methyl-2-phenyl-4-pentenol (39): 40 mg (39%): $[\alpha]^{21}_D$ +2.99° (c 1.64, MeOH). A mixture of 41 (20 mg, 0.11 mmol), (–)-MTPA-Cl (1-methoxy-1-(trifluoromethyl)phenylacetyl chloride) (37 mg, 0.15 mmol), CCl_4 (50 μL), and pyridine (20 μL) was stirred at room temperature overnight under argon. The reaction mixture was quenched with water and extracted with ether. Thin-layer chromatography on SiO_2 ($CHCl_3$) gave 2-methyl-2-phenyl-4-pentenyl 1-methoxy-1-(trifluoromethyl)phenylacetate (42): 44 mg (94%); ^1H NMR (100 MHz, $CDCl_3$) δ 1.32 (s, 1.68 H), 1.36 (s, 1.32 H), 2.16–2.18 (m, 2 H), 3.20–3.40 (m, 3 H), 4.29 and 4.30 (d, J = 12 Hz, 1 H), 4.46 and 4.48 (d, J = 12 Hz, 1 H), 4.70–5.06 (m, 2 H), 5.22–5.72 (m, 1 H), 7.26 (s, 5 H), 7.29 (s, 5 H).

Acyclic Control of Stereochemistry via a Reiterative (*E* or *Z*)-1-Propenyllithium-Derived Cuprate Opening of a Chiral Epoxide/Reepoxidation Sequence

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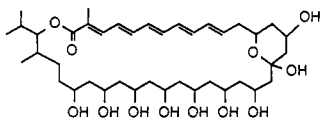
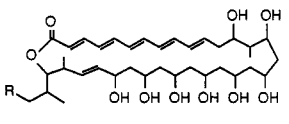
The 1,3-relationship between syn hydroxyl and syn or anti methyl groups can be established in a homochiral fashion by using a regioselective (*Z*)- or (*E*)-propenyllithium-based cuprate opening of a chiral epoxide, followed by stereoselective reepoxidation. The two-step sequence is reiterative.

As part of our program in polyene macrolide synthesis with emphasis on the 36-membered pentaene roflamycoin,[2] we developed a two-pot reiterative protocol[3] for arriving at the key polyol sections in homochiral form.[4] The



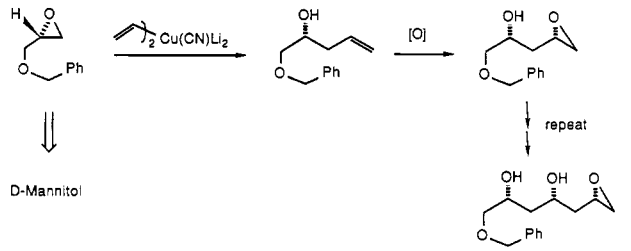
Roflamycoin



Mycoticin A (R = H)
Mycoticin B (R = CH_3)

method relies on a higher order (HO) vinyl cuprate opening of a chiral epoxide to afford a homoallylic alcohol, followed by stereoselective reepoxidation (Scheme I).[3] Although this approach permits construction of polyacetate-derived systems, many macrolides of this type contain one or more propionate portions, the Mycoticins being two such representative examples.[5] Since even the relative stereochemistry of all but two of the polyene macrolides is as yet unknown,[6] a synthetic strategy aimed at establishing vicinal hydroxy–methyl arrays must be sufficiently flexible to respond to either a syn or anti disposition between the two groups. We now report that the conceptually straightforward use of an (*E*)- or (*Z*)-propenyllithium-based HO cuprate, in place of the simple vinyllithium-derived reagent used previously (Scheme I),[3] allows rapid construction of these desired stereochemical relationships.

Scheme I



Results and Discussion

Treatment of readily available,[7] optically pure (*S*)-epoxide 1 with the HO cuprate derived from (*Z*)- or (*E*)-propenyllithium[8] regiospecifically affords homoallylic alcohols 2[9] and 3,[9] respectively (Scheme II). Epoxidation of 2 to 4 (R = H), and 3 to 5 (R = H), using the modified Cardillo route[10] developed earlier[3] (procedure A in Scheme II), proceeds in a one-pot, four-step sequence to give the required syn disposition of the two newly generated chiral centers. More efficient oxirane formation could be achieved by using the Mihelich procedure,[11] which is also easier to carry out and leads to identical products 4 (94%) and 5 (84%). Interestingly, both routes were essentially stereospecific, as judged by capillary GLC analyses[12] of the crude reaction mixtures.

With epoxides 4 and 5 in hand, it was anticipated that their electrophilic cuprate couplings would follow the traditional pathway[13] of reaction at the least hindered, desired position (i.e., next to the methyl group) so as to

(1) A. P. Sloan Foundation Fellow, 1984–1988; Camile and Henry Dreyfus Teacher-Scholar, 1984–1989.

(2) Afzal, M.; Nimer, N. D.; Nazar, M. *Zeit. Allg. Mikrobiol.* **1983**, *23*, 411. Schlegel, R.; Thrum, H.; Zielinski, J.; Borowski, E. *J. Antibiot.* **1981**, *34*, 122. Grigorjev, P.; Schlegel, R.; Thrum, H.; Ermishkin, L. *Biochem. Biophys. Acta* **1985**, *821*, 297.

(3) Lipshutz, B. H.; Kozlowski, J. A. *J. Org. Chem.* **1984**, *49*, 1147.

(4) Lipshutz, B. H.; Kotsuki, H.; Lew, W. *Tetrahedron Lett.* **1986**, *27*, 4825.

(5) Wasserman, H. H.; Van Verth, J. E.; McCaustland, D. J.; Borowitz, I. J.; Kamber, B. *J. Am. Chem. Soc.* **1967**, *89*, 1535.

(6) *Antibiotics, Chemotherapeutics, and Antibacterial Agents for Disease Control*; Grayson, M., Ed.; Wiley: New York, 1982; p 275–301. See also, Pawlak, J.; Nakanishi, K.; Iwashita, T.; Borowski, E. *J. Org. Chem.* **1987**, *52*, 2896. However, for some recent developments that suggest that the all-syn nature of the polyol portion of Amphotericin B may be the exception rather than the rule, see: Pawlak, J.; Nakanishi, K.; Iwashita, T.; Borowski, E. *J. Org. Chem.* **1987**, *52*, 2896. Schrieber, S. L.; Goulet, M. T.; Schulte, G. *J. Am. Chem. Soc.* **1987**, *109*, 4718.

