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A Convenient Multigram Synthesis of Highly Enantioenriched Methyl 3-Silylglycidates

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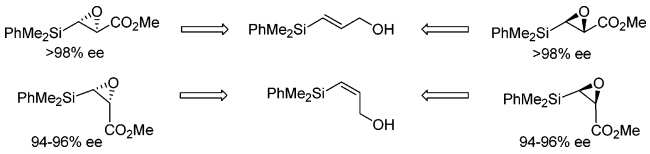

A multigram scale synthesis of the four stereoisomers of methyl 3-silylglycidates (epoxysilanes) with high enantiopurity is described. Key reactions include a Sharpless asymmetric epoxidation (SAE) of a *trans*-vinylsilane and an enzymatic resolution of a racemic *cis*-epoxysilane to establish the desired configurations. Few chromatographic separations (5 columns out of 13 steps) are required for purification, establishing a convenient reaction sequence for both the *trans*- and *cis*-isomers.

Epoxysilanes have received attention from the chemical community due to their ease of preparation and versatility as building blocks and synthetic intermediates.[1] Methods to generate these substrates in enantioenriched form have also become widely available.[2] This interest is, in part, due to their predictable behavior in nucleophilic epoxide ring openings, wherein the steric and electronic effects imparted through the electropositive nature of silicon may influence the regioselectivity.[1f,3] The synthesis of a wide range of functionalized β-hydroxysilanes is the direct result of this regiocontrol (eq 1, Figure 1). These derived β-hydroxysilanes, in turn, have found numerous synthetic applications in the stereocontrolled access to diols,[4] alkenes,[1f,5] lactones,[1c] tetrahydrofurans,[6] and other functional groups.[7]

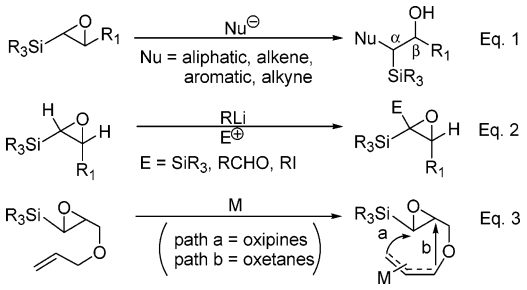

FIGURE 1. Representative transformations of epoxysilanes.

Epoxysilanes can also be converted to their lithium anion by deprotonation with strong base; subsequent electrophilic addition at the carbon bearing the silicon group affords the substituted epoxysilane (Eq 2, Figure 1).[8] They may also undergo rearrangements involving anionic intermediates to form oxetanes and oxipines (Eq 3, Figure 1).[9] Interestingly, silyl-substituted glycidates as a subclass of epoxysilanes remain undeveloped (Eq 1, $R_1 = CO_2R$).[10]

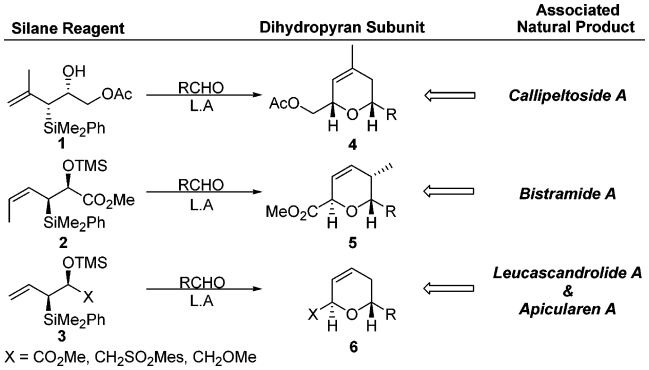

FIGURE 2. [4 + 2]-Annulations with crotyl- and allylsilane reagents.

