Supporting Information for:

# Complete stereodivergence in the synthesis of 2-amino-1,3-diols from allenes

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## I. Complete Reference 6.

Gaussian 09, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2010.

## II. General Information.

Unless otherwise specified, all glassware was either oven-dried overnight at 130 °C or flame-dried under vacuum and purged with dry nitrogen prior to use. Unless otherwise specified, reagents were used as obtained from the vendor without further purification. Tetrahydrofuran and diethyl ether were freshly distilled from purple Na/benzophenone ketyl. Dichloromethane, acetonitrile and toluene were dried over $CaH_2$ and freshly distilled prior to use. 1,2-Dichloroethane was used as purchased from Sigma Aldrich. All other solvents were purified in accordance with "Purification of Laboratory Chemicals".[1] Air- and moisture- sensitive reactions were performed using standard Schlenk techniques under an atmosphere of nitrogen. Analytical thin layer chromatography (TLC) was performed utilizing pre-coated silica gel 60 $F_{254}$ plates

containing a fluorescent indicator, while preparative chromatography was performed using SilicaFlash P60 silica gel (230-400 mesh) via Still's method.[2] Unless otherwise stated, the mobile phases for column chromatography were mixtures of hexanes/ethyl acetate. Columns were typically run using a gradient increasing the polarity using ethyl acetate. Various stains were used to visualize reaction products, including *p*-anisaldehyde, $KMnO_4$, ceric ammonium molybdate (CAM stain) and iodine powder. High-pressure liquid chromatography (HPLC) analyses were performed at 215 and 225 nm using a Shimadzu HPLC, Model LC-20AB. Further details are given in Section XV.

$^1H$ NMR and $^{13}C$ NMR spectra were obtained using Bruker-300, Varian Inova-500, Varian Unity-500 or Varian Inova-600 NMR spectrometers. For $^1H$ NMR, chemical shifts are reported relative to residual protiated solvent peaks (δ 7.26, 2.49, 7.15 and 4.80 ppm for $CDCl_3$, $(CD_3)_2SO$, $C_6D_6$ and $CD_3OD$ respectively). $^{13}C$ NMR spectra were measured at either 125 MHz or 150 MHz on the same instruments noted above for recording $^1H$ NMR spectra. Chemical shifts were again reported in accordance to residual protiated solvent peaks (δ 77.0, 39.5, 128.0 and 49.0 ppm for $CDCl_3$, $(CD_3)_2SO$, $C_6D_6$, and $CD_3OD$, respectively). Accurate mass measurements were acquired at the University of Wisconsin, Madison using a Micromass LCT (electrospray ionization, time-of-flight analyzer or electron impact methods). When two or more significant isotopes were present in the molecule, a monoisotopic approach was used, focusing on the isotope with the lowest mass ($^{35}Cl$ and $^{79}Br$). The NMR and Mass Spectrometry facilities are funded by the NSF (CHE-9974839, CHE-9304546, CHE-9208463, CHE-9629688) and the University of Wisconsin, as well as the NIH (RR08389-01).

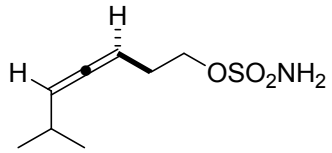
**III. Preparation of homoallenic sulfamates.**

General procedure A: The following procedure is taken from a published literature procedure by Du Bois.[3] Formic acid (1.5 equiv) was added over 10 min to a rapidly stirred solution of neat chlorosulfonyl isocyanate (1.5 equiv) at 0 °C (Caution: significant gas evolution!). After the addition was completed, the mixture was stirred for an additional 5 min to yield a white solid. Dichloromethane was added (1.9 M) and the resulting solution stirred at room temperature for 6-8 h. The solution was cooled to 0 °C and a mixture of the homoallenic alcohol (1.0 equiv) and pyridine (1.5 equiv) in dichloromethane (1.4 M in alcohol) was added dropwise. The flask was warmed to room temperature and stirred for 1 h. The mixture was quenched with EtOAc and $H_2O$, the biphasic mixture extracted with three portions of EtOAc and the combined organics washed with brine. Silica gel chromatography (hexanes/ethyl acetate gradient) afforded the sulfamate esters.

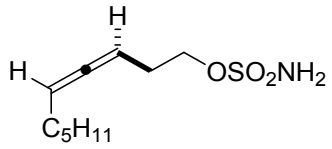
General procedure B: The following procedure is taken from a published literature procedure by Du Bois.[4] Formic acid (2.5 equiv) was added over 2-3 min to a rapidly stirred solution of neat chlorosulfonyl isocyanate (2.5 equiv) at 0 °C. Vigorous gas evolution was observed during the addition process, resulting in solidification of the mixture to a white solid within 5 min. Acetonitrile was added to the resulting white mass (6 mL per mmol of alcohol) and the contents warmed to 23 °C. After stirring for 4-8 h, the mixture was cooled to 0 °C and a solution of the corresponding homoallenic alcohol (1.0 equiv) in N,N-dimethylacetamide (DMA, same volume as for acetonitrile) was added *via* syringe. The reaction was warmed to 23 °C and stirred for 1.5-2 h (Note: TLC monitoring can be attempted, but the product and starting material often have the same $R_f$ values). After the reaction was complete, the mixture was carefully quenched by the addition of $H_2O$ and poured into a separatory funnel containing $Et_2O$. The organic phase was collected and the aqueous layer was extracted twice with portions of $H_2O$. The combined

organic extracts were washed five times with $H_2O$, once with a saturated solution of NaCl and then dried over $Na_2SO_4$. The solution was decanted and concentrated by rotary evaporation to give a crude oil that was purified by silica gel chromatography (hexanes/EtOAc gradient) to afford the sulfamate ester.

(Note: Either method can be used for all substrates described in the SI; the choice of method was based on the preference of the individual authors.)

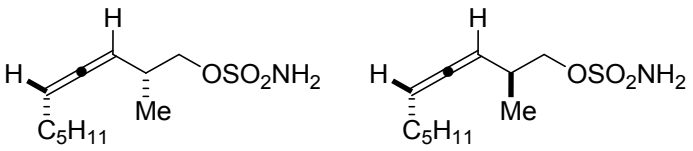



**Sulfamate precursor for compound 5**. Following general procedure A, 2.54 g of the homoallenic alcohol (20.1 mmol) yielded upon silica gel chromatography (10-30% EtOAc in hexanes) 3.18 g of the sulfamate (15.5 mmol, 77%). $^1$H NMR (400.2 MHz, $CDCl_3$) δ 5.21 (m, 1H), 5.14 (m, 1H), 5.03 (br s, 2H), 4.25 (t, $J$ = 6.7 Hz, 2H), 2.44 (app qd, $J$ = 6.7, 2.9 Hz, 2H), 2.29 (m, 1H), 1.01 (d, $J$ = 6.7 Hz, 6H). $^{13}$C NMR (100.6 MHz, $CDCl_3$) δ 203.1, 99.8, 86.7, 70.4, 28.5, 27.7, 22.3, 22.3. HRMS (ESI) *m*/*z* calculated for $C_8H_{19}N_2O_3S$ [M+$NH_4^+$] 223.1111, found 223.1105.

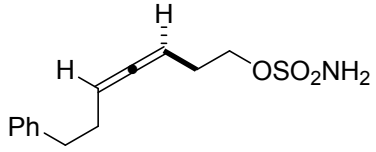



**Sulfamate precursor for compound 11.** Following general procedure B, 2.0 g of homoallenic alcohol (13.0 mmol) yielded upon silica gel chromatography (10% to 30% EtOAc in Hexanes)

2.63 g of the sulfamate (11.3 mmol, 87%). Spectral data was consistent with the reported values.[5]

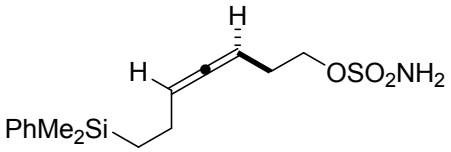



**Sulfamate precursors for compound 12.** Following general procedure A, 6.80 g of homoallenic alcohol (40.4 mmol, ~1.25:1 mixture of isomers) yielded upon silica gel chromatography (10% to 30% EtOAc in hexanes) 6.84 g of the two homoallenic sulfamates as an inseparable mixture of isomers (27.7 mmol, 68%, in a ratio of ~ 1.25:1). $^{1}$H NMR (500.0 MHz, $CDCl_3$) δ 5.22 (m, 1H), 5.10 (m, 1H), 4.80 (br s, 2H), 4.14 (app dd, *J* = 9.1, 6.1 Hz, 1H), 4.01 (m, 1H), 2.59 (m, 1H), 1.99 (app qd, *J* = 7.2, 2.8 Hz, 2H), 1.36-1.44 (m, 2H), 1.27-1.34 (m, 4H), 1.10 (d, *J* = 6.7 Hz, 3H), 0.89 (t, *J* = 6.2 Hz, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 203.5, 93.5, 93.4, 91.9, 75.3, 75.3, 32.8, 32.7, 31.3, 28.8, 28.7, 28.7, 22.5, 16.6, 16.5, 14.0. HRMS (ESI) *m*/*z* calculated for $C_{11}H_{25}N_2O_3S$ [M + $NH_4^+$] 265.1581, found 265.1572.

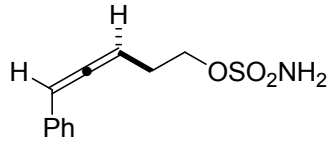



**Sulfamate precursor for compound 13.** Following general procedure B, 3.07 g of homoallenic alcohol (16.3 mmol) yielded upon silica gel chromatography (10% to 40% EtOAc/hexane) 3.45 g of the sulfamate (12.9 mmol, 79%). $^{1}$H NMR (500.0 MHz, $CDCl_3$) δ 7.28 (m, 2H), 7.19 (m, 3H), 5.22 (qt, *J* = 6.3, 2.8 Hz, 1H), 5.09 (qt, *J* = 6.3, 2.8 Hz), 4.67 (bs, 2H), 4.16 (app td, *J* = 6.8, 2.8 Hz, 2H), 2.73 (m, 2H), 2.35 (m, 4H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 204.8, 141.5, 128.5,

128.3, 125.9, 91.7, 86.1, 70.3, 35.1, 30.1, 28.3. HRMS (ESI) *m/z* calculated for $C_{13}H_{21}N_2O_3S$ [M + $NH_4^+$] 285.1268, found 285.1279.