(7) Takano, S.; Goto, E.; Hirama, M.; Ogasawara, K. *Heterocycles* **1981**, *16*, 381.

(8) Whitesides, G. M.; Casey, C. P.; Krieger, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 1379.

(9) Mosher esters of both 2 and 3 were prepared and served to confirm the optical purity (>98%) of each; cf. Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(10) Cardillo, G.; Bongini, A.; Orena, M.; Porzi, G.; Sandri, S. *J. Org. Chem.* **1982**, *47*, 4626.

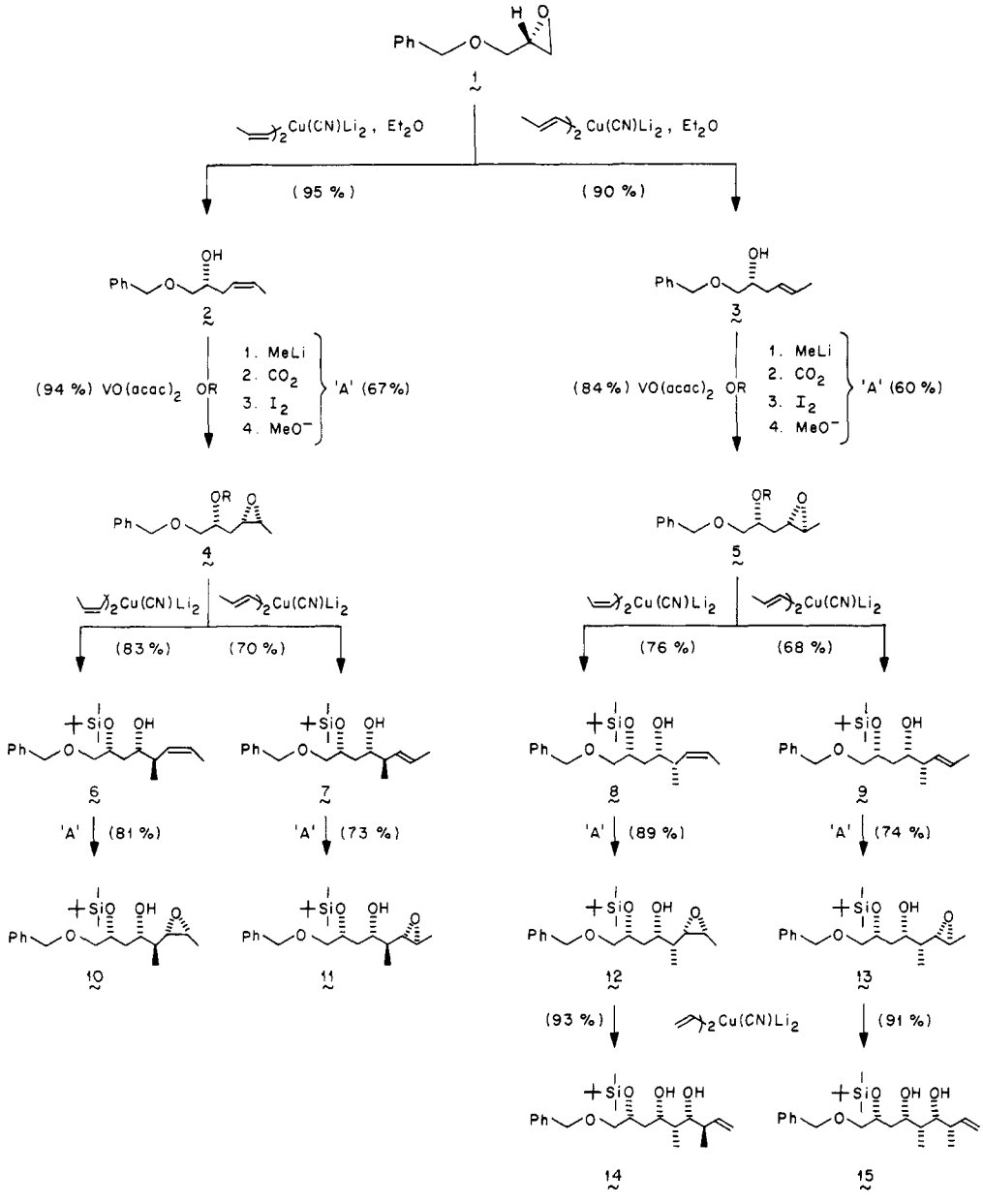
(11) Mihelich, E. D.; Daniels, K.; Eickhoff, D. *J. Am. Chem. Soc.* **1981**, *103*, 7690. Use of cumene hydroxperoxide, in place of *tert*-butyl hydroperoxide gives identical results.

(12) Analyses were performed on a 60-m J&W DB-S capillary column between 200 and 300 °C.

(13) Posner, G. H. *Org. React. (N.Y.)* **1975**, *22*, 253.

0022-3263/88/1953-4495$01.50/0

Scheme II



form the corresponding 1,3-*syn*-diol. The configuration of the carbon-bearing methyl was assured by virtue of the inversion process well-known to occur with cuprate-mediated openings of epoxides.[14] Hence, from **4** (R = TBDMS), products **6** and **7** may be obtained, depending again upon the choice of (*Z*)- or (*E*)-propenyllithium-derived cuprates. Similarly, epoxide **5** (R = TBDMS) leads to **8** or **9**. Although each of these four cuprate alkylations is an extremely efficient process, variable ratios of regioisomers are obtained in all cases. Hence, the following results have been observed: for **4** → **6**, 83% 1,3-diol, 16% 1,4-diol (99% total yield); for **4** → **7**, 70% 1,3-diol, 20% 1,4-diol (90% total yield); for **5** → **8**, 76% 1,3-diol, 21% 1,4-diol (97% total yield); and for **5** → **9**, 68% 1,3-diol, 26% 1,4-diol (94% total yield). The desired 1,3-diols could, in each case, be readily separated via flash chromatography on SiO_2 in the usual fashion (see the Experimental Section).

The choice of hydroxyl protecting group for epoxy alcohols **4** and **5** is apparently quite limited. Attempted cuprate displacements with R equal to SEM, Ph_2MeSi, or Li^+ (i.e., the lithium alkoxide) were unsuccessful, starting material being cleanly recovered.