Recent efforts in our laboratories have focused on the preparation of enantioenriched silyl-substituted glycidate and glycidol derivatives to access novel crotyl- and allylsilane reagents **1**−**3** (Figure 2). For instance, organosilanes have been used for the formation of dihydropyrans **4**−**6** via a [4 + 2]-annulation strategy, which has been employed in the synthesis of several complex natural products and advanced intermediates.[11]

(1) (a) Chakraborty, T. K.; Laxman, P. *Tetrahedron Lett.* **2003**, *44*, 4989. (b) Hudrlik, P. F.; Gebreselassie, P.; Tafesse, L.; Hudrlik, A. M. *Tetrahedron Lett.* **2003**, *44*, 3409. (c) Kim, K.; Okamoto, S.; Takayama, Y.; Sato, F. *Tetrahedron Lett.* **2002**, *43*, 4237. (d) Whitham, G. H. *Sci. Synth.* **2002**, *4*, 633. (e) Babudri, F.; Fiandanese, V.; Marchese, G.; Punzi, A. *Tetrahedron* **2001**, *57*, 549. (f) Hudrlik, P. F.; Hudrlik, A. M. *Advances in Silicon Chemistry*; JAI Press: Greenwich, CT, 1993; Vol. 2, p 1. (g) Chakraborty, T. K.; Reddy, G. V. *Tetrahedron Lett.* **1990**, *31*, 1335.

(2) For examples of SAE to generate epoxysilanes, see: (a) Chauret, D. C.; Chong, J. M.; Ye, Q. *Tetrahedron: Asymmetry* **1999**, *10*, 3601. (b) Kobayashi, Y.; Ito, T.; Yamakawa, I.; Urabe, H.; Sato, F. *Synlett* **1991**, 811. (c) Takeda, Y.; Matsumoto, T.; Sato, F. *J. Org. Chem.* **1986**, *51*, 4731. For an example of Shi epoxidation, see: (d) Heffron, T. P.; Jamison, T. F. *Org. Lett.* **2003**, *5*, 2339. For examples of kinetic resolutions, see: (e) Carlier, P. R.; Mungall, W. S.; Schroder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 2978. (f) Kitano, Y.; Matsumoto, T.; Sato, F. *J. Chem. Soc., Chem. Commun.* **1986**, *17*, 1323. For substrate-directed epoxidations using $VO(acac)_2$, see: (g) Kobayashi, Y.; Uchiyama, H.; Kanbara, H.; Sato, F. *J. Am. Chem. Soc.* **1985**, *107*, 5541.

(3) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063.

(4) Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 4412.

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(7) β-hydroxysilanes not derived from epoxysilanes, see: (a) Adam, J.-M.; de Fays, L.; Laguerre, M.; Ghosez, L. *Tetrahedron* **2004**, *60*, 7325. (b) Landais, Y.; Mahieux, C.; Schenk, K.; Surange, S. S. *J. Org. Chem.* **2003**, *68*, 2779. (c) Ohi, H.; Inoue, S.; Iwabuchi, Y.; Irie, H.; Hatakeyama, S. *Synlett* **1999**, *11*, 1757 and references therein.

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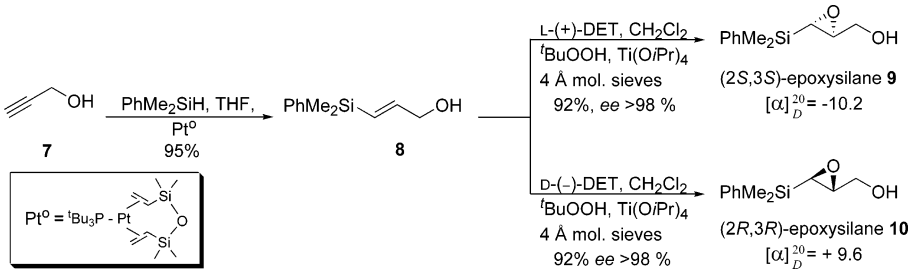
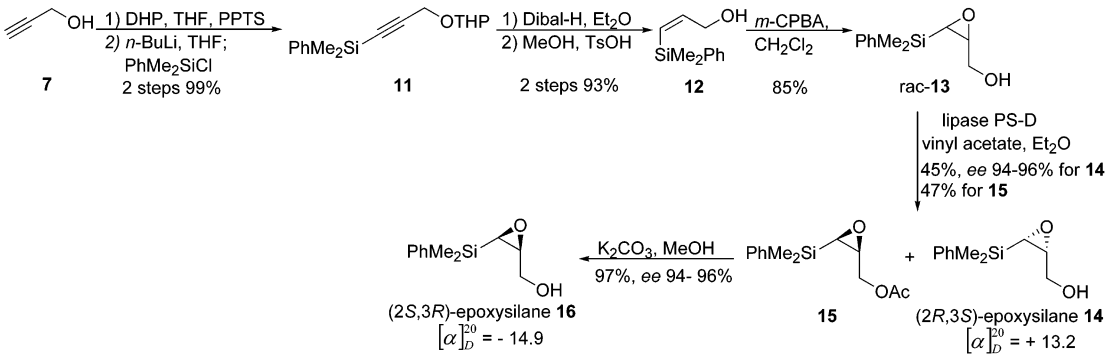
SCHEME 1. Synthesis of Both Enantiomers of *trans*-Epoxysilanes using SAE



