 (s), 167.7 (s); exact mass (electrospray) m/z calcd for $C_{28}H_{35}N_2O_3$ (M + H) 447.2642, found 447.2641.

[(7*R*)-6-Benzyl-7-(hydroxymethyl)-5*H*,6*H*,7*H*-pyrido[3,2-*c*]-azepin-8-yl]methanol (25j). DIBAL-H (1.0 M in PhMe, 0.14 mL, 0.14 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **25i** (12.1 mg, 0.027 mmol) in THF (0.6 mL). Stirring at −78 °C was continued for 3 h, the cold bath was left in place but not recharged, and stirring was continued for 4 h. MeOH (0.1 mL) and a saturated aqueous solution of Rochelle's salt (ca. 3 mL) were then added sequentially. Stirring was continued for 1 h, and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (0.6 × 8 cm), using 1:25 MeOH/EtOAc, gave **25j** (2.7 mg, 34%) as an yellow solid: $[\alpha]^{20}_D$ 69.92 (c 1.15, $CHCl_3$); FTIR ($CHCl_3$, cast) 3346, 3062 3028, 2922, 2855, 1650, 1582, 1494, 1444 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.18 (s, 1 H), 3.35 (s, 1 H), 3.46−3.60 (m, 3 H), 3.66 (d, J = 16.0 Hz, 1 H), 3.82 (dd, J = 5.0, 9.5 Hz, 1 H), 3.89−3.94 (m, 1 H), 4.18 (d, J = 15.5 Hz, 1 H), 4.24 (AB q, J = 13.5 Hz, $\Delta\nu_{AB}$ = 19.1 Hz, 2 H), 7.02 (s, 1 H), 7.12 (dd, J = 5.0, 7.5 Hz, 1 H), 7.18 (d, J = 7.5 Hz, 2 H), 7.28−7.35 (m, 4 H), 8.57 (d, J = 5.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 49.6 (t), 57.1 (t), 62.5 (t), 66.0 (d), 67.3 (t), 121.6 (d), 127.6 (d), 128.5 (d), 129.0 (d), 130.5 (d), 133.8 (s), 137.3 (d), 137.9 (s), 145.2 (s), 148.3 (d), 154.1 (s); exact mass (electrospray) m/z calcd for $C_{18}H_{21}N_2O_2$ (M + H) 297.1598, found 297.1597.

■ ASSOCIATED CONTENT

Supporting Information

Flowchart for the preparation of amine **26**; X-ray data (cif) for compounds **epi-18**, **19d**, **19f**, **23i**, and **24k**; and copies of NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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