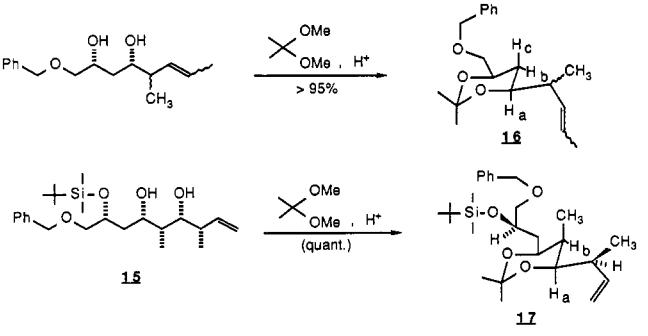
Each of the newly prepared homoallylic alcohols **6** → **9** could then, in principle, be re-epoxidized to **10**–**13**, respectively. Unfortunately, the $VO(acac)_2$ protocol,[11] which worked flawlessly with both **2** and **3**, was nonselective and quite inefficient with each new substrate (**6**–**9**). It was very gratifying to find, therefore, that the iodocyclization route[3] (procedure A above) works extremely well for this series, resulting in products **10**–**13**. Again, the stereoselectivity of *syn*-epoxide formation appears to be excellent; virtually none of the anti isomers could be detected. Final couplings were carried out on **12** and **13** with use of excess (ca. 10 equiv) $(CH_2{=}CH)_2Cu(CN)Li_2$ to establish the anti (cf. **14**) and syn (cf. **15**) relationships between the 1,3-disposed methyl groups. The regioselectivity of cuprate attack observed was significantly enhanced in these latter two cases,[15] not surprising in light of recent reports by Katsuki.[16] The presence of a syn (or anti) methyl group on

(14) Lipshutz, B. H.; Kozlowski, J. A.; Wilhelm, R. S. *J. Am. Chem. Soc.* **1982**, *104*, 2305.

(15) None of the corresponding 1,4-diol was detected by TLC or VPC analyses of the crude reaction mixture.

the backbone in, e.g., **12** and **13**, leads presumably via additional steric hindrance to a more selective cuprate attack (as opposed to the cases of **4** and **5**) such that only the desired 1,3-relationships are realized.[15] Interestingly, it was essential to use **12** and **13** as their free alcohols (compare with reactions of **4** and **5**, vide supra). Both the TMS and TBDMS ethers, as well as the acetonides formed from the desilylated materials, lead to no reaction with each educt. Attempts to couple a variety of other nucleophiles, such as vinyllithium, vinyl Grignard, diethylvinylaluminum (with and without $BF_3 \cdot Et_2O$), and lithiodithiane in the presence of DMPU did not give synthetically useful results.

The stereochemical assignments follow from high-field (500-MHz) ^1H NMR analyses of the four acetonides formed from desilylated **6–9** (see **16**). The syn orientation of the hydroxyl groups in each 1,3-diol was clear from the determination of coupling constants observed (J_{ab} = 1.6 Hz, J_{ac} = 10.5 Hz), which requires in each case that the configuration be as shown in **16**. Likewise, conversion of **15** to its acetonide **17** also supplied via ^1H NMR analysis confirming evidence for (in this case) an axial location of the methyl moiety (J_{ab} = 2.5 Hz) and hence, the all-syn arrangement as indicated.



Conclusions

In summary, control of acyclic stereochemistry has been demonstrated by employing two one-pot reactions in a reiterative sense. The 1,3-*syn*-diol relationship derives from a virtually stereospecific epoxidation of a homoallylic alcohol, while the 1,3-dimethyl configuration is established by choice of an (*E*)- or (*Z*)-propenyllithium-derived cuprate opening of the epoxy alcohol so formed. This allows rapid and efficient construction of polypropionate relationships, so long as *syn*-1,3-polyols are of interest.

Experimental Section

General Methods. Proton NMR spectra were measured in $CDCl_3$ at 300 or 500 MHz. Carbon NMR spectra were determined in $CDCl_3$ at 75 or 125 MHz. GC analyses were conducted on a 60-m J&W DB-5 capillary column. Optical rotations were determined on a Rudolph Research Autopol III polarimeter.

CuCN was purchased from Mallinckrodt. All solvents were distilled from sodium/benzophenone ketyl. (*Z*)-Propenyllithium and (*E*)-propenyllithium were prepared from *cis*-bromopropene and *trans*-chloropropene, respectively, by the procedure of Whitesides.[8] Vinyllithium was purchased from Organometallics. The alkenyllithiums were titrated according to the method of Watson and Eastham.[17] (*S*)-(−)-Benzyl-2,3-epoxypropyl ether was prepared by the method of Anisuzzaman.[18] Flash chromatographic separations were performed with 230–400-mesh silica gel (Fisher Scientific Co.). The purity of all characterized products was found to be greater than 95% by TLC and GC analysis.

(2*R*)-(*Z*)-1-(Phenylmethoxy)-4-hexen-2-ol (2). An oven-dried flask containing cuprous cyanide (273 mg, 3.05 mmol), previously dried in an Abderholden apparatus, was purged with argon four times. THF (4 mL) was added via syringe, the resulting slurry was cooled to −78 °C (acetone/CO_2), and (*Z*)-propenyllithium (7 mL, 6.10 mmol, 0.87 M in Et_2O) was added. The mixture was then warmed by removing the ice bath until the CuCN dissolved, forming a homogeneous brown solution and then recooled to −78 °C. (*S*)-Benzyl-2,3-epoxypropyl ether (1) (454 mg, 2.77 mmol) was then added in 2 mL of Et_2O giving an instantaneous reaction (by TLC). The mixture was warmed above 0 °C and quenched with 10% concentrated NH_4OH in saturated NH_4Cl. Ethereal extraction and column chromatography (10:1 petroleum ether/acetone) gave 568 mg (99%) of **2** as a clear oil: IR 3580, 3026, 2910, 2862, 2246, 1454, 1364, 1206, 1103, 910 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 5.6 (m, 1 H), 5.4 (m, 1 H), 4.5 (s, 2 H), 3.9 (m, 1 H), 3.5 (dd, J = 3.3, J = 9.5, 1 H), 3.4 (dd, J = 7.2, J = 9.5), 2.4 (s, 1 H), 2.3 (dt, J = 7.2, J = 1, 2 H), 1.6 (dd, J = 6.6, J = 1, 3 H); ^{13}C NMR δ 137.7, 128.0, 127.3, 126.0, 125.9, 125.5, 73.7, 72.9, 69.9, 30.7, 12.6; MS, *m/e* (relative intensity), 206 (M^+, 20), 188 (18), 170 (10), 91 (100), 65 (10), 55 (10); $[\alpha]^{23}_D$ +2.11° (*c* 4.7, Et_2O).