SCHEME 2. Synthesis of Both Enantiomers of *cis*-Epoxysilanes using a Enzymatic Resolution



To maximize structural and stereochemical variations in the synthesis of new organosilane reagents, we designed a route that had the potential to access all four stereoisomers of the epoxysilanes. To the best of our knowledge, there is only one report of a multigram synthesis of an enantioenriched epoxysilane[12] and no reports describing the synthesis of all four stereoisomers. Herein, we describe a straightforward multigram synthesis accessing these versatile building blocks with high enantiopurity.

The synthesis of both *cis*- and *trans*-epoxysilanes began with commercially available propargyl alcohol. The *trans*-isomers were accessed through a *syn*-hydrosilylation of **7** using previously described conditions,[13] resulting in >95% yield of a single stereo- and regioisomer (Scheme 1). (*E*)-Vinylsilane **8** was then subjected to a SAE using (+)- or (−)-diethyl tartrate under slightly modified conditions.[14] The resulting epoxysilyl alcohols **9** and **10** were obtained in a two-step yield of 87% and with >98% enantiomeric excess.[15]

Generation of the *cis*-epoxysilane began with the protection of propargyl alcohol as a THP ether, which was subsequently silylated to obtain **11** (Scheme 2). This substrate underwent regio- and stereoselective hydroalumination to give a (*Z*)-olefin. Removal of the THP ether yielded the (*Z*)-vinylsilane **12** in 92% yield over four steps.

A Sharpless asymmetric epoxidation on the complementary (*Z*)-vinylsilane was attempted but provided less than 5% conversion using conditions described for the (*E*)-vinylsilane.[16] Accordingly, we explored the possibility of an enzymatic resolution of the racemic epoxide. Epoxidation with *m*-CPBA gave a racemic mixture of epoxy alcohols **13** that seemed a suitable substrate for enzymatic resolution.

Several lipase enzymes were surveyed for their ability to effectively resolve racemic epoxysilyl alcohols.[17] Best results were obtained using Amano PS-D lipase in the presence of vinyl acetate (a transesterifying agent) to provide primary alcohol **14** and acetate **15** in high yields and enantiomeric excess. Base-catalyzed methanolysis of the acetate group in **15** gave the desired *cis*-epoxysilane **16**.[18]

Completion of the synthesis began with the oxidation of **9** with $NaIO_4$ and catalytic $RuCl_3$[19] to provide acid **17**, which was immediately esterified to give *trans*-silyl glycidate **18** (72% from **9**, respectively). The *trans*-epoxides were obtained in an overall four-step sequence capable of generating >20 g of material in high enantiopurity (Scheme 3). With an efficient route to the *trans*-epoxy esters, we next turned our efforts toward the synthesis of the *cis*-isomer.

The *cis*-epoxide **14** underwent the oxidation/esterification sequence described for the *trans*-epoxides to give **20**. However, upon scale-up, a significant amount of aldehyde was observed (ca. 20%) using previously reported conditions.[11a] The sequence resulted in a two-step 55% isolated yield of **20** after DCC coupling. During the course of oxidation, the reaction solution became a dark green color with the formation of a black suspension, suggesting an inactive catalytic system.[19] To drive

(10) For references pertaining to the asymmetric synthesis of glycidates (without silicon), see: Imashiro, R.; Seki, M. *J. Org. Chem.* **2004**, *69*, 4216 and references therein.

(11) (a) Lowe, J. T.; Panek, J. S. *Org. Lett.* **2005**, *7*, 3231. (b) Su, Q.; Panek, J. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 1223. (c) Su, Q.; Panek, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 2425. (d) Huang, H.; Panek, J. S. *Org. Lett.* **2003**, *5*, 1991. (e) Huang, H.; Panek, J. S. *J. Am. Chem. Soc*. **2000**, *122*, 9836.