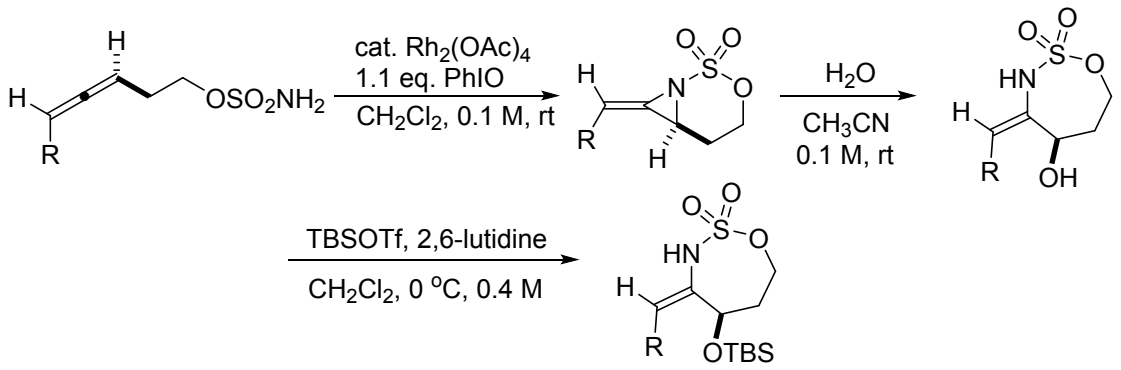



**Sulfamate precursor for compound 14.** Following general procedure A, 1.26 g of homoallenic alcohol (5.11 mmol) yielded upon silica gel chromatography (5% to 20% EtOAc in hexanes) 1.20 g of the sulfamate (3.69 mmol, 72%). $^1$H NMR (500.0 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.36 (m, 3H), 5.24 (m, 1H), 5.10 (m, 1H), 4.66 (br s, 2H), 4.23 (t, *J* = 6.7 Hz, 2H), 2.42 (app qd, *J* = 6.7, 2.8 Hz, 2H), 2.02 (m, 2H), 0.87 (m, 2H), 0.28 (s, 6H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 204.1, 139.1, 133.6, 128.9, 127.8, 95.2, 86.4, 70.4, 28.5, 23.0, 15.0, -3.1. HRMS (ESI) *m/z* calculated for $C_{15}H_{27}N_2O_3SSi$ [M+$NH_4^+$] 343.1507, found 343.1496.



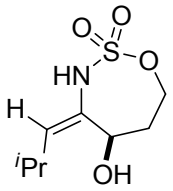

**Sulfamate precursor for compound 15.** Following general procedure B, 2.00 g of the homoallenic alcohol (12.5 mmol) yielded upon silica gel chromatography (0% to 30% EtOAc/hexane) 2.20 g of the sulfamate (9.21 mmol, 74%). $^1$H NMR (500.0 MHz, $CDCl_3$) δ 7.35-7.29 (m, 4H), 7.22 (m, 1H), 6.24 (dt, *J* = 6.4, 3.0 Hz, 1H), 5.61 (q, *J* = 6.4 Hz, 1H), 4.52 (bs, 2H), 4.34 (t, *J* = 6.4 Hz, 2H), 2.59 (qd, *J* = 6.4, 3.0 Hz, 2H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 205.8, 134.0, 128.7, 127.3, 126.8, 96.0, 90.0, 69.7, 28.1. HRMS (ESI) *m/z* calculated for $C_{11}H_{17}N_2O_3S$ [M+$NH_4^+$] 257.0955, found 257.0961.

**IV. One-pot synthesis of enesulfamates from homoallenic sulfamates.**

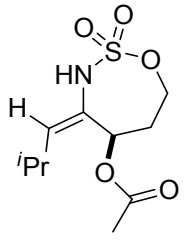



General procedure: A flame-dried roundbottom flask equipped with a stir bar was charged with the appropriate homoallenic sulfamate (1.0 equiv) and $Rh_2(OAc)_4$ (0.005 equiv). Dry dichloromethane was added to prepare a 0.1 M solution, and the mixture stirred vigorously to yield a faint green-blue solution. Iodosylbenzene (1.1 equiv) was added in one portion, and the resulting suspension stirred at room temperature for approximately 1 h. The reaction was monitored by TLC for consumption of starting material (~30% EtOAc/hex or 100% $CH_2Cl_2$ solvent system, CAM stain). Upon complete consumption of the starting material, the solution was concentrated by rotary evaporation, and $CH_3CN$ was added to the residue to prepare a 0.1 M solution. Water (50 equiv) was added, and the solution stirred at room temperature for approximately 1 h until TLC indicated complete consumption of the intermediate bicyclic methylene aziridine (~30% EtOAc/hex or 100% $CH_2Cl_2$ solvent system, CAM stain). Upon completion, the reaction was poured into a beaker of appropriate size and diluted by a factor of 2-3 with $CH_2Cl_2$. The solution was dried by the addition of $Na_2SO_4$ until the initially cloudy solution turned clear, and the resulting suspension decanted. The residual material was washed twice with $CH_2Cl_2$, the organic portions combined and concentrated by rotary evaporation. The residue was then dissolved in dry $CH_2Cl_2$ (0.4 M) and cooled to 0 ºC. A portion of 2,6-lutidine was added all at once, followed by the slow addition of TBSOTf over approximately 1 min. The

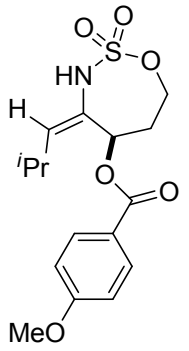
reaction was stirred at 0 °C until complete consumption of the starting material was observed by TLC, usually within 30 min (~30% EtOAc/hex or 100% $CH_2Cl_2$ solvent system, CAM stain). The reaction mixture was diluted with $CH_2Cl_2$ and washed twice with portions of saturated $NH_4Cl$ and NaCl solutions. The organic layer was dried over $Na_2SO_4$ and concentrated by rotary evaporation to yield a crude oil that is purified by silica gel chromatography to yield the (*E*)-enesulfamate typically as oils.




**Compound 1.** A 0.430 g portion of the homoallenic sulfamate (2.09 mmol) was subjected to aziridination/ring-opening conditions. The water-opened intermediate was purified by column chromatography (10-40% EtOAc in Hexanes) to yield 0.367 g product as a white solid (1.66 mmol, 79%). $^1$H NMR (500 MHz, $CDCl_3$) δ 6.59 (br s, 1H), 5.61 (d, *J* = 10.5 Hz, 1H), 4.94 (td, *J* = 3.2, 2.8 Hz, 1H), 4.72 (dd, *J* = 13.0, 12.5 Hz, 1H), 4.19 (dt, *J* = 13.0, 3.2 Hz, 1H), 2.55 (d sep, *J* = 10.5, 6.8 Hz, 1H), 2.52 (d, *J* = 3.2 Hz, 1H), 2.15 (ddt, *J* = 15.2, 12.5, 3.2 Hz, 1H), 2.04 (dt, *J* = 15.3, 2.8 Hz, 1H), 1.05 (d, *J* = 6.8 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 1H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 138.4, 129.2, 64.8, 64.0, 36.8, 26.7, 22.7, 22.7. HRMS (ESI) *m*/*z* calculated for $C_8H_{19}N_2O_4S$ [M+$NH_4^+$] 239.1061, found 239.1061.

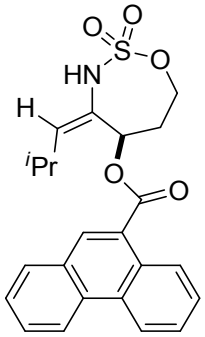


**Compound 2.** A portion of 0.267 g of the homoallenic sulfamate precursor (1.30 mmol) was subjected to aziridination conditions. After 2 h, 0.446 mL AcOH (7.80 mmol, 6 equiv) was added and the reaction was stirred overnight. The reaction mixture was then filtered through Celite and concentrated to yield a crude oil. Purification by column chromatography (5% to 25% EtOAc in hexanes) yielded the product as a white solid (0.234 g, 0.931 mmol, 72%). $^{1}$H NMR (500.0 MHz, $CDCl_3$) δ 6.01 (br s, 1H), 5.93 (t, *J* = 3.4 Hz, 1H), 5.79 (d, *J* = 10.5 Hz, 1H), 4.62 (dd, *J* = 13.1, 12.2 Hz, 1H), 4.23 (dt, *J* = 13.1, 3.4 Hz, 1H), 2.64 (d sep, *J* = 10.5, 6.6 Hz, 1H), 2.22 (ddt, *J* = 15.9, 12.2, 3.4 Hz, 1H), 2.10-2.15 (m, 4H), 1.06 (d, *J* = 6.6 Hz, 3H), 1.04 (d, *J* = 6.6 Hz, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 169.1, 143.0, 125.5, 66.8, 65.0, 34.7, 27.1, 22.6, 22.3, 21.1. HRMS (ESI) *m/z* calculated for $C_{10}H_{21}N_2O_5S$ [M+$NH_4^+$] 281.116, found 281.1164.



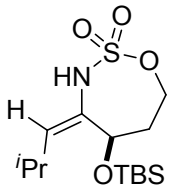

**Compound 3.** A portion of 0.267 g of the homoallenic sulfamate (1.30 mmol) was subjected to aziridination conditions. After 2 h, 0.297 g of *p*-anisic acid (1.95 mmol, 1.50 equiv) was added and the mixture filtered through Celite. The filtrate was concentrated and the residue redissolved in 1.3 mL of dry $CH_3CN$. The solution was heated to 50 °C for 1 h. The crude reaction mixture was then diluted with dichloromethane, washed with aqueous $NaHCO_3$, and concentrated. Purification of the crude residue by column chromatography (5 to 25% EtOAc in Hexanes) yielded the product as a white solid (0.316 g, 0.889 mmol, 68%). $^{1}$H NMR (500.0 MHz, $CDCl_3$)

δ 7.99 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.15 (t, *J* = 3.3 Hz, 1H), 6.12 (br s, 1H), 5.81 (d, *J* = 10.5 Hz, 1H), 4.74 (ddd, *J* = 13.1, 10.8, 1.4 Hz, 1H), 4.30 (dt, *J* = 13.1, 3.3 Hz, 1H), 3.89 (s, 3H), 2.73 (d sep, *J* = 10.5, 6.7 Hz, 1H), 2.25-2.38 (m, 2H), 1.09 (d, *J* = 6.7 Hz, 3H), 1.07 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ164.5, 164.0, 143.1, 131.8, 125.8, 121.3, 114.0, 67.0, 65.3, 55.5, 34.8, 27.2, 22.7, 22.4. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{25}N_2O_6S$ [M+$NH_4^+$] 373.1428, found 373.1436.