(2*R*)-(*E*)-1-(Phenylmethoxy)-4-hexen-2-ol (3). Epoxide (1) was added in 2 mL of Et_2O to the cuprate prepared from CuCN (706 mg, 7.9 mmol) and (*E*)-propenyllithium (12 mL, 15.8 mmol, 1.31 M in Et_2O) as described above for (**2**) at −78 °C. Warming above 0 °C and quenching with NH_4OH in saturated NH_4Cl followed by ethereal extraction and chromatography (10:1 petroleum ether/acetone) gave 1.23 g (90%) of **3** as a clear oil: IR 3440, 3040, 2920, 1720, 1450, 1270, 1200, 1100, 970, 750, 690 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 5.5 (m, 2 H), 4.5 (s, 2 H), 3.8 (m, 1 H), 3.5 (dd, J = 9.6, J = 3.3, 1 H), 3.4 (dd, J = 7.2, J = 9.6, 1 H), 2.3 (s, 1 H), 2.2 (t, J = 7.2, 2 H), 1.7 (dd, J = 5.7, J = 1.0); ^{13}C NMR δ 137.9, 128.3, 128.2, 127.6, 126.4, 73.9, 73.3, 70.0, 36.7, 18.0; MS, *m/e* (relative intensity), 206 (M^+, 10), 188 (10), 151 (70), 146 (30), 144 (25), 131 (18), 121 (27), 91 (100), 65 (10), 55 (10); $[\alpha]^{23}_D$ 1.52° (*c* 4.7, Et_2O); HRCIMS calcd for $C_{13}H_{19}O_2$ (M + 1) 207.1385, found 207.1402.

(2*R*,4*S*,5*R*)-4,5-Epoxy-1-(phenylmethoxy)hexan-2-ol (4, R = H) via the Modified Cardillo Procedure. A 10-mL two-neck round-bottom flask with a stirbar was fitted with a rubber septum and a glass two-way valve connected to a vacuum and an argon source and then flame-dried and flushed with argon. Alcohol **2** (112 mg, 0.54 mmol) in 2 mL of THF was added and cooled to −78 °C. MeLi (1.3 mL, 1.15 mmol, 0.85 M in THF) was added, and the solution was stirred for 0.5 h. Dry CO_2 was then bubbled through the solution for 1 h, followed by the addition of azeotropically dried I_2 (0.544 g, 2.18 mmol) in 2 mL of THF and then stirred for 1.5 h, with continued bubbling of CO_2. The THF was then removed in vacuo, requiring warming to room temperature, and replaced with 5 mL of freshly distilled methanol. The septum was removed and ~0.3 g K_2CO_3 was added after the solution was recooled to −78 °C, and it was then stirred for 2 h. The solution was then warmed to 0 °C, and another ~0.3 g K_2CO_3 was added and allowed to stir for 4 h. The mixture was poured into 10 mL of H_2O and extracted with CH_2Cl_2 (3 × 30 mL) and washed with saturated sodium thiosulfate solution (2 × 20 mL) followed by saturated NaCl and finally dried with Na_2SO_4. Column chromatography (1:1 petroleum ether/Et_2O) gave **4** (81 mg, 67%) as a clear oil.

Product 4 (R = H) via the Mihelich Procedure. Compound **2** (651 mg, 3.2 mmol) was added to a dry 10-mL round-bottom flask equipped with a stribar and containing 4 mL of dry CH_2Cl_2. $VO(AcAc)_2$ (13 mg, catalytic) was added followed by the addition of *tert*-butyl hydroperoxide (2.0 mL, 5.4 mmol, 2.7 M in toluene), and the solution was stirred overnight. Filtration through a silica plug and solvent removal followed by column chromatography (1:1 petroleum ether/Et_2O) gave **4** (670 mg, 94%) as a clear oil: IR 3577, 2924, 2867, 2248, 1497, 1454, 1393, 1365, 1206, 1095, 1029,

(16) Hanamoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 6195; **1987**, *28*, 6191. For some recent related work on epoxidations and/or cuprate openings, see: Kurth, M. J.; Abreo, M. A. *Ibid.* **1987**, *28*, 5631. Kramer, T.; Hoppe, D. *Ibid.* **1987**, *28*, 5149. Hull, C.; Mortlock, S. V.; Thomas, E. J. *Ibid.* **1987**, *28*, 5343. Hoppe, D.; Luzzman, J.; Jones, P. G.; Schmidt, D.; Sheldrick, G. M. *Ibid.* **1986**, *27*, 3591. Mulzer, J.; Autenrieth-Ansorge, L.; Kirstein, H.; Matsuoka, T.; Munch, W. *J. Org. Chem.* **1987**, *52*, 3784.

(17) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

(18) Anisuzzaman, A. K. M.; Owen, L. N. *J. Chem. Soc. C* **1967**, 1201.

843, 806, 620 cm^{-1}; ^1H NMR 7.3 (s, 5 H), 4.6 (s, 2 H), 4.1 (s, 1 H), 3.5 (m, 2 H), 3.1 (m, 2 H), 2.7 (s, 1 H), 1.8 (dt, J = 14.4, J = 4.8, 1 H), 1.7 (q, J = 7.2, 1 H), 1.3 (d, J = 8, 2 H); ^{13}C NMR δ 137.5, 127.8, 127.1, 73.6, 72.7, 68.2, 53.7, 51.4, 30.9, 12.7; MS, m/e (relative intensity), 222 (M^+, 10), 204 (18), 203 (20), 149 (8), 107 (13), 101 (10), 92 (20), 91 (100), 83 (10), 65 (13), 57 (20), 55 (10); $[\alpha]^{23}_D$ +2.31° (c 5.4, Et_2O); HRCIMS calcd for $C_{13}H_{17}O_3$ (M − 1) 221.1118, found 221.1148.