(12) For the 19.5 g preparation of (2*R*,3*R*)-3-(triphenylsilyl)-2,3-epoxypropan-l-ol, see: Raubo, P.; Wicha, J. *Tetrahedron: Asymmetry* **1995**, *6*, 577.

(13) Beresis, R. T.; Solomon, J. S.; Yang, M.; Jain, N. F.; Panek, J. S. *Org. Synth.* **1997**, *75*, 78.

(14) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

(15) The enantiomeric excess was determined to be 98% for both **9** and **10** as observed using Chiralcel OD 99/1 (hexanes/IPA) at 1 mL/min. (t_R 35.92 for **9** and 45.17 for **10**).

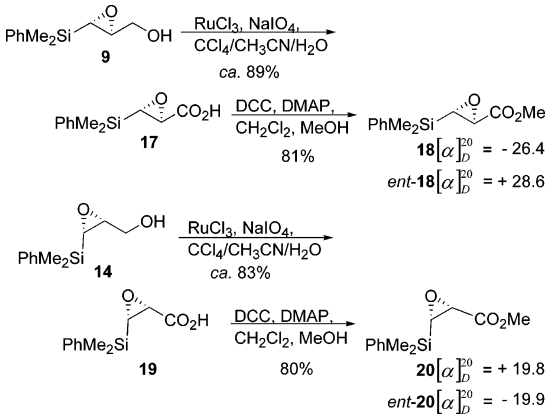
(16) Elevated temperatures (−20, 0, and +25 °C) did not provide the desired epoxide.

(17) Lipase AK "Amano" 20, Lipase PS "Amano", and Lipase PS-D "Amano" were screened.

(18) The enantiomeric excess was determined to vary between 94 and 96% for both **14** and **16** as observed using Chiralcel OD 85/15 (hexanes/IPA) at 1 mL/min (t_R 5.03 for **14** and 7.08 for **16**).

(19) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

SCHEME 3. Synthesis of Methyl 3-Silyl Glycidates



the reaction to completion, catalyst loading was increased and extended reaction times were explored with little success. Fortunately, a reset of the catalytic system provided complete conversion. Thus, applying two sequential catalytic ruthenium oxidations followed by esterification using DCC/DMAP afforded the silyl glycidate **20** in a comparable 66% yield for the two-step sequence (Scheme 3). This oxidation/esterification sequence was also successfully applied to the primary alcohols of **10** and **16** with nearly identical results.

In summary, we have developed a convenient, versatile synthesis of the stereoisomers of methyl 3-silyl glycidates. These epoxysilanes possess utility as chiral building blocks in organic synthesis, portions of which were previously demonstrated. A Sharpless asymmetric epoxidation and an enzymatic resolution were employed to obtain the enantiomerically enriched epoxysilyl alcohols, thus providing access to all four stereoisomers in both the *cis*/*trans* series. Each enantiomer was prepared in greater than 20 g quantities with high enantiomeric purity and yields for all intermediate substrates.

Experimental Section

(*E*)-3-(Dimethylphenylsilanyl)prop-2-en-1-ol (8). To a solution of 2-propyn-1-ol (38 g, 677.8 mmol) in tetrahydrofuran (1000 mL) were added dimethylphenylsilane (97 g, 712.0 mmol), sodium (0.020 g), and platinum(0) hydrosilylation catalyst[13] (0.14 g, 0.24 mmol) under an atmosphere of nitrogen. The solution was then refluxed overnight and the solvent removed in vacuo to give an orange oil. The oil was run over a silica plug with hexanes followed by 100% ethyl acetate to provide 124.1 g (95%) of **8** as a light yellow oil. The ^{1}H and ^{13}C NMR and IR spectra of compound **8** were in complete agreement with those found in ref 12.