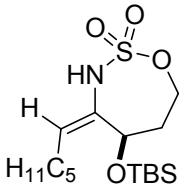



**Compound 4.** Silver triflate (0.565 g, 2.20 mmol, 2.2 equiv) was mixed with 10 mL of dry dichloromethane and the mixture cooled to 0 °C. A portion of 0.481 g of 9-phenanthroyl chloride (2.00 mmol, 1.0 equiv) was added and the slurry stirred for 30 min. The 9-phenanthroyl triflate solution was then cooled to -78 °C, and 0.433 g of **1** (2.00 mmol) was added in 5 mL dry dichloromethane containing 2,6-lutidine (0.255 mL, 2.20 mmol, 1.10 equiv). After stirring for 20 min, the cold bath was removed and the reaction warmed to room temperature for 30 min. The crude solution was filtered over Celite, washed with aqueous $NH_4Cl$, dried with $MgSO_4$ and concentrated to a crude oil. The residue was purified by column chromatography (6 to 30% EtOAc in hexanes) to give the product as an off-white solid (0.623 g, 1.46 mmol, 73%). $^1$H NMR (500.0 MHz, $CDCl_3$) δ 8.81 (d, *J* = 8.1 Hz, 1H), 8.76 (d, *J* = 7.9 Hz, 1H), 8.71 (d, *J* = 8.4 Hz, 1H), 8.42 (s, 1H), 8.02 (d, *J* = 7.9 Hz, 1H), 7.80 (t, *J* = 7.9 Hz, 1H), 7.67-7.76 (m, 3H), 6.32

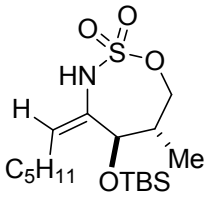
(t, $J$ = 3.1 Hz, 1H), 6.14 (br s, 1H), 5.89 (d, $J$ = 10.4 Hz, 1H), 4.80 (m, 1H), 4.36 (dt, $J$ = 13.2, 3.2 Hz, 1H), 2.83 (d sep, $J$ = 10.4, 6.5 Hz, 1H), 2.40-2.47 (m, 2H), 1.14 (app d, $J$ = 6.5 Hz, 6H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 165.7, 143.6, 132.6, 132.4, 130.8, 130.2, 129.7, 129.5, 128.7, 127.7, 127.3, 127.3, 126.1, 125.7, 125.1, 123.1, 122.7, 67.7, 65.4, 34.8, 27.4, 22.7, 22.5. HRMS (ESI) $m/z$ calculated for $C_{23}H_{26}NNaO_5S$ [M+Na$^+$] 448.1190, found 448.1190.




**Compound 5.** The general procedure was employed to convert 0.100 g of the precursor homoallenic sulfamate (0.487 mmol) to 0.119 g of enesulfamate as a clear oil (0.355 mmol, 73% yield) after silica gel chromatography (9:1 hexanes:EtOAc). $^1$H NMR (500.0 MHz, $CDCl_3$) δ 6.33 (br s, 1H), 5.60 (d, $J$ = 10.6 Hz, 1H), 4.83 (t, J = 2.8 Hz, 1H), 4.68 (t, $J$ = 12.7 Hz, 1H), 4.15 (dt, $J$ = 12.7, 2.8 Hz, 1H), 2.51 (m, 1H), 2.09 (ddt, $J$ = 15.1, 12.7, 2.8 Hz, 1H), 1.86 (dt, $J$ = 15.1, 2.8 Hz, 1H), 1.05 (d, $J$ = 6.6 Hz, 3H), 1.03 (d, $J$ = 6.4 Hz, 3H), 0.90 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H). 13C NMR (125.7 MHz, $CDCl_3$) δ 136.9, 129.4, 64.9, 64.5, 38.2, 26.8, 25.7, 22.8, 22.5, 18.1, -4.9, -5.1. HRMS (ESI) $m/z$ calculated for $C_{14}H_{30}NO_4SSi$ [M+H$^+$] 336.1660, found 336.1657.

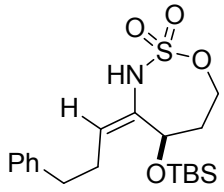


**Compound 10.** According to the general procedure, 1.51 g of the homoallenic sulfamate precursor (6.48 mmol) yielded 1.29 g of enesulfamate (3.55 mmol, 55% yield) after silica gel chromatography (0% to 15% EtOAc/hexane). The product was a colorless liquid that solidified upon storage in a 0 °C freezer. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 6.35 (s, 1H), 5.75 (t, 7.8 Hz, 1H), 4.81 (t, *J* = 3.0 Hz, 1H), 4.68 (t, *J* = 12.7 Hz, 1H), 4.16 (dt, *J* = 12.7, 3.0 Hz, 1H), 2.08 (m, 3H), 1.84 (dt, *J* = 15.0, 3.3 Hz, 1H), 1.47-1.39 (m, 2H), 1.36-1.26 (m, 4H), 0.92-0.88 (m, 12H), 0.10 (s, 3H), 0.08 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 131.2, 130.3, 64.7, 64.6, 37.7, 31.4, 28.7, 26.7, 25.7, 22.4, 18.1, 13.9, -4.9, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{37}N_2O_4SSi$ [M+$NH_4^+$] 381.2238, found 381.2248.

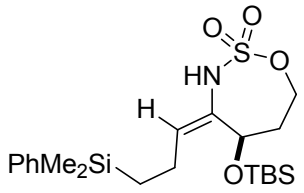



**Compound 12.** The compound was prepared by a modification of the general procedure. The homoallenic sulfamate precursor (2.00 g, 8.01 mmol), prepared as a 1.25:1 mixture of diastereomers, were subjected to the aziridination/water ring-opening conditions. After dilution with dichloromethane, drying, filtration, and concentration, the crude enesulfamate was purified by column chromatography on silica gel (10%-50% EtOAc in hexanes) to separate the *anti* and *syn* stereoisomers prior to silylation (1.67 g, 6.34 mmol, 79% yield, *dr* ~ 1.25:1 *anti*:*syn*). The silyl protection was performed on each individual alcohol using TBSOTf and 2,6-lutidine as outlined in the general procedure. Silylation of 0.770 g of the *anti*-isomer yielded 0.903 g (2.39 mmol, 82%) of **12** as a white solid. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 6.29 (s, 1H), 5.85 (dd, *J* = 8.3, 6.9 Hz, 1H), 4.75 (d, *J* = 12.9 Hz, 1H), 4.49 (d, *J* = 3.0 Hz, 1H), 3.92 (dd, *J* = 12.9, 2.6 Hz,

1H), 2.08 (m, 2H), 1.92 (m, 1H), 1.30-1.50 (m, 6H), 1.08 (d, $J$ = 7.3 Hz, 3H), 0.89 (m, 12H), 0.10 (s, 3H), 0.07 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 132.9, 128.9, 69.7, 68.9, 41.3, 31.5, 28.7, 27.5, 25.7, 22.4, 18.1, 13.9, 13.1, -4.9, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{39}N_2O_4SSi$ [M+$NH_4^+$] 395.2395, found 395.2384.

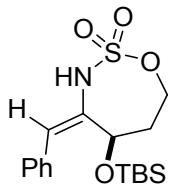



**Compound 13.** According to the general procedure, 2.50 g of the homoallenic sulfamate precursor (9.36 mmol) yielded 2.27 g of enesulfamate as a faint yellow liquid (5.70 mmol, 61% yield) after silica gel chromatography (10% to 40% EtOAc in hexane). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.30 (m, 2H), 7.22-7.16 (m, 3H), 6.33 (s, 1H), 5.80 (t, $J$ = 7.9 Hz, 1H), 4.66 (t, $J$ = 2.9 Hz, 1H), 4.60 (t, $J$ = 12.5 Hz, 1H), 4.04 (dt, $J$ = 12.5, 3.1 Hz, 1H), 2.75 (m, 2H), 2.44 (m, 1H), 2.34 (m, 1H), 1.65 (dt, $J$ = 15.0, 3.0 Hz, 1H), 1.55 (ddt, $J$ = 15.0, 12.0, 3.0 Hz, 1H), 0.87 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 140.7, 132.0, 129.0, 128.7, 128.6, 126.2, 64.6, 64.5, 37.3, 35.2, 29.3, 25.6, 18.1, -5.0, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{35}N_2O_4SSi$ [M+$NH_4^+$] 415.2082, found 415.2089.




**Compound 14.** According to the general procedure, 1.00 g of the homoallenic sulfamate precursor (3.07 mmol) yielded 0.918 g of enesulfamate as an oil (2.03 mmol, 66% yield) after

purification by silica gel chromatography (9:1 hexanes:EtOAc). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.37 (m, 3H), 6.30 (br s, 1H), 5.76 (dd, *J* = 8.3, 7.2 Hz, 1H), 4.62-4.68 (m, 2H), 4.12 (dt, *J* = 13.0, 3.2 Hz, 1H), 1.95-2.10 (m, 3H), 1.76 (dt, *J* = 15.0, 3.2 Hz, 1H), 0.82-0.89 (m, 10H), 0.28-0.32 (m, 7H), 0.04 (s, 3H), 0.02 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 138.2, 133.5, 132.5, 130.1, 129.1, 127.9, 64.5, 64.5, 37.7, 25.6, 21.1, 18.1, 15.7, -3.3, -3.3, -5.0, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{21}H_{41}N_2O_4SSi_2$ [M+$NH_4^+$] 473.2321, found 473.2321.