(2*R*,4*S*,5*S*)-4,5-Epoxy-1-(phenylmethoxy)hexan-2-ol (5, R = H) via the Modified Cardillo Route. Compound **3** (72 mg, 0.35 mmol) was treated with MeLi (0.5 mL, 6 mmol, 1.2 M in Et_2O) followed by CO_2 addition as described above for the preparation of **4**. Iodocyclization was effected with I_2 (200 mg, 0.8 mmol), and addition of K_2CO_3 with stirring as described above, followed by quench, ethereal workup, and chromatography (1:1 Et_2O/petroleum ether) gave **5** (47 mg, 60%), along with 16 mg of starting material recovered.

Product 5 (R = H) via the Mihelich Procedure. To a solution of compound **3** (413 mg, 2.0 mmol) in 4 mL of dry CH_2Cl_2 was added $VO(acac)_2$ (10 mg, catalytic) followed by cumene hydroperoxide (0.44 mL, 2.4 mmol), and the mixture was allowed to stir for 10 h. Filtration through a silica plug, solvent removal, and column chromatography (1:1 Et_2O/petroleum ether) gave **5** (373 mg, 84%) as a clear oil: IR 3450, 2920, 2860, 1448, 1380, 1350, 1200, 1090, 1025, 940, 850, 800, 740, 690 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 4.5 (s, 2 H), 4.0 (m, 1 H), 3.5 (m, 2 H), 2.8 (m, 3 H), 1.8 (dt, J = 5, J = 14, 1 H), 1.6 (q, J = 6.6, 1 H), 1.3 (d, J = 5, 3 H); ^{13}C NMR 137.7, 128.3, 127.6, 79.8, 79.2, 68.5, 56.7, 54.1, 35.5, 17.4; MS, m/e (relative intensity) 222 (5, M^+), 108 (12), 107 (30), 101 (80), 92 (15), 91 (100), 83 (10), 79 (8), 65 (15), 57 (98), 55 (20), 45 (8), 43 (18); $[\alpha]^{23}_D$ −10.21° (c 4.8, Et_2O); HRCIMS calcd for $C_{13}H_{18}O_3$ 222.1256, found 222.1290.

(2*R*,4*S*,5*R*)-4,5-Epoxy-1-(phenylmethoxy)hexan-2-ol (1,1-Dimethylethyl)dimethylsilyl Ether (4, R = TBDMS). Compound **4**, R = H, (267 mg, 1.2 mmol) was combined with 2 mL of dry DMF, TBDMSCl (236 mg, 1.56 mmol), and dry Et_3N (0.33 mL, 2.4 mmol). A catalytic amount of DMAP (10 mg) was added, and the reaction mixture was stirred overnight. Ethereal extraction and column chromatography (10:1 petroleum ether/acetone) gave **4**, R = TBDMS, (385 mg, 94%) as a clear oil: IR 2920, 2860, 1740, 1450, 1360, 1250, 1210, 1100, 1005, 830, 775, 695, 660 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 4.5 (s, 2 H), 4.0 (p, J = 5.7, 1 H), 3.5 (m, 2 H), 3.1 (dt, J = 5.4, 2 H), 1.8 (m, 2 H), 1.3 (d, J = 5.4, 3 H), 0.9 (s, 9 H), 0.1 (s, 6 H); MS, m/e (relative intensity) 230 (5), 221 (10), 205 (15), 203 (13), 201 (10), 107 (13), 97 (5), 93 (13), 92 (15), 91 (100), 79 (10), 69 (8); $[\alpha]^{23}_D$ +3.93° (c 5.5, Et_2O); HRCIMS calcd for $C_{19}H_{33}O_3Si$ (M + 1) 337.2199, found 337.2171.

(2*R*,4*S*,5*S*)-4,5-Epoxy-1-(phenylmethoxy)hexan-2-ol (1,1-Dimethylethyl)dimethylsilyl Ether (5, R = TBDMS). Compound **5**, R = H, (346 mg, 1.56 mmol) was combined with 2 mL of dry DMF, TBDMSCl (306 mg, 2.03 mmol), and dry Et_3N (0.44 mL, 3.12 mmol). A catalytic amount of DMAP (10 mg) was added, and the reaction mixture was stirred overnight. Ethereal extraction and column chromatography (10:1 petroleum ether/acetone) gave **5**, R = TBDMS, (490 mg, 92%) as a clear oil: IR 2920, 2860, 1450, 1385, 1360, 1250, 1205, 1110, 1030, 1005, 940, 830, 770, 730, 690, 660 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 4.5 (s, 2 H), 4.0 (p, J = 5.4, 1 H), 3.5 (m, 2 H), 3.1 (dt, J = 5.4, J = 18, 2 H), 1.8 (m, 2 H), 1.3 (d, J = 5.4, 3 H), 0.9 (s, 9 H), 0.1 (s, 6 H); MS, m/e (relative intensity), 230 (5), 171 (13), 159 (8), 145 (7), 131 (5), 117 (13), 107 (10), 93 (17), 92 (13), 91 (100), 83 (8), 75 (10), 69 (13); $[\alpha]^{23}_D$ −2.00° (c 7.1, Et_2O); HRCIMS calcd for $C_{19}H_{33}O_3Si$ (M + 1) 337.2199, found 337.2176.