[(2*S*,3*S*)-3-(Dimethylphenylsilanyl)oxiranyl]methanol (9). A solution of 4 Å molecular sieves (23.1 g) and (+)-diethyl-L-tartrate (10.5 mL, 50.9 mmol) in dichloromethane (1300 mL) was blanketed with an atmosphere of argon and cooled to −40 °C. To the above solution was added titanium tetraisopropoxide (15.0 mL, 50.8 mmol) followed by a slow addition of a 3.5 M solution of *tert*-butyl hydroperoxide in toluene[20] (242 mL). The solution was allowed to stir for 1 h before (*E*)-3-(dimethylphenylsilanyl)prop-2-en-1-ol **8** (82.5 g, 429 mmol) in dichloromethane (225 mL) was added via cannula and stirred for an additional 48 h at −40 °C. The reaction was warmed to 0 °C, and a premixed solution of ferrous sulfate heptahydrate (144 g, 517 mmol) and tartaric acid (44.1 g, 294 mmol) in water (435 mL) cooled to 0 °C was slowly added and stirred for 30 min. The reaction was then filtered through a pad of Celite and extracted with dichloromethane. The combined organic layers were again cooled to 0 °C, and a solution containing 126 g of NaOH in 420 mL of a brine solution was added and stirred for 2 h. The reaction was diluted with 500 mL of water and then extracted with 1:1 hexane/diethyl ether, dried over $MgSO_4$, filtered, and concentrated to obtain an oil. The oil was chromatographed over silica gel using hexanes/ethyl acetate (90/10 to 60/40) to get 82.4 g (92% yield, >98% ee) of **9** as a clear oil: $[\alpha]^{20}_D$ −10.2 (*c* 1.48 $CHCl_3$).[21] For **10** (92% yield, > 98% ee): $[\alpha]^{20}_D$ +9.6 (*c* 2.39 $CHCl_3$). The ^{1}H and ^{13}C NMR and IR spectra of compounds **9** and **10** were in complete agreement with those found in ref 12.

(2*S*,3*S*)-3-(Dimethylphenylsilanyl)oxirane-2-carboxylic Acid (17). Epoxy alcohol **9** (27.7 g, 133 mmol) was added into a 3 L round-bottom flask followed by acetonitrile (440 mL), CCl_4 (440 mL), and water (660 mL). Sodium metaperiodate (114 g, 532 mmol) was then added as a solid in one portion followed by ruthenium(III) chloride hydrate (0.98 g, 4.3 mmol). The reaction was allowed to rapidly stir overnight at room temperature. Dichloromethane (500 mL) was then added and the reaction mixture stirred for 30 min before adding an additional 500 mL of water. The aqueous layer was then extracted with dichloromethane, combined and dried over $MgSO_4$, filtered, and concentrated to get 26.2 g of **17** as a colored (red/pink on dilution) oil which was immediately taken to the next step: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.51 (m, 2H), 7.41−7.35 (m, 3H), 3.26 (d, J = 3.2 Hz, 1H), 2.66 (d, J = 3.6 Hz, 1H), 0.39 (s, 3H), 0.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 134.0, 133.8, 130.0, 128.1, 51.9, 50.4, −5.4, −5.5; IR (film) ν_{max} 3071, 2582, 1738 cm^{-1}; HRMS(CI, NH_3) *m*/*z* calcd for $C_{11}H_{14}O_3Si$ $[M]^+$ 222.0712, found 222.0689; $[\alpha]^{20}_D$ −15.96 (*c* 1.83, $CHCl_3$). For *ent*-**17**: $[\alpha]^{20}_D$ +17.50 (*c* 2.0, $CHCl_3$).

(2*S*,3*S*)-Methyl 3-(Dimethylphenylsilanyl)oxirane-2-carboxylate (18). A solution of epoxy acid **17** (25.4 g, 114 mmol) in dichloromethane (325 mL) was slowly added to a solution of DCC (36.9 g, 179 mmol), DMAP (1.78 g, 14.6 mmol), and methanol (18.2 mL, 441 mmol) in dichloromethane (70 mL) at 0 °C. The reaction was allowed to stir overnight at room temperature. The solution was then filtered and dried in vacuo to yield **18** as a oil. Further purification over silica gel (hexanes/ethyl acetate 100% to 90/10) gave 21.9 g (81%) of a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (m, 2H), 7.38 (m, 3H), 3.74 (s, 3H), 3.24 (d, J = 3.2 Hz, 1H), 2.64 (d, J = 3.2 Hz, 1H), 0.37 (s, 3H), 0.34 (s, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 170.3, 134.2, 133.7, 129.7, 127.8, 52.1, 51.0, 50.6, −5.6, −5.7; IR (film) ν_{max} 1755, 1290, 1207 cm^{-1}; HRMS (CI, NH_3) *m*/*z* calcd for $C_{12}H_{16}O_3Si$ $[M]^+$ 236.0869, found 236.0877; $[\alpha]^{20}_D$ −26.39 (*c* 1.95, $CHCl_3$). For *ent*-**18**: $[\alpha]^{20}_D$ +28.56 (*c* 1.67, $CHCl_3$).