**Compound 15.** Due to the instability of the intermediate methylene aziridine, a modified procedure was used to access compound **15**. To a 100 mL roundbottom flask was added the homoallenic sulfamate precursor (598 mg, 2.50 mmol, 1 equiv) and rhodium (II) triphenylacetate (34.0 mg, 0.0251 mmol, 0.01 equiv, prepared according to the procedure of Huard and Lebel[6]). A portion of $CH_2Cl_2$ (25 mL, 0.1 M) was added, and the green solution was stirred for 2-3 min prior to addition of PhIO (1.10 g, 5.02 mmol, 2 equiv) in one portion at rt. The solution was stirred at rt for 30 min, at which point TLC (100% $CH_2Cl_2$, CAM stain) indicated complete consumption of the starting allene. The solution was filtered through a pad of Celite with $CH_2Cl_2$ and concentrated by rotary evaporation at room temperature (higher temperatures promoted product decomposition). The residue was dissolved in 15 mL $CH_3CN$ and cooled to 0 °C in an ethylene glycol/water bath cooled by a chiller. Water (15 mL) was added, and the mixture was stirred at 0 °C for two days (higher temperatures gave lower yields due to decomposition of the methylene aziridine). After two days, the mixture was poured into a beaker

and diluted five-fold with $CH_2Cl_2$. $Na_2SO_4$ was added, and the mixture was stirred until the cloudy solution turned transparent. The solution was decanted and concentrated by rotary evaporation. The residue was dissolved in 7 mL $CH_2Cl_2$, cooled to 0 °C and 2,6-lutidine (0.29 mL, 2.51 mmol, 1 equiv) was added slowly, followed by TBSOTf (0.58 mL, 2.51 mmol, 1 equiv). A TLC sample taken at 15 min (100% $CH_2Cl_2$, CAM stain) indicated incomplete reaction, so an additional 0.5 equiv of 2,6-lutidine and TBSOTf were added. After an additional 40 min at 0 °C, the reaction was quenched by the addition of a saturated solution of $NH_4Cl$. The mixture was extracted with $CH_2Cl_2$, the combined organic layers washed with saturated $NH_4Cl$ and brine. The organic layer was dried over $Na_2SO_4$, decanted and the volatiles removed under reduced pressure. Purification of the crude oil was attempted *via* silica gel chromatography (0% to 15% EtOAc in hexanes), but the product was contaminated with $Rh_2TPA_4$ and an unknown yellow oil. Pure product was obtained by recrystallization from a mixture of hexanes/EtOAc. The solid was heated in boiling hexanes, and small portions of EtOAc added gradually until complete dissolution was achieved. Upon cooling, the white solid was filtered and the recrystallization repeated to yield a combined 310.2 mg (0.838 mmol, 33%) of a white crystalline solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.36 (m, 3H), 7.18 (app d, $J$ = 7.0 Hz, 2H), 6.84 (s, 1H), 6.64 (bs, 1H), 4.91 (t, $J$ = 2.9 Hz, 1H), 4.79 (t, $J$ = 12.6 Hz, 1H), 4.27 (dt, $J$ = 12.6, 3.1 Hz, 1H), 2.37 (ddt, $J$ = 15.2, 12.5, 3.1 Hz, 1H), 1.95 (dt, $J$ = 15.2, 3.0 Hz, 1H), 0.83 (s, 9H), -0.06 (s, 3H), -0.07 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 133.7, 133.2, 130.1, 128.6, 128.5, 128.2, 64.8, 64.7, 38.1, 25.6, 18.0, -5.1, -5.2. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{31}N_2O_4SSi$ [M+$NH_4^+$] 387.1769, found 387.1768.

**V. Computational models for enesulfamates 5 and (*Z*)-5.**

The geometries for enesulfamate **5** and **(*Z*)-5** were optimized using a suite of Gaussian 09 software at B3LYP/6-31G(d) level of theory.[6]

Enesulfamate **5** RB3LYP Energy = -1594.27176634 Hartree.

Cartesian coordinates for enesulfamate **5**:

C 0.00000000 0.00000000 0.00000000

C -1.00001800 0.01710100 -1.14616600

N -0.98779600 -1.19354600 -1.92352300

S -2.08224000 -2.40756200 -1.49816600

O -2.14227500 -2.32269700 0.14254700

C -0.87813400 -2.29170000 0.85671200

C -0.47487400 -0.85707600 1.19038800

H 0.34284800 -0.89221200 1.92160200

H -1.32760700 -0.36140600 1.66972900

H -0.10616400 -2.82111100 0.28966000

H -1.06868100 -2.85617000 1.77253200

O -3.42355100 -2.04341000 -1.90831400

O -1.45158000 -3.65619400 -1.90891700

H -0.05726800 -1.60790700 -1.96418500

C -1.87822700 0.98073500 -1.45226800

C -2.12660500 2.27995800 -0.73085800

C -1.99328600 3.46514900 -1.70611000

H -2.71644800 3.37768000 -2.52618700

H -2.18352300 4.41407200 -1.19137900

H -0.99121100 3.51058900 -2.14704300

C -3.52415100 2.26383400 -0.07754600

H -4.30689800 2.13483400 -0.83448400

H -3.61957300 1.44292200 0.64077700

H -3.71457200 3.20733600 0.44752000

H -1.38481500 2.41117300 0.06749100

H -2.52399300 0.78988500 -2.30917700

O 1.24058000 -0.54668000 -0.46285500

Si 2.54732500 0.32503300 -1.10505400

C 2.19843600 0.75760300 -2.91021300

H 2.10554400 -0.13759100 -3.53589600

H 1.26200800 1.32000400 -3.00329100

H 2.99929700 1.37604800 -3.33337300

C 2.78761300 1.91835300 -0.11468800

H 2.86296400 1.72779400 0.96180600

H 3.70895000 2.42570800 -0.42525400

H 1.96540700 2.62609700 -0.27416200

C 4.03477800 -0.86186000 -0.92926300

C 3.72098400 -2.20383700 -1.62570500

H 2.85020800 -2.69796800 -1.18042600

H 3.52440300 -2.07505200 -2.69713300

H 4.57456500 -2.89053100 -1.53258000

C 5.28471000 -0.23297500 -1.58412000

H 6.14854000 -0.90401600 -1.47526500

H 5.14429300 -0.05752500 -2.65758100

H 5.55849200 0.72310600 -1.12038100

C 4.32400900 -1.12678100 0.56380100

H 5.16395300 -1.82794400 0.67169500

H 4.59673300 -0.20849600 1.09827900

H 3.45822800 -1.56744600 1.07121900

H 0.15528100 1.02047100 0.36685000

Enesulfamate **(*Z*)-5** RB3LYP Energy = -1594.27473013 Hartree

Cartesian coordinates for enesulfamate **(*Z*)-5**:

C 0.00000000 0.00000000 0.00000000

C -1.10981700 0.38327800 -0.96764000

N -1.22418700 -0.50186600 -2.09463300

S -2.24922200 -1.84107600 -1.97174300

O -2.14035100 -2.28275900 -0.39602300

C -0.81077000 -2.45758200 0.16470400

C -0.36415800 -1.19674800 0.89916800

H 0.51966700 -1.44545600 1.50049500

H -1.16175500 -0.89645600 1.58907000

H -0.10566200 -2.75864500 -0.61604500

H -0.91832200 -3.29068800 0.86305900

| | | | |
|---|---|---|---|
| O | -3.63386600 | -1.43409000 | -2.11359000 |
| O | -1.64908800 | -2.86196800 | -2.82220700 |
| H | -0.30673700 | -0.84381400 | -2.38158800 |
| C | -1.91032100 | 1.44344800 | -0.80631200 |
| H | -1.74097500 | 2.05410400 | 0.08326900 |
| C | -3.02795000 | 1.89915000 | -1.70571900 |
| C | -4.38551100 | 1.78478600 | -0.98528600 |
| H | -4.60136800 | 0.74519800 | -0.72377500 |
| H | -4.40086800 | 2.38748200 | -0.06756400 |
| H | -5.19068600 | 2.14665100 | -1.63532400 |
| C | -2.76768900 | 3.34499400 | -2.17024500 |
| H | -1.82189100 | 3.42548000 | -2.71755700 |
| H | -3.57274600 | 3.68526500 | -2.83170400 |
| H | -2.72448900 | 4.03470500 | -1.31698700 |
| H | -3.05283200 | 1.24449600 | -2.58258300 |
| O | 1.16938300 | -0.35510200 | -0.74930000 |
| Si | 2.49746800 | 0.65653200 | -1.04631400 |
| C | 1.95786300 | 2.14048700 | -2.08315100 |
| H | 1.57417800 | 1.83771700 | -3.06388200 |
| H | 1.16110800 | 2.70148200 | -1.58076800 |
| H | 2.79288000 | 2.83187400 | -2.24900100 |
| C | 3.19206300 | 1.27380000 | 0.60096300 |
| H | 3.48172300 | 0.44710700 | 1.25916800 |

H 4.07988100 1.89690200 0.43852300

H 2.46501000 1.89127500 1.14242300

C 3.73753300 -0.46288700 -1.97271000

C 3.10339300 -0.99648600 -3.27569600

H 2.21324500 -1.60435800 -3.07605700

H 2.81470500 -0.18680700 -3.95698300

H 3.81917000 -1.63392600 -3.81405200

C 5.00403200 0.34905800 -2.32464000

H 5.72759200 -0.28722300 -2.85359500

H 4.78138800 1.19958100 -2.98077200

H 5.50802700 0.73689400 -1.43059700

C 4.13459900 -1.66113200 -1.08363800

H 4.83564200 -2.31716400 -1.61910300

H 4.63059000 -1.34051200 -0.15939800

H 3.26236500 -2.26336000 -0.80582500

H 0.20477000 0.85848700 0.65359200

**VI. Preparation of dimethyldioxirane (DMDO).** Dimethyldioxirane was prepared as a solution in acetone using a variation on the procedure of Murray and Singh,[7] then extracted into $CH_2Cl_2$ according to the procedure of Messeguer.[8,9] A 2 L, three-necked, roundbottom flask equipped with a magnetic stir bar was charged with water (160 mL), acetone (100 mL) and sodium bicarbonate (192 g). The flask was fitted with a pressure-equalizing addition funnel containing water (120 mL) and acetone (120 mL) and an air condenser. The outlet of the air

condenser was attached to a receiving flask (cooled in a dry ice/acetone bath) and a dry ice/acetone trap. The dry ice/acetone trap was connected using Tygon tubing (not rubber) to an oil bubbler capable of carefully monitoring gas flow. Oxone (monopersulfate compound, 360 g total) was added portionwise to the stirred solution over ~30 minutes while the acetone/water mixture was simultaneously added to the flask in a dropwise fashion. A yellow solution of dimethyldioxirane in acetone collected in the receiving flask throughout the course of the addition. Vigorous stirring was continued for an additional 15 min while a slight vacuum (ca. 30 mm using a water aspirator) was applied to the cold trap. Approximately 100 mL of a yellow DMDO-acetone (0.05 – 0.1 M) solution was obtained that could be stored for several months at -70 °C or 1-2 weeks at 0 °C.