(2*R*,4*S*,5*R*)-(6*Z*)-2-[(1,1-Dimethylethyl)dimethylsilyl]oxy]-5-methyl-1-(phenylmethoxy)-6-octen-4-ol (6). Compound **4**, R = TBDMS, (100 mg, 0.28 mmol) was azeotropically dried with toluene (3 × 1 mL) in a 10-mL two-neck round-bottom flask equipped with stirbar and fitted with a septum. Et_2O (2 mL) was then added under Ar, and the solution was added to 3 equiv of the (*Z*)-propenyl cuprate prepared as described above for the preparation of **2** with CuCN (76 mg, 0.85 mmol) and (*Z*)-propenyllithium (2.0 mL, 1.70 mmol, 0.87 M in Et_2O). Warming the mixture to 0 °C and stirring for 0.5 h followed by quench, ethereal workup, and column chromatography (20:1 petroleum ether/acetone) gave **6** (89 mg, 83%): IR 3500, 3050, 2920, 2820, 1450, 1360, 1250, 1200, 1090, 1030, 1005, 960, 830, 810, 780, 730, 695 cm^{-1}; ^1H NMR δ 7.2 (s, 5 H), 5.5 (m, 1 H), 5.2 (m, 1 H), 4.5 (s, 2 H), 4.0 (m, 1 H), 3.6 (m, 1 H), 3.4 (m, 2 H), 2.8 (d, J = 1.5, 1 H), 2.5 (m, 1 H), 1.7 (m, 1 H), 1.6 (dd, J = 3, J = 7.5, 3 H), 1.4 (m, 1 H), 0.9 (d, J = 7.0, 3 H), 0.8 (s, 9 H), 0.1 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR δ 138.1, 132.4, 128.2, 127.6, 124.7, 74.6, 73.3, 73.2, 71.9, 38.7, 37.4, 25.8, 17.9, 16.6, 13.1, −4.3, −4.8; MS, m/e (relative intensity) 379 (M + 1, 10), 361 (20), 321 (15), 269 (50), 257 (25), 255 (20), 213 (8), 201 (20), 159 (10), 119 (10), 117 (10), 91 (100), 69 (10); $[\alpha]^{23}_D$ −15.22° (c 5.4, Et_2O); HRCIMS calcd for $C_{22}H_{39}O_3Si$ (M + 1) 379.2668, found 379.2655.

(2*R*,4*S*,5*R*)-(6*E*)-2-[(1,1-Dimethylethyl)dimethylsilyl]oxy]-5-methyl-1-(phenylmethoxy)-6-octen-4-ol (7). Compound **4**, R = TBDMS, (77 mg, 0.23 mmol) was azeotropically dried with toluene (3 × 1 mL) in a 10-mL two-neck round-bottom flask equipped with a stirbar and fitted with a septum. Et_2O (2 mL) was then added under Ar, and the solution was transferred into 3 equiv of the (*E*)-propenyl cuprate prepared as described above for the preparation of **2** with CuCN (61 mg, 0.68 mmol) and (*E*)-propenyllithium (1.47 mL, 1.35 mmol, 0.92 M in Et_2O). Warming the mixture to 0 °C and stirring for 0.5 h followed by quench, ethereal workup, and column chromatography (20:1 petroleum ether/acetone) gave **7** (61 mg, 70%); IR 3480, 3050, 2930, 2860, 1700, 1450, 1360, 1320, 1250, 1200, 1090, 1025, 1005, 930, 830, 775, 730, 690 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 5.5 (m, 2 H), 4.5 (s, 2 H), 4.1 (dt, J = 5.1, J = 6.9, 1 H), 3.6 (m, 1 H), 3.4 (m, 2 H), 2.8 (s, 1 H), 2.2 (m, 1 H), 1.8 (m, 1 H), 1.7 (d, J = 5.1, 3 H), 1.6 (m, 1 H), 1.0 (d, J = 6.9, 3 H), 0.9 (s, 9 H), 0.11 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR δ 138.1, 133.0, 128.3, 127.6, 125.9, 74.9, 73.3, 72.9, 71.3, 42.3, 38.5, 25.8, 18.1, 16.0, −4.3, −4.8; MS, m/e (relative intensity) 269 (65), 213 (8), 201 (17), 159 (8), 121 (10), 117 (23), 107 (10), 95 (10), 93 (10), 92 (12), 91 (100), 75 (90), 73 (22), 69 (17), 57 (10), 45 (10); $[\alpha]^{23}_D$ −3.10° (c 3.9, Et_2O); HCRIMS calcd for $C_{22}H_{39}O_3Si$ (M + 1) 379.2668, found 379.2687.

(2*R*,4*S*,5*S*)-(6*Z*)-2-[(1,1-Dimethylethyl)dimethylsilyl]oxy]-5-methyl-1-(phenylmethoxy)-6-octen-4-ol (8). Compound **5**, R = TBDMS, (91 mg, 0.26 mmol) was azeotropically dried with toluene (3 × 1 mL) in a 10-mL two-neck round-bottom flask equipped with stirbar and fitted with a septum. Et_2O (2 mL) was then added under Ar, and the solution was transferred into 3 equiv of the (*Z*)-propenyl cuprate, prepared as described above for formation of **2** with CuCN (70 mg, 0.78 mmol) and (*Z*)-propenyllithium (1.80 mL, 1.56 mmol, 0.87 M in Et_2O). Warming the mixture to 0 °C and stirring for 0.5 h followed by quench, ethereal workup, and column chromatography (20:1 petroleum ether/acetone) gave **8** (76 mg, 76%) as a clear oil. IR 3490, 3040, 2920, 2875, 1450, 1370, 1250, 1200, 1090, 1030, 1005, 940, 830, 775, 730, 695 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 5.4 (m, 1 H), 5.2 (m, 1 H), 4.5 (s, 2 H), 4.1 (m, 1 H), 3.6 (m, 1 H), 3.5 (m, 2 H), 2.5 (m, 1 H), 2.2 (m, 1 H), 1.8 (m, 1 H), 1.7 (dd, J = 24, J = 1.8, 3 H), 1.6 (m, 1 H), 0.08 (s, 3 H); ^{13}C NMR δ 137.9, 133.3, 128.2, 127.6, 124.1, 74.7, 73.9, 73.3, 71.7, 39.1, 38.1, 25.8, 16.5, −4.3, −4.8; MS, m/e (relative intensity) 201 (10), 159 (8), 117 (12), 92 (10), 91 (100), 75 (10), 73 (12), 59 (8); $[\alpha]^{23}_D$ +5.56° (c 4.3, Et_2O); HRCIMS calcd for $C_{22}H_{39}O_3Si$ (M + 1) 379.2668, found 379.2662.