Dimethylphenyl[3-(tetrahydropyran-2-yloxy)prop-1-ynyl]silane (11). Propargyl alcohol (40.0 g, 713 mmol) and dichloromethane (1400 mL) were added into a 3 L round-bottom flask and cooled to 0 °C. Dihydropyran (68.3 mL, 749 mmol) was added followed by *p*-toluenesulfonic acid (1.23 g, 7.12 mmol) and the mixture stirred for 1 h. A saturated solution of sodium bicarbonate was slowly added and the mixture stirred until gas evolution ceased. The remaining aqueous layer was extracted with dichloromethane and dried over $MgSO_4$. After filtering, the reaction was concentrated to get a clean oil (94 g) that was reacted directly.

Tetrahydro-2-(2-propynyloxy)-2*H*-pyran (ca. 48 g, 340 mmol) was added to a 2 L round-bottom flask followed by THF (360 mL). The reaction was cooled to −78 °C, and 1.05 equiv of 2.5 M *n*-BuLi in hexanes (140 mL) was slowly added over 2 h via a syringe pump. After the solution was stirred for 30 min, chlorodimethylphenylsilane (59.8 mL, 360 mmol) was added dropwise. The reaction mixture was stirred for an additional 30 min at −78 °C and then warmed to room temperature and stirred for 3 h. The resulting solution was poured into ice−water and diluted with hexanes. The aqueous layer was extracted with hexanes, and the organics were dried over $MgSO_4$, filtered, and concentrated in vacuo to yield 93 g (99%) of **11** as a light yellow oil that can be used without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (m, 2H), 7.36

(20) For the preparation of anhydrous TBHP, see: Hill, J. G.; Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3607.

(21) Le Bideau, F.; Gilloir, F.; Nilsson, Y.; Aubert, C.; Malacria, M. *Tetrahedron* **1996**, *52*, 7487.

(m, 3H), 4.82 (t, 3.2 Hz, 1H), 4.34−4.30 (d, J_{ab}= 16 Hz, 1H), 4.28−4.24 (d, J_{ab}= 15.2 Hz, 1H), 3.83 (m, 1H), 3.51 (m, 1H), 1.84−1.75 (m, 1H), 1.76−1.69 (m, 1H), 1.64−1.59 (m, 2H), 1.56−1.50 (m, 2H), 0.40 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.7, 133.6, 129.4, 127.8, 103.3, 96.7, 88.8, 61.9, 54.8, 30.2, 25.3, 19.0, −1.00; IR (film) ν_{max} 2944, 2176, 1428, 1250, 1118, cm^{-1}; HRMS (CI, NH_3) *m*/*z* calcd for $C_{16}H_{22}O_2Si$ [M]$^+$ 274.1389, found 274.1366.

(*Z*)-3-(Dimethylphenylsilanyl)prop-2-en-1-ol (12). Alkyne **11** (95.0 g, 346 mmol) was dissolved in diethyl ether (218 mL) and cooled to 0 °C. A 1 M solution of DIBAL-H in hexanes (381 mL) was added and the reaction allowed to reach room temperature and stir for an additional 24 h. The reaction was then slowly poured into 1 L of a 1 M HCl/ice solution and allowed to stir until solution became clear (ca. 2 h). The mixture was extracted with diethyl ether, dried over $MgSO_4$, filtered over silica, and concentrated to yield 90 g (94%) of an oil that was used without further purification.