Extraction of DMDO into $CH_2Cl_2$: The freshly distilled DMDO solution in acetone (cooled to at least 0 °C) was diluted with an equal volume of cold water (the solution bubbles vigorously upon addition) and transferred to a separatory funnel. The solution was extracted four times with $CH_2Cl_2$ (4 x 1/20$^{th}$ of the initial volume of the acetone solution). The first extract typically could not be separated and was collected with the second extract. The combined extracts were washed five times with cold 0.01 M phosphate buffer, pH 7.0 (1.5 volume with respect to the volume to be washed) to remove excess acetone and water. The remaining solution was stored over $Na_2SO_4$ in a roundbottom flask sealed with a glass stopper. The flask was stored in a -70 ºC freezer (decomposition of the DMDO occurs more readily at 0 ºC, but it is typically stable for at least a week).

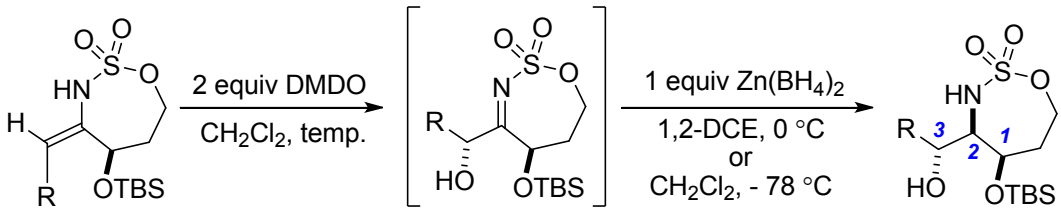
Titration of the DMDO/$CH_2Cl_2$ solution: The concentration of DMDO in solution was measured by the oxidation of a known amount of thioanisole to methyl phenyl sulfoxide (and a minor amount of methyl phenyl sulfone). In a typical titration, 10.0 mg (0.0805 mmol) of thioanisole is

added to a 2 mL screw cap flask equipped with a stir bar. $CH_2Cl_2$ (0.5 mL) is added, and then DMDO (~0.25 M in $CH_2Cl_2$ if prepared by the above method, 0.1 mL, ~0.025 mmol) is added. The solution is stirred at rt for 1 h, then concentrated by rotary evaporation at rt. A crude $^1H$ NMR in $CDCl_3$ is taken with a relaxation delay (d1) of at least 5 s. Comparison of the ratio of thioanisole (~2.5 ppm) to methyl phenyl sulfoxide (~2.8 ppm) and methyl phenyl sulfone (~3.0 ppm), and based on the known mass of starting thioanisole, the concentration of the DMDO solution can be determined (typically 0.2 – 0.3 M).

**VII. Determination of *dr* for reaction of -OTBS protected enesulfamates with DMDO.**

General procedure: The purified (*E*)-enesulfamate (1 equiv) is added to a roundbottom flask and the flask is cooled to the specified temperature (see Tables 1, 2 and 5 in the manuscript). A solution of DMDO in $CH_2Cl_2$ (2 equiv) is added, the flask is capped and the solution stirred until complete consumption of the starting material is observed by TLC (~30% EtOAc/hex, CAM stain). At this point, the solution is concentrated by rotary evaporation and the ratio of the imine diastereomers is measured by crude $^1H$ NMR in $CDCl_3$.

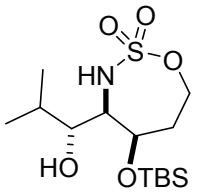
**VIII. Synthesis of 1,2-*syn*:2,3-*anti* stereotriads.**



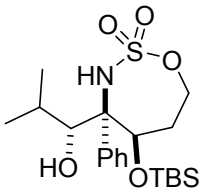

General procedure A: The appropriate (*E*)-enesulfamate (1 equiv) is added to a roundbottom flask and cooled to the specified temperature (see the individual entries for temperature). DMDO is added (2 equiv as a solution in $CH_2Cl_2$), the flask is capped and the resulting solution

stirred at the specified temperature until complete consumption of the starting material was indicated by TLC (~ 30% EtOAc/hex, CAM stain). The solution is concentrated by rotary evaporation at room temperature, and 1,2-dichloroethane (0.05 - 0.1 M) is added. The solution is cooled to 0 °C, and 1 equiv of $Zn(BH_4)_2$ (0.5 M in THF, prepared according to the procedure of Narasimhan and Balakumar)[10] is added *via* syringe. The reaction is stirred at 0 °C until the reaction is complete and then quenched by the addition of a saturated solution of $NH_4Cl$. The mixture is transferred to a separatory funnel, diluted with additional $CH_2Cl_2$, then washed twice with saturated $NH_4Cl$ and once with brine. The organic layer is dried over $Na_2SO_4$ and concentrated by rotary evaporation to give a crude oil, which is purified by silica gel chromatography to give the desired 1,2-*syn*;2,3-*anti* stereotriad, along with minor diastereomers. The *dr* and yield for the reaction are calculated based on the isolated masses of each diastereomer. As a rule, the isolated *dr* closely matches the *dr* of the crude material, as measured by $^1H$ NMR.

General procedure B: The reaction is run in a fashion identical to procedure A until completion of the DMDO oxidation. The reaction mixture is concentrated under vacuum at rt and $CH_2Cl_2$ added to the residue. The solution is cooled to -78 °C in an acetone/dry ice bath and 1 equiv of $Zn(BH_4)_2$ (0.5 M in THF) added. The mixture is stirred under TLC indicates complete consumption of the starting material, at which point the reaction is quenched by the addition of a saturated solution of $NH_4Cl$. Workup, purification, and determination of product yield and *dr* are performed in a manner identical to that described in General Procedure A.

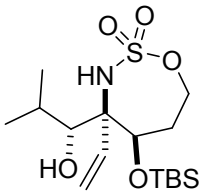



**Compound 21.** A portion of 0.500 g of enesulfamate **5** (1.49 mmol) was subjected to General Procedure A, using 1.5 equiv DMDO in $CH_2Cl_2$ at 25 °C over 2.5 hours. This yielded 0.423 g of the stereotriad **21** as an oil (1.20 mmol, 80% yield) after silica gel chromatography (4-20% EtOAc in hexanes). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.22 (d, *J* = 10.4 Hz, 1H), 4.58 (app t, *J* = 12.5 Hz, 1H), 4.56 (s, 1H), 4.16 (dt, *J* = 12.5, 3.1 Hz, 1H), 3.22-3.32 (m, 2H), 2.22 (sep d, *J* = 7.1, 1.9 Hz, 1H), 2.12 (ddt, *J* = 15.3, 12.5, 3.1 Hz, 1H), 1.89 (dt, *J* = 15.3, 3.1 Hz, 1H), 1.33 (d, *J* = 5.2 Hz, 1H), 1.00 (d, *J* = 7.1 Hz, 1H), 0.91-0.94 (m, 12H), 0.12 (s, 3H), 0.12 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 73.7, 65.7, 64.3, 57.8, 36.7, 28.2, 25.8, 20.2, 18.0, 13.4, -4.4, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{35}N_2O_5SSi$ [M+$NH_4^+$] 371.2031, found 371.2031.



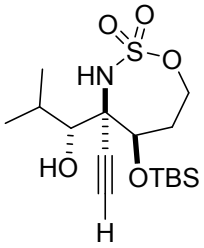

**Compound 22.** A portion of 0.100 g of enesulfamate **5** (0.298 mmol) was oxidized using 1.5 equiv DMDO in $CH_2Cl_2$ at 25 °C over 2.5 hours. After concentration, the crude imine was dissolved in 3.0 mL dry 1,2-dichloroethane, and the solution was cooled to 0 °C. 0.373 mL PhMgCl (2.0 M in THF, 0.745 mmol, 2.5 equiv) was injected and the solution was stirred for 1 hour. Workup was performed as described in General Procedure A. This yielded 0.108 g of the stereotriad **22** as a white solid (0.251 mmol, 84% yield) after silica gel chromatography (4-20% EtOAc in Hexanes). $^1$H NMR (500.0 MHz, $CDCl_3$) δ 7.30-7.70 (m, 5H), 5.16 (d, *J* = 5.7 Hz,

1H), 5.04 (s, 1H), 4.73 (td, *J* = 12.2, 1.0 Hz, 1H), 4.03 (dt, *J* = 12.2, 3.4 Hz, 1H), 3.44 (dd, *J* = 10.4, 2.0 Hz, 1H), 2.41 (dddd, *J* = 15.9, 12.2, 3.4, 1.0 Hz, 1H), 2.12 (sep d, *J* = 6.9, 2.0 Hz, 1H), 1.84 (m, 1H), 1.26 (d, *J* = 10.4 Hz, 1H), 1.00 (s, 9H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.22 (s, 3H), 0.19 (s, 3H), 0.06 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 133.7, 128.1, 128.1, 128.1, 77.7, 71.6, 70.2, 65.1, 31.7, 27.1, 25.9, 23.8, 18.2, 15.4, -4.2, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{20}H_{39}N_2O_5SSi$ [M+$NH_4^+$] 447.2344, found 447.2339.