(2*R*,4*S*,5*S*)-(6*E*)-2-[(1,1-Dimethylethyl)dimethylsilyl]oxy]-5-methyl-1-(phenylmethoxy)-6-octen-4-ol (9). Compound **5**, R = TBDMS, (89 mg, 0.261 mmol) was azeotropically dried with toluene (3 × 1 mL in a 10-mL two-neck round-bottom flask equipped with a stirbar and fitted with a septum. Et_2O (2 mL) was added under Ar, and the solution was transferred into 3 equiv of the (*E*)-propenyl cuprate, prepared as described above for the formation of compound **2** with CuCN (70 mg, 0.78 μmol) and (*E*)-propenyllithium (1.70 mL, 1.6 mmol, 0.92 M in Et_2O). Warming the mixture to 0 °C and stirring for 0.5 h followed by quench, ethereal workup, and column chromatography (20:1 petroleum ether/acetone) gave **9** (68 mg, 68%) as a clear oil: IR 3500, 3020, 2930, 2860, 1450, 1410, 1360, 1250, 1205, 1090, 1030, 1005, 970, 830, 775, 730, 695 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 5.5 (m, 2 H), 4.5 (s, 2 H), 4.0 (m, 1 H), 3.6 (m, 1 H), 3.4 (m, 2 H), 2.9 (m, 1 H), 2.2 (m, 1 H), 1.9 (m, 1 H), 1.7 (dd, J = 5.4, J = 1.0, 3 H), 1.5 (m, 1 H), 1.0 (d, J = 6.3, 3 H), 0.9 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR δ 138.0, 133.6, 128.2, 127.5, 125.1, 74.6, 73.2, 71.4, 42.8, 38.6, 37.7, 25.7, 18.0, 15.7, −4.3, −4.8; MS, m/e (relative intensity) 213 (8), 201 (25), 159 (7), 121 (12), 117 (25), 115 (12), 107 (15), 95 (13), 93 (17), 92 (18), 91 (100), 79 (16), 75 (87), 73 (22), 69 (25), 57 (13), 45 (12), 44 (10); $[\alpha]^{23}_D$ −2.49° (c 8.7, Et_2O);

HCRIMS calcd for $C_{22}H_{39}O_3Si$ (M + 1) 379.2668, found 379.2687.

(2*R*,4*S*,5*S*,6*S*,7*R*)-6,7-Epoxy-2-[(1,1-dimethylethyl)dimethylsiloxy]-5-methyl-1-(phenylmethoxy)octan-4-ol (10). Compound **6** (13 mg, 34 mmol) was subjected to the modified Cardillo epoxidation conditions as described above for compound **4**, R = H, with MeLi (0.033 mL, 50 mmol, 1.52 M in Et_2O) followed by CO_2 bubbling for 3 h. Addition of I_2 (25 mg, 100 mmol) in THF with stirring with continued CO_2 addition over 1 h gave the intermediate iodocarbonate. After treatment with MeOH saturated with K_2CO_3 at −78 °C, warming to 20 °C, and stirring for 10 h, the reaction was quenched. Ethereal extraction and column chromatography (15:1 petroleum ether/acetone) gave **10** (11 mg, 81%): IR 3400, 2930, 2860, 1630, 1450, 1410, 1360, 1320, 1250, 1215, 1095, 1025, 1000, 940, 830, 760, 730, 690 cm^{-1}; ^1H NMR δ 7.4 (s, 5 H), 4.5 (s, 2 H), 4.1 (m, 1 H), 3.9 (dq, J = 2.5, J = 7, 1 H), 3.8 (m, 2 H), 3.6 (s, 1 H), 3.5 (m, 1 H), 3.4 (m, 1 H), 1.8 (m, 1 H), 1.5 (m, 2 H), 1.2 (d, J = 6.5, 3 H), 1.0 (d, J = 5, 3 H), 0.9 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H); MS, m/e (relative intensity) 395 (M + 1, 20) 337 (18), 287 (12), 245 (10), 227 (17), 171 (8), 137 (7), 115 (53), 91 (100), 75 (10), 57 (10); $[\alpha]^{23}_D$ −4.31° (*c* 6.4, Et_2O); HRCIMS calcd for $C_{22}H_{39}O_4Si$ (M + 1) 395.2618, found 395.2619.

(2*R*,4*S*,5*S*,6*S*,7*S*)-6,7-Epoxy-2-[(1,1-dimethylethyl)dimethylsiloxy]-5-methyl-1-(phenylmethoxy)octan-4-ol (11). Compound **7** (190 mg, 0.5 mmol) was subjected to the modified Cardillo epoxidation conditions described above for compound **10** with MeLi (0.63 mL, 0.75 mmol, 1.2 M in Et_2O) and I_2 (203 mg, 0.8 mmol). Quench, workup, and column chromatography as described above gave **11** (144 mg, 73%): IR 3400, 2920, 2870, 1630, 1440, 1410, 1350, 1250, 1210, 1100, 1020, 995, 935, 830, 740, 690 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 4.5 (s, 2 H), 4.1 (m, 1 H), 3.9 (m, 1 H), 3.4 (m, 2 H), 3.3 (s, 1 H), 2.9 (m, 1 H), 2.7 (m, 1 H), 1.8 (m, 1 H), 1.7 (m, 1 H), 1.3 (d, J = 3.3, 3 H), 1.2 (m,1 H), 1.0 (d, J = 6.6, 3 H), 0.9 (s, 9 H), 0.11 (s, 3 H), 0.08 (s, 3 H); MS, m/e (relative intensity) 395 (M + 1, 15) 337 (15), 287 (8), 245 (15), 227 (20), 115 (45), 91 (100), 75 (13), 57 (10); $[\alpha]^{23}_D$ +2.42° (*c* 5.0, Et_2O); HRCIMS calcd for $C_{22}H_{39}O_4Si$ (M + 1) 395.2618, found 395.2647.

(2*R*,4*S*,5*R*,6*S*,7*R*)-6,7-Epoxy-2-[(1,1-dimethylethyl)dimethylsiloxy]-5-methyl-1-(phenylmethoxy)octan-4-ol (12). Compound **8** (28 mg, 73 μmol) was subjected to the modified Cardillo epoxidation conditions described above for compound **10** with MeLi (0.08 mL, 100 μmol, 1.2 M in Et_2O) and I_2 (51 mg, 200 μmol). Quench, workup, and column chromatography as described above gave **12** (26 mg, 89%): IR 3400, 2940, 2880, 1640, 1440, 1400, 1360, 1230, 1210, 1090, 1995, 1030, 1000, 830, 730, 690 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 4.5 (s, 2 H), 4.1 (m, 1 H), 4.0 (m, 1 H), 3.5 (m, 2 H), 3.2 (s, 1 H), 2.8 (m, 1 H), 2.7 (m, 1 H), 1.7 (m, 2 H), 1.3 (d, J = 5.1, 3 H), 1.0 (d, J = 6.9, 3 H), 1.2 (m, 1 H), 0.11 (s, 3 H), 0.07 (s, 3 H); MS, m/e (relative intensity), 395 (M + 1, 18), 337 (13), 287 (10), 245 (15), 227 (20), 115 (40), 91 (100), 75 (12), 57 (8); $[\alpha]^{23}_D$ +7.61° (*c* 8.7, Et_2O); HCRIMS calcd for $C_{22}H_{37}O_4Si$ (M − 1) 393.2461, found 393.2437.