This oil (ca. 90 g, 300 mmol) was added into a 1 L round-bottom flask followed by methanol (580 mL) and a catalytic amount of *p*-toluenesulfonic acid (0.620 g, 3.2 mmol). The reaction was allowed to stir for 3 h before addition of triethylamine (0.45 mL, 3.2 mmol). The reaction was then filtered through a pad of silica gel and concentrated in vacuo to give 60 g (99%) of **12** as a clear oil that can be used without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.34 (m, 3H), 6.54 (dt, J = 14.4, 6.0 Hz, 1H), 5.85 (d appt t, 14, 1.2 Hz, 1H), 4.05 (dd, J = 6.4, 1.6 Hz, 2H), 0.37 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.0, 139.1, 133.5, 129.8, 129.1, 127.8, 63.2, −0.97; IR (film) ν_{max} 3346, 2956, 1607 cm^{-1}; HRMS (CI, NH_3) *m*/*z* calcd for $C_{11}H_{16}OSi$ [M]$^+$ 192.0970, found 192.0972.

[3-(Dimethylphenylsilanyl)oxiranyl]methanol (13). A solution of allylic alcohol **12** (51.3 g, 267 mmol) in dichloromethane (1250 mL) was added into a 3 L round-bottom flask and cooled to 0 °C. *m*-CPBA (119 g, 531 mmol of max 77%) was then added. The solution was allowed to warm to room temperature and stir for an additional 3.5 h. The entire solution was then poured SLOWLY into a mixture of saturated $Na_2S_2O_3$ solution (1 L) where it was allowed to stir for 30 min. A 1.5-L portion of saturated $NaHCO_3$ was then SLOWLY added, and the combined mixture was stirred for an additional 1.5 h. The solution was then extracted with dichloromethane. The combined organics were washed carefully with saturated $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated in vacuo to get an oil. Further purification over silica gel (hexanes/ethyl acetate: 95/5 to 50/50) yielded 46.8 g (85%) of **13** as a light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (m, 2H), 7.40 (m, 3H), 3.68 (q, J = 9.6 Hz, 1H), 3.37 (m, 2H), 2.71 (br. s, 1H), 2.52 (m, 1H), 0.42 (s, 3H), 0.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 133.7, 129.6, 128.0, 63.2, 57.7, 49.4, −2.9, −3.3; IR (film) ν_{max} 3418, 2958, 1427 cm^{-1}; HRMS (CI, NH_3) *m*/*z* calcd for $C_{11}H_{16}O_2Si$ [M]$^+$ 208.0920, found 208.0881.

Acetic Acid (2*S*,3*R*)-3-(Dimethylphenylsilanyl)oxiranyl Methyl Ester and [(2*R*,3*S*)-3-(Dimethylphenylsilanyl)oxiranyl]methanol (15 and 14). A solution of racemic epoxide **13** (50 g, 240 mmol) and vinyl acetate (11 mL, 120 mmol, 0.5 equiv) in diethyl ether (3000 mL) was added to a 4 L round-bottom flask. After the addition of lipase PS-D (6 g), the reaction was allowed to stir for 15 h at room temperature. The solution was then filtered and concentrated in vacuo to get an oil. Further purification over silica gel (hexanes/ethyl acetate: 95/5 to 80/20) yielded 28.5 g (47%) of **15** as a clear oil and 22.5 g (45%, 94−96% ee) of **14** as a light yellow oil. Acetate **15**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (m, 2H), 7.38 (m, 3H), 4.17 (dd, J = 12, 3.2 Hz, 1H), 3.74 (dd, J = 12, 7.6 Hz, 1H), 3.40 (m, 1H), 2.49 (d, J = 5.6 Hz, 1H), 2.04 (s, 3H), 0.42 (s, 3H), 0.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 135.9, 133.7, 129.7, 128.0, 65.1, 54.5, 48.7, 20.7, −3.1, −3.5; IR (film) ν_{max} 2957, 1740, 1428, 1372, 1232 cm^{-1}; HRMS (CI, NH_3) *m*/*z* calcd for $C_{13}H_{18}O_3Si$ [M]$^+$ 250.1025, found 250.1021. For **15**: $[\alpha]^{20}_D$ −8.68 (*c* 1.51, $CHCl_3$). For spectral properties of **14**, see **13**. For **14**: $[\alpha]^{20}_D$ +13.2 (*c* 1.14, $CHCl_3$).