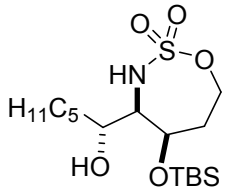

**Compound 23.** A portion of 0.0500 g of enesulfamate **5** (0.149 mmol) was oxidized using 2.0 equiv DMDO in $CH_2Cl_2$ at 25 °C over 2.0 hours. After concentration, the crude imine was dissolved in 1.5 mL dry diethyl ether, and the solution was cooled to -78 °C. 0.447 mL vinylmagnesium bromide (1.0 M in THF, 0.447 mmol, 3.0 equiv) was injected and the solution was stirred for 30 minutes. Workup was performed as described in General Procedure A. This yielded 0.0417 g of the stereotriad **23** as a colorless oil (0.110 mmol, 74% yield) after silica gel chromatography (4-20% EtOAc in Hexanes) along with 5.0 mg of a separable minor diastereomer (0.013 mmol, 9% yield). Major Isomer: $^1$H NMR (500.0 MHz, $CDCl_3$) δ 6.56 (dd, *J* = 18.4, 12.0 Hz, 1H), 5.46 (d, *J* = 12.0 Hz, 1H), 5.17 (br s, 1H), 5.13 (d, *J* = 18.4 Hz, 1H), 4.55-4.67 (m, 2H), 4.10 (dt, *J* = 12.8, 3.3 Hz, 1H), 3.33 (dd, *J* = 11.1, 3.7 Hz, 1H), 2.56 (dddd, *J* = 15.7, 12.8, 3.3, 2.0 Hz, 1H), 2.11 (sep d, *J* = 6.9, 3.7 Hz, 1H), 1.68 (dt, *J* = 15.7, 3.3 Hz, 1H), 1.47 (d, *J* = 11.1 Hz, 1H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.94 (s, 9H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.16 (s, 3H), 0.13 (s, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 132.9, 117.9, 77.3, 69.2, 67.9, 64.4, 32.1,

28.7, 25.9, 22.8, 18.1, 17.7, -4.5, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{34}NO_5SSi$ [M+H$^+$] 380.1922, found 380.1925. Minor Diastereomer: $^1$H NMR (400.2 MHz, $CDCl_3$) δ 5.85 (dd, *J* = 17.3, 10.8 Hz, 1H), 5.34 (d, *J* = 17.3 Hz, 1H), 5.30 (d, *J* = 10.8 Hz, 1H), 5.06 (br s, 1H), 4.63 (app t, *J* = 11.9 Hz, 1H), 4.36 (d, *J* = 5.2 Hz, 1H), 4.28 (br s, 1H), 4.15 (ddd, *J* = 11.9, 4.0, 3.0 Hz, 1H), 2.51 (m, 1H), 2.13 (sep d, *J* = 6.8, 1.3 Hz, 1H), 1.89 (dt, *J* = 15.6, 4.7 Hz, 1H), 1.58 (s, 1H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H). HRMS (ESI) *m*/*z* calculated for $C_{16}H_{37}N_2O_5SSi$ [M+NH$_4^+$] 397.2187, found 397.2187.

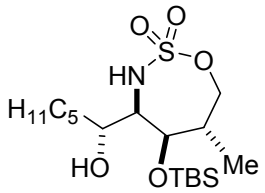



**Compound 24.** 0.100 g of enesulfamate **5** (0.298 mmol) was oxidized using 2.0 equiv DMDO in $CH_2Cl_2$ at 25 °C over 2.0 hours. After concentration, the crude imine was dissolved in 3.0 mL dry THF, and the solution was cooled to 0 °C. 1.79 mL ethynylmagnesium bromide (0.5 M in THF, 0.894 mmol, 3.0 equiv) was injected and the solution was stirred for 60 minutes. Workup was performed as described in General Procedure A. This yielded 0.0906 g of the stereotriad **24** as a colorless oil (0.240 mmol, 81% yield) after silica gel chromatography (4-20% EtOAc in Hexanes) along with 12.0 mg of a separable minor diastereomer (0.0318 mmol, 11% yield). Major Isomer: $^1$H NMR (500.0 MHz, $CDCl_3$) δ 5.16 (br s, 1H), 4.63 (app t, *J* = 12.6 Hz, 1H), 4.49 (dd, *J* = 4.3, 1.8 Hz, 1H), 4.18 (dt, *J* = 12.6, 3.0 Hz, 1H), 3.28 (dd, *J* = 11.3, 4.0 Hz, 1H), 2.80 (s, 1H), 2.73 (dddd, *J* = 16.0, 12.6, 3.0, 1.8 Hz, 1H), 2.25 (sep d, *J* = 6.9, 4.0 Hz, 1H), 1.78 (dt, *J* = 16.0, 4.3 Hz, 1H), 1.66 (d, *J* = 11.3 Hz, 1H), 1.07 (d, *J* = 6.9 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 81.5, 76.4, 75.1,

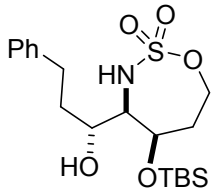
70.6, 64.1, 62.1, 33.3, 29.8, 25.8, 22.1, 18.0, 16.7, -4.5, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{35}N_2O_5SSi$ [M+$NH_4^+$] 395.2031, found 395.2036. Minor Isomer: $^1$H NMR (500.0 MHz, $CDCl_3$) δ 5.62 (br d, *J* = 10.8 Hz, 1H), 4.62-4.69 (m, 1H), 4.16 (dt, *J* = 12.8, 3.2 Hz, 1H), 3.55 (d, *J* = 10.8 Hz, 1H), 2.49 (s, 1H), 2.14 (s, 1H), 2.04-2.14 (m, 2H), 1.92 (dt, *J* = 15.7, 3.2 Hz, 1H), 1.05-1.10 (2 x d, *J* = 6.9 Hz, 6H), 0.93 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 82.9, 75.7, 74.6, 65.5, 64.3, 58.6, 37.3, 35.3, 26.0, 18.1, 17.5, 16.2, -3.8, -4.0. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{35}N_2O_5SSi$ [M+$NH_4^+$] 395.2031, found 395.2015.




**Compound 25.** A portion of 0.150 g of the enesulfamate **11** (0.413 mmol) was subjected to General Procedure A using 4.0 equiv of DMDO in $CH_2Cl_2$ at -20 °C. The stereotriad **25** was isolated as an oil (0.108 g, 0.283 mmol, 68%) along with the separable 1,2-*anti*:2,3-*anti* isomer (21.2 mg, 0.0556 mmol, 13%) after silica gel chromatography (4-20% EtOAc in hexanes). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.29 (d, *J* = 10.6 Hz, 1H), 4.58 (m, 2H), 4.16 (dt, *J* = 12.9, 2.9 Hz, 1H), 3.37 (m, 1H), 3.13 (t, *J* = 10.6 Hz, 1H), 2.11 (ddt, *J* = 15.2, 12.6, 2.3 Hz, 1H), 1.95 (app t, *J* = 12.6 Hz, 1H), 1.88 (dt, *J* = 15.2, 3.7 Hz, 1H), 1.52 (m, 1H), 1.44 (m, 1H), 1.43 (d, *J* = 5.4 Hz, 1H), 1.32 (m, 5H), 0.92 (s, 9H), 0.90 (t, *J* = 6.7 H, 3H), 0.13 (s, 3H), 0.12 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 69.9, 65.3, 64.3, 60.5, 36.7, 33.9, 31.6, 25.8, 24.7, 22.5, 18.0, 14.0, -4.4, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{36}NO_5SSi$ [M+$H^+$] 382.2078, found 382.2068.

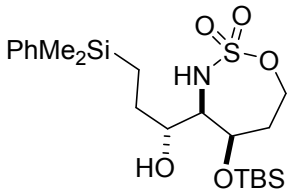



**Compound 26**. 0.100 g of the enesulfamate **12** (0.265 mmol) was subjected to General Procedure A using 2.5 equiv DMDO at 25 °C over 5.5 hours. This yielded 0.0776 g of stereotriad **26** as an oil (0.196 mmol, 74% yield) after purification by silica gel chromatography (4-20% EtOAc in hexanes). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 5.25 (d, *J* = 10.1 Hz, 1H), 4.66 (d, *J* = 12.9 Hz, 1H), 4.23 (d, *J* = 3.0 Hz, 1H), 3.96 (dd, *J* = 12.9, 3.0 Hz, 1H), 3.36 (m, 1H), 3.13 (app t, *J* = 10.1 Hz, 1H), 1.85-2.00 (m, 2H), 1.22-1.60 (m, 8H), 1.14 (d, *J* = 7.4 Hz, 3H), 0.92 (s, 9H), 0.90 (t, *J* = 6.1 Hz, 3H), 0.12 (s, 3H), 0.11 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 70.3, 69.6, 68.4, 56.3, 39.4, 34.0, 31.6, 25.8, 24.8, 22.5, 18.0, 14.0, 13.3, -4.5, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{41}N_2O_5SSi$ [M+$NH_4^+$] 413.2500, found 413.2520.



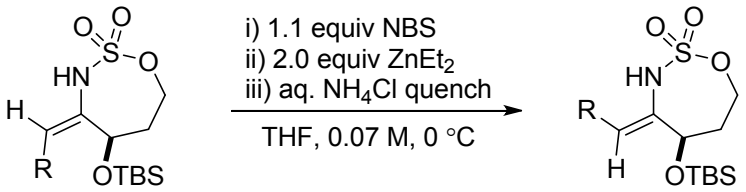

**Compound 27.** The enesulfamate **13** (67.7 mg, 0.170 mmol, 1 equiv.) was subjected to General Procedure B using 2.5 equiv. DMDO at 40 °C over 70 minutes. This yielded 56.6 mg of stereotriad **27** and a minor diastereomer (0.136 mmol, 80%) as an inseparable mixture after purification by silica gel chromatography (5% to 30% EtOAc in hexanes). The diastereomers were eventually separated by silica gel chromatography on a Combiflash RF (0% to 5% MeOH in $CH_2Cl_2$). Major diastereomer: $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.20 (m, 3H), 5.23 (d, *J* = 10.7 Hz, 1H), 4.55 (t, *J* = 12.5 Hz, 1H), 4.54 (app t, *J* = 3.0 Hz, 1H), 4.15 (dt, *J* =

12.5, 3.1 Hz), 3.34 (m, 1H), 3.17 (app t, $J$ = 10.7 Hz, 1H), 2.87 (ddd, $J$ = 13.7, 8.5, 5.3 Hz, 1H), 2.72 (dt, $J$ = 13.7, 8.2 Hz, 1H), 2.31 (dtd, $J$ = 14.7, 8.4, 2.4 Hz, 1H), 2.09 (ddt, $J$ = 15.2, 12.4, 2.7 Hz, 1H), 1.86 (dt, $J$ = 15.7, 3.5 Hz, 1H), 1.78 (dtd, $J$ = 14.2, 8.2, 5.5 Hz, 1H), 1.36 (d, $J$ = 5.8 Hz, 1H), 0.85 (s, 9H), 0.07 (s, 3H), 0.02 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 141.0, 128.6, 128.5, 126.2, 69.0, 65.2, 64.4, 60.3, 36.7, 35.3, 31.3, 25.7, 17.9, -4.4, -5.0. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{37}N_2O_5SSi$ [M+$NH_4^+$] 433.2187, found 433.2196.

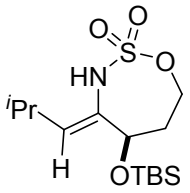



**Compound 28.** The enesulfamate **14** (0.0500 g, 0.110 mmol, 1.0 equiv) was subjected to General Procedure A using 4.0 equiv of DMDO in $CH_2Cl_2$ at -20 °C. The stereotriad **28** was isolated as an oil (0.0288 g, 0.0616 mmol, 56%) along with the separable 1,2-*anti*:2,3-*anti* isomer (8.3 mg, 0.0176 mmol, 16%) after silica gel chromatography (4-20% EtOAc in hexanes). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.52 (m, 2H), 7.36 (m, 3H), 5.23 (d, $J$ = 10.8 Hz, 1H), 4.56 (app t, $J$ = 12.6 Hz, 1H), 4.54 (t, $J$ = 3.1 Hz, 1H), 4.14 (dt, $J$ = 12.6, 3.1 Hz, 1H), 3.33 (m, 1H), 3.16 (app t, $J$ = 10.8 Hz, 1H), 2.08 (ddt, $J$ = 15.3, 12.6, 3.1 Hz, 1H), 1.83-1.92 (m, 2H), 1.50-1.63 (m, 1H), 1.42 (br d, $J$ = 5.4 Hz, 1H), 0.88-0.98 (m, 10H), 0.67 (td, $J$ = 13.2, 4.4 Hz, 1H), 0.30 (s, 3H), 0.30 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 138.7, 133.6, 129.0, 127.9, 71.1, 65.4, 64.3, 59.4, 36.7, 27.8, 25.8, 18.0, 9.4, -3.2, -3.3, -4.5, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{21}H_{43}N_2O_5SSi_2$ [M+$NH_4^+$] 491.2426, found 491.2424.

## IX. *E*/*Z* Isomerization of enesulfamates.

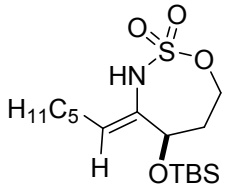



General procedure: The appropriate (*E*)-enesulfamate is added to a roundbottom flask and enough THF added to prepare a 0.07 M solution. The solution is cooled to 0 °C, and N-bromosuccinimide (1.1 equiv) added in one portion. The reaction mixture is stirred for 15 min and $ZnEt_2$ (1.0 M in hexane, 2 equiv) added *via* syringe. The solution is stirred at 0 °C for an additional 20 min and the reaction quenched by the addition of a saturated solution of $NH_4Cl$. (Note: reaction monitoring with TLC is generally not necessary for this reaction.) The mixture is transferred to a separatory funnel, diluted with $CH_2Cl_2$ and washed twice with saturated $NH_4Cl$ and once with brine. The organic layer is dried over $Na_2SO_4$ and concentrated by rotary evaporation to yield the (*Z*)-isomer as a crude oil. The product can be purified by silica gel chromatography or used as the crude material due to the clean and high-yielding nature of the reaction. In this instance, the yield of the (*Z*)-isomer was determined by $^1H$ NMR with mesitylene as an internal standard, and the material used in subsequent transformations as a solution of known concentration in $CDCl_3$.

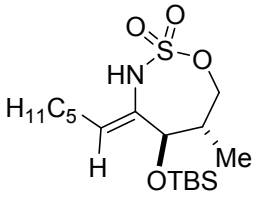


**Compound (*Z*)-5.** The (*E*)-enesulfamate **5** (0.500 g, 1.49 mmol, 1.0 equiv) was subjected to the general procedure to provide **(*Z*)-5** (0.483 g, 1.44 mmol, 97% yield) as a white solid after chromatography (10% EtOAc in hexanes). $^1H$ NMR (500 MHz, $CDCl_3$) δ 6.01 (br s, 1H), 5.33

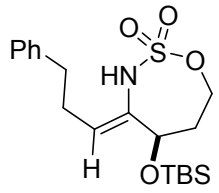
(d, $J$ = 10.2 Hz, 1H), 4.67 (app t, $J$ = 12.9 Hz, 1H), 4.37 (t, $J$ = 2.4 Hz, 1H), 4.17 (dt, $J$ = 12.9, 2.4 Hz, 1H), 3.05 (d sep, $J$ = 10.2, 6.6 Hz, 1H), 2.17 (ddt, $J$ = 14.9, 12.9, 2.4 Hz, 1H), 1.85 (dt, $J$ = 14.9, 2.4 Hz, 1H), 1.03 (d, $J$ = 6.6 Hz, 3H), 0.95 (d, $J$ = 6.6 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 138.0, 129.0, 71.1, 64.7, 38.3, 26.1, 25.7, 22.3, 21.9, 18.1, -5.0. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{33}N_2O_4SSi$ [M+$NH_4^+$] 353.1925, found 353.1913.



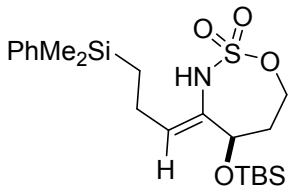

**Compound (*Z*)-11.** The (*E*)-enesulfamate **11** (0.300 g, 0.824 mmol, 1.0 equiv) was subjected to the general procedure to provide **(*Z*)-11** (0.763 mmol, 97% yield by $^1$H NMR with a mesitylene standard). The product was not purified further and was used in later reactions as a 0.25 M solution in $CDCl_3$. $^1$H NMR (500 MHz, $CDCl_3$) δ 6.08 (s, 1H), 5.55 (dd, $J$ = 8.9, 5.8 Hz, 1H), 4.67 (t, $J$ = 12.6 Hz, 1H), 4.42 (t, $J$ = 3.2 Hz, 1H), 4.17 (dt, $J$ = 12.6, 3.3 Hz, 1H), 2.44 (m, 1H), 2.18 (m, 2H), 1.85 (dt, $J$ = 15.0, 3.6 Hz, 1H), 1.42 (m, 1H), 1.30 (m, 5H), 0.89 (s, 9H), 0.88 (t, $J$ = 6.9 Hz, 3H), 0.09 (s, 3H), 0.06 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 131.0, 71.0, 64.7, 38.2, 31.3, 28.3, 26.5, 25.6, 22.4, 18.1, 14.0, -5.0, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{37}N_2O_4SSi$ [M+$NH_4^+$] 381.2238, found 381.2224.



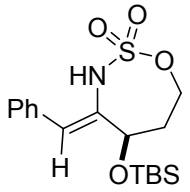
**Compound (*Z*)-12.** The (*E*)-enesulfamate **12** (0.983 g, 2.60 mmol, 1.0 equiv) was subjected to the general procedure to provide the (*Z*)-isomer **(*Z*)-12** (0.779 g, 2.06 mmol, 79%) as a colorless oil after chromatography (10% EtOAc in hexanes). $^1$H NMR (500 MHz, $CDCl_3$) δ 6.02 (br s, 1H), 5.47 (dd, *J* = 8.0, 5.9 Hz, 1H), 4.74 (d, *J* = 12.9 Hz, 1H), 3.99 (d, *J* = 3.0 Hz, 1H), 3.93 (dd, *J* = 12.9, 2.7 Hz, 1H), 2.45 (app dq, *J* = 15.0, 8.0 Hz, 1H), 2.26 (dtq, *J* = 15.0, 8.0, 5.9 Hz, 1H), 1.84 (m, 1H), 1.25-1.48 (m, 6H), 1.06 (d, *J* = 7.2 Hz, 3H), 0.85-0.91 (m, 12H), 0.08 (s, 3H), 0.06 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 133.0, 128.3, 76.5, 68.8, 40.2, 31.4, 28.4, 26.7, 25.7, 22.4, 18.1, 14.0, 13.3, -5.0, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{39}N_2O_4SSi$ [M+$NH_4^+$] 395.2395, found 395.2405.




**Compound (*Z*)-13.** The (*E*)-enesulfamate **13** (1.00 g, 2.51 mmol, 1.0 equiv) was subjected to the general procedure to provide **(*Z*)-13** (2.23 mmol, 89% yield by $^1$H NMR with a mesitylene standard). The product was not purified further and was used in later reactions as a 0.74 M solution in $CDCl_3$. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.27 (m, 2H), 7.19 (m, 3H), 6.05 (bs, 1H), 5.52 (app dd, *J* = 8.1, 6.1 Hz, 1H), 4.66 (t, *J* = 12.9 Hz, 1H), 4.36 (t, *J* = 3.1 Hz, 1H), 4.17 (dt, *J* = 12.9, 3.3 Hz, 1H), 2.76 (m, 2H), 2.67 (m, 1H), 2.60 (m, 1H), 2.14 (ddt, *J* = 15.0, 12.0, 3.0, 1H), 1.83 (dt, *J* = 15.0, 3.5 Hz, 1H), 0.86 (s, 9H), 0.03 (s 3H), -0.02 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 141.1, 131.7, 129.5, 128.5, 128.4, 126.0, 70.9, 64.8, 38.3, 34.7, 28.1, 25.7, 18.1, -5.06, -5.07. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{35}N_2O_4SSi$ [M+$NH_4^+$] 415.2082, found 415.2086.



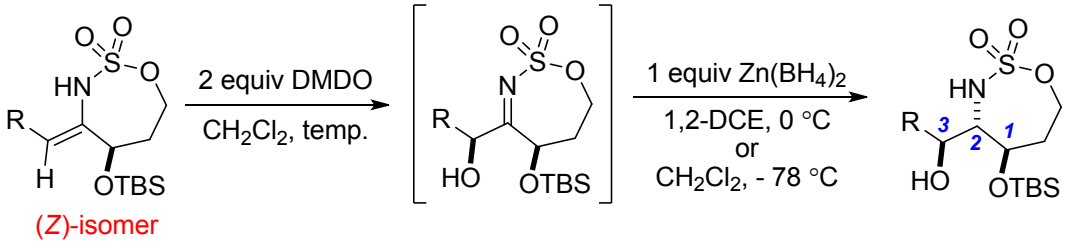

**Compound (*Z*)-14.** The (*E*)-enesulfamate **14** (0.810 g, 1.78 mmol, 1.0 equiv) was subjected to the general procedure, providing the product **(*Z*)-14** (0.690 g, 1.51 mmol, 85%) after chromatography (10% EtOAc in hexanes) as a colorless oil that solidified upon standing. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.35 (m, 3H), 6.01 (br s, 1H), 5.51 (t, *J* = 7.2 Hz, 1H), 4.66 (t, *J* = 12.4 Hz, 1H), 4.35 (t, *J* = 3.2 Hz, 1H), 4.15 (dt, *J* = 12.4, 3.2 Hz, 1H), 2.26-2.42 (m, 2H), 2.12 (ddt, *J* = 15.1, 12.4, 3.2 Hz, 1H), 1.82 (dt, *J* = 15.1, 3.2 Hz, 1H), 0.82-0.92 (m, 10H), 0.76 (ddd, *J* = 14.4, 11.1, 5.8 Hz, 1H), 0.30 (s, 3H), 0.29 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 139.1, 133.6, 133.3, 129.8, 128.9, 127.8, 71.0, 64.7, 38.2, 25.7, 21.2, 18.1, 15.0, -3.2, -3.2, -5.0. HRMS (ESI) *m/z* calculated for $C_{21}H_{41}N_2O_4SSi_2$ [M+$NH_4^+$] 474.2399, found 474.2391.




**Compound (*Z*)-15.** The (*E*)-enesulfamate **15** (20.1 mg, 0.0543 mmol, 1.0 equiv) was subjected to the general procedure to provide **(*Z*)-15** (0.0535 mmol, 98% yield by $^{1}$H NMR with a mesitylene standard). The product was not purified further and was used in later reactions as a 0.0535 M solution in $CDCl_3$. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.64 (app d, *J* = 7.4 Hz, 1H), 7.36 (app t, *J* = 7.4 Hz, 1H), 7.29 (app tt, *J* = 7.4, 1.2 Hz, 1H), 6.41 (bs, 1H), 6.30 (s, 1H), 4.66 (m, 2H), 4.30 (ddd, *J* = 12.6, 5.9, 3.0 Hz, 1H), 2.26 (ddt, *J* = 15.1, 9.7, 2.7, 1H), 2.04 (dtd, *J* = 15.1,

5.8, 1.8, 1H), 0.93 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 133.3, 131.9, 129.3, 128.5, 128.4, 122.2, 71.4, 65.9, 38.4, 25.7, 18.1, -4.9. -5.0. HRMS (ESI) *m/z* calculated for $C_{17}H_{31}N_2O_4SSi$ [M+$NH_4^+$] 387.1769, found 387.1762.

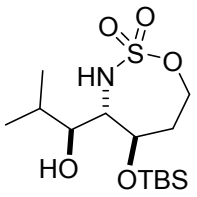
**X. Synthesis of 1,2-*anti*:2,3-*anti* stereotriads.**




General procedure A: The appropriate (*Z*)-enesulfamate is added to a roundbottom flask and cooled to the desired temperature (see the individual entries). DMDO is added to the flask (2 equiv as a solution in $CH_2Cl_2$), the flask capped and the solution stirred until TLC indicates complete consumption of the starting material (30% EtOAc/hex, CAM stain). Upon completion of the reaction, the solution is concentrated by rotary evaporation at rt and 1,2-dichloroethane (0.05 – 0.1 M) is added. The solution is cooled to 0 °C and 1 equiv of $Zn(BH_4)_2$ (0.5 M in THF) is added *via* syringe. The reaction is stirred at 0 °C until TLC indicates complete consumption of the starting material and then quenched by the addition of a saturated solution of $NH_4Cl$. The mixture is transferred to a separatory funnel, diluted with additional $CH_2Cl_2$, then washed twice with saturated $NH_4Cl$ and once with brine. The organic layer is dried over $Na_2SO_4$ and concentrated by rotary evaporation to give a crude oil, which is purified by silica gel chromatography to give the desired 1,2-*anti*;2,3-*anti* stereotriad, in addition to minor diastereomers. The *dr* and yield for the reaction are calculated based on the isolated masses of

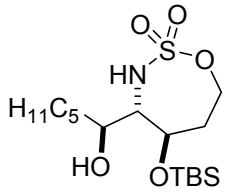
each diastereomer. As a rule, the isolated *dr* closely matches the *dr* of the crude material, as measured by $^1$H NMR.

General procedure B: The reaction is run in a manner identical to procedure A until completion of the DMDO oxidation. After concentration of the reaction mixture under reduced pressure at rt, $CH_2Cl_2$ (0.05 – 0.1 M) is added to the residue and the resulting solution is cooled to -78 °C in an acetone/dry ice bath. A solution of 1 equiv of $Zn(BH_4)_2$ (0.5 M in THF) is added, and the reaction mixture is stirred until TLC indicates complete consumption of the starting material. Workup, purification, and determination of product yield and *dr* are performed in a manner identical to that described in General Procedure A.

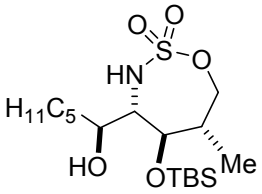



**Compound 35.** The enesulfamate **(*Z*)-5** (0.200 g, 0.596 mmol, 1.0 equiv) was subjected to General Procedure A using 4.0 equiv of DMDO in $CH_2Cl_2$ at -20 °C for 23 h. Purification by column chromatography (4% to 20% EtOAc in hexanes) resulted in the isolation of the 1,2-*anti*;2,3-*anti* stereotriad **35** (0.156 g, 0.441 mmol, 74%) with 31.6 mg of the 1,2-*anti*;2,3-*syn* stereotriad isolated (0.0894 mmol, 15%) as a separable mixture of diastereomers. $^1$H NMR (500 MHz, $CDCl_3$) δ 5.18 (d, *J* = 7.2 Hz, 1H), 4.51 (dd, *J* = 12.8, 9.4 Hz, 1H), 4.25 (td, *J* = 6.2, 2.6 Hz, 1H), 4.19 (ddd, *J* = 12.8, 6.2, 1.8 Hz, 1H), 3.80 (m, 1H), 3.27 (dt, *J* = 7.2, 6.2 Hz, 1H), 2.22-2.32 (m, 2H), 2.17 (sep d, *J* = 6.6, 3.9 Hz, 1H), 1.96 (dt, *J* = 15.9, 6.2 Hz, 1H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H). $^{13}$C NMR (125 MHz,

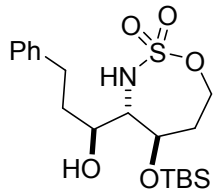
$CDCl_3$) δ 75.3, 71.2, 65.0, 60.4, 35.3, 29.3, 25.7, 19.7, 17.9, 15.0, -4.4, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{35}N_2O_5SSi$ [M+$NH_4^+$] 371.2031, found 371.2036.




**Compound 36.** The enesulfamate **(*Z*)-11** (0.44 mL of a 0.25 M solution in $CDCl_3$, 0.110 mmol, 1.0 equiv) was subjected to General Procedure A using 2.0 equiv of DMDO at 0 °C for 1 h for the oxidation step. Purification by column chromatography (0% to 10% EtOAc in $CH_2Cl_2$) yielded 26.2 mg (0.0686 mmol, 62%) of the major diastereomer **36**. Two minor diastereomers (8.4 mg) were also obtained, but the material was slightly contaminated with an unknown impurity, so this mass was not included in the yield. $^1$H NMR analysis of the crude product mixture showed an 11.7:1.7:1 *dr*. Major diastereomer: $^1$H NMR (500 MHz, $CDCl_3$) δ 5.22 (d, *J* = 8.0 Hz, 1H), 4.44 (ddd, *J* = 12.9, 5.2, 1.5 Hz, 1H), 4.23 (ddd, *J* = 12.9, 8.4, 1.5 Hz, 1H), 4.10 (td, *J* = 7.0, 3.1 Hz, 1H), 3.98 (bs, 1H), 3.25 (app q, *J* = 7.0 Hz, 1H), 2.24 (m, 2H), 1.98 (dtd, *J* = 15.6, 7.8, 1.7 Hz, 1H), 1.72 (m, 1H), 1.56 (m, 1H), 1.32 (m, 6H), 0.90 (app s, 12H), 0.10 (app s, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 70.7, 70.5, 65.6, 63.3, 36.3, 33.2, 31.8, 25.7, 25.2, 22.6, 17.9, 14.0, -4.1, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{36}NO_5SSi$ [M+$H^+$] 382.2078, found 382.2065.

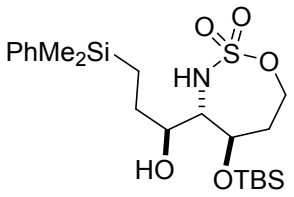


**Compound 37.** Following the general procedure for the synthesis of the 1,2-*syn*:2,3-*syn* stereotriads (see Section XII), the enesulfamate **(*Z*)-12** (0.050 g, 0.132 mmol, 1.0 equiv) was oxidized with 2.0 equiv DMDO at 25 °C over 2 hours. Reduction and chromatography (4% to 20% EtOAc in hexanes) yielded 0.0367 g (0.0927 mmol, 70%) of the 1,2-*anti*;2,3-*anti* stereotriad **37**. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 5.28 (d, *J* = 10.4 Hz, 1H), 4.41 (s, 1H), 4.37 (dd, *J* = 12.9, 10.9 Hz, 1H), 3.83 (dd, *J* = 12.9, 2.0 Hz, 1H), 3.35 (m, 1H), 3.11 (t, *J* = 10.4 Hz, 1H), 2.12 (m, 1H), 2.01 (m, 1H), 1.25-1.58 (m, 8H), 0.85-0.95 (m, 12H), 0.90 (t, *J* = 6.4 Hz, 3H), 0.15 (s, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 69.9, 69.4, 68.7, 61.3, 40.3, 34.0, 31.5, 26.3, 24.7, 22.5, 18.5, 15.0, 14.0, -3.7, -4.0. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{38}NO_5SSi$ [M+H$^+$] 396.2235, found 396.2244.

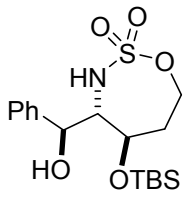



**Compound 38.** The enesulfamate **(*Z*)-13** (40.0 mg, 0.101 mmol, 1.0 equiv.) was subjected to General Procedure A using 2.0 equiv of DMDO at 0 °C for 1.5 h for the oxidation step. Purification by column chromatography (0% to 5% EtOAc in $CH_2Cl_2$) yielded 30.0 mg of the clean 1,2-*anti*:2,3-*anti* product **38**, and 7.0 mg of two minor diastereomers in a 1:0.4 ratio. Taken together, this equates to a total of 37.0 mg (0.0889 mmol, 88%) and a 15:2.5:1 *dr*. Major diastereomer: $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.28 (m, 2H), 7.22 (m, 2H), 7.18 (m, 1H), 5.16 (d, *J* = 8.0 Hz, 