(2*R*,4*S*,5*R*,6*S*,7*S*)-6,7-Epoxy-2-[(1,1-dimethylethyl)dimethylsiloxy]-5-methyl-1-(phenylmethoxy)octan-4-ol (13). Compound **9** (150 mg, 0.40 mmol) was subjected to the modified Cardillo epoxidation procedure described above for compound **10** with MeLi (0.42 mL, 0.48 mmol, 1.2 M in Et_2O) and I_2 (158 mg, 0.63 mmol). Quench, workup, and column chromatography as described above gave **13** (116 mg, 74%): IR 3400, 2960, 2880, 1650, 1445, 1400, 1355, 1240, 1215, 1095, 1020, 990, 870, 770, 685 cm^{-1}; ^1H NMR δ 7.2 (s, 5 H), 4.4 (s, 2 H), 4.0 (m, 1 H), 3.8 (m, 1 H), 3.3 (m, 2 H), 3.2 (s, 1 H), 2.7 (m, 1 H), 2.5 (m, 1 H), 1.6 (m, 2 H), 1.3 (m, 1 H), 1.1 (d, J = 6.0, 3 H), 0.9 (d, J = 6.9, 3 H), 0.8 (s, 9 H), 0.10 (s, 3 H), 0.07 (s, 3 H); MS, m/e (relative intensity) 395 (M + 1, 22), 337 (15), 287 (15), 245 (20), 227 (18), 115 (48), 91 (100), 75 (10), 57 (7); $[\alpha]_D$ −6.40° (*c* 4.2, Et_2O); HRCIMS calcd for $C_{22}H_{39}O_4Si$ (M + 1) 395.2618, found 395.2620.

(2*R*,4*S*,5*R*,6*R*,7*R*)-2-[(1,1-Dimethylethyl)dimethylsiloxy]-5,7-dimethyl-1-(phenylmethoxy)-8-nonene-4,6-diol (14). Compound **12** (11 mg, 28 μmol) was azeotropically dried with toluene (3 × 1 mL) in a 10-mL two-neck round-bottom flask equipped with a septum and stirbar. Et_2O (1 mL) was then added under Ar, and the mixture was combined with 10 equiv of the vinyl cuprate, propared as described for compound **2** above with CuCN (25 mg, 280 μmol) and vinyllithium (0.29 mL, 560 μmol, 1.9 M in THF), at −78 °C and warming to 0 °C with stirring for 4 h. Warming to room temperature, quench, ethereal workup, and column chromatography (10:1 petroleum ether/acetone) gave **14** (11 mg, 93%) as a clear oil: IR 3400, 3020, 2980, 2930, 2860, 1680, 1450, 1420, 1370, 1250, 1100, 1005, 960, 940, 910, 835, 810, 775, 735, 690 cm^{-1}; ^1H NMR δ 7.4 (s, 5 H), 5.9 (m, 1 H), 5.1 (m, 2 H), 4.5 (s, 2 H), 4.1 (m, 2 H), 3.9 (s, 1 H), 3.7 (s, 1 H), 3.4 (m, 3 H), 2.3 (m, 1 H), 1.8 (m, 2 H), 1.3 (m, 1 H), 1.2 (d, J = 6.1, 3 H), 1.1 (d, J = 6.5, 3 H), 0.9 (s, 9 H), 0.10 (s, 3 h), 0.07 (s, 3 H); MS, m/e (relative intensity), 423 (M + 1, 14) 273 (10), 201 (18), 165 (9), 159 (8), 147 (11), 117 (11), 107 (9), 92 (10), 91 (100), 81 (10), 75 (10); $[\alpha]^{23}_D$ −0.375° (*c* 0.8, Et_2O); HRCIMS calcd for $C_{24}H_{43}O_4Si$ (M + 1) 423.2931, found 423.2913.

(2*R*,4*S*,5*R*,6*R*,7*S*)-2-[(1,1-Dimethylethyl)dimethylsiloxy]-5,7-dimethyl-1-(phenylmethoxy)-8-nonene-4,6-diol (15). Compound **13** (7 mg, 17 μmol) was azeotropically dried with toluene (3 × 1 mL) in a 10-mL two-neck round-bottom flask equipped with a septum and stirbar. Et_2O (1 mL) was added under Ar, and the mixture was combined with 10 equiv of the vinyl cuprate, prepared as described for compound **2** with CuCN (16 mg, 170 μmol) and vinyllithium (0.16 mL, 350 μmol, 2.2 M in Et_2O), at −78 °C and warming with stirring for 4 h. Warming to room temperature, quench, and ethereal workup followed by column chromatography (10:1 petroleum ether/acetone) gave **15** (7 mg, 91%) as a clear oil: IR 3400, 1950, 2860, 1720, 1450, 1380, 1360, 1260, 1200, 1100, 1030, 1010, 910, 835, 810, 775, 760, 710, 690 cm^{-1}; ^1H NMR δ 7.3 (s, 5 H), 5.6 (m, 1 H), 5.0 (m, 2 H), 4.5 (s, 2 H), 4.1 (m, 1 H), 3.9 (m, 1 H), 3.8 (m, 1 H), 3.6 (m, 2 H), 3.3 (s, 1 H), 2.9 (m, 1 H), 2.1 (m, 1 H), 1.3 (d, J = 6.0, 3 H), 1.2 (m, 2 H), 1.0 (d, J = 7.5, 3 H), 0.9 (s, 9 H), 0.07 (s, 3 H), 0.05 (s, 3 H); MS, m/e (relative intensity) 423 (M + 1, 15), 273 (10), 201 (15), 165 (10), 159 (12), 147 (10), 117 (9), 107 (10), 92 (15), 91 (100), 81 (12), 75 (8); $[\alpha]^{23}_D$ +2.42° (*c* 0.4, Et_2O); HRCIMS calcd for $C_{24}H_{43}O_4Si$ (M + 1) 423.2931, found 423.2956.

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