[(2*S*,3*R*)-3-(Dimethylphenylsilanyl)oxiranyl]methanol (16). A solution of acetate **15** (58 g, 232 mmol) in methanol (600 mL) was added to a 2 L round-bottom flask. K_2CO_3 was added (0.64 g, 4.6 mmol) and the reaction stirred for 2 h at room temperature. Water was added to the flask followed by ether. The aqueous layer was subsequently extracted twice more with ether. The combined organics were then dried over $MgSO_4$, filtered, and concentrated in vacuo to get an oil. The oil was flashed over silica gel with hexanes/ethyl acetate (80/20) to get 46.5 g (97%, 94−96% ee) of **16** as a clear oil: $[\alpha]^{20}_D$ −14.90 (*c* 1.56, $CHCl_3$). The ^{1}H and ^{13}C NMR and IR spectra and HRMS of compound **16** were in complete agreement with those found for **13** as reported above.

(2*R*,3*S*)-3-(Dimethylphenylsilanyl)oxirane-2-carboxylic Acid (19). Epoxy alcohol **14** (47.0 g, 226 mmol) was added into a 5 L round-bottom flask followed by acetonitrile (750 mL), CCl_4 (750 mL), and water (1138 mL). Sodium metaperiodate (193 g, 902 mmol) was then added as a solid in one portion followed by ruthenium(III) chloride hydrate (3.00 g, 14 mmol). The reaction was allowed to stir at room temperature for 4 h. Dichloromethane (2500 mL) was then added and the reaction mixture stirred for an additional 30 min. The aqueous layer was extracted with dichloromethane, and the combined extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to give 45.53 g of a colored (red/pink) oil (ca. 20% aldehyde). The oil may be taken on crude or added into a 5 L round-bottom flask with acetonitrile (750 mL), CCl_4 (750 mL), and water (1138 mL). Sodium metaperiodate (43.4 g, 175 mmol) was then added followed by ruthenium(III) chloride hydrate (0.49 g, 2.2 mmol). The reaction was allowed to stir at room temperature for 4 h. Workup followed as described above to give 41.43 g (83%) of **19** as a colored (lavender) oil that was immediately taken to the next step: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.35 (m, 3H), 3.68 (d, J = 5.2 Hz, 1H), 2.68 (d, J = 6.0 Hz, 1H), 0.44 (s, 3H), 0.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 133.8, 133.7, 129.7, 127.9, 52.1, 51.4, −3.5, −4.8; IR (film) ν_{max} 3071, 2958, 1723, 1251 cm^{-1}; HRMS (CI, NH_3) *m*/*z* calcd for $C_{11}H_{14}O_3Si$ [M]$^+$ 222.0712, found 222.0698; $[\alpha]^{20}_D$ +10.94 (*c* 1.92, $CHCl_3$). For *ent*-**19**: $[\alpha]^{20}_D$ −10.23 (*c* 1.76, $CHCl_3$).

(2*R*,3*S*)-Methyl 3-(Dimethylphenylsilanyl)oxirane-2-carboxylate (20). A solution of epoxy acid **19** (41.43 g, 186.4 mmol) in dichloromethane (260 mL) was added to a solution of DCC (57.7 g, 280 mmol), DMAP (2.96 g, 24.2 mmol), and methanol (30.2 mL, 745 mmol) in dichloromethane (104 mL) at 0 °C. The reaction was allowed to stir overnight at room temperature. The solution was then filtered and concentrated in vacuo to yield an oil. Further purification by column chromatography (hexanes/ethyl acetate: 95/5) gave 35.34 g (80%) of **20** as a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.35 (m, 3H), 3.65 (d, J = 5.6 Hz, 1H), 3.48 (s, 3H), 2.68 (d, J = 5.6 Hz, 1H), 0.42 (s, 3H), 0.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 135.7, 129.3, 127.7, 52.3, 51.6, 50.5, −3.3, −5.0; IR (film) ν_{max} 2954, 1756, 1428, 1211 cm^{-1}; HRMS (CI, NH_3) *m*/*z* calcd for $C_{12}H_{16}O_3Si$ [M]$^+$ 236.0869, found 236.0877; $[\alpha]^{20}_D$ +19.8 (*c* 1.97, $CHCl_3$). For *ent*-**20**: $[\alpha]^{20}_D$ −19.9 (c 2.10, $CHCl_3$).

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Supporting Information Available: ^{1}H and ^{13}C NMR and IR spectra and HPLC data. This material is available free of charge via the Internet at http://pubs.acs.org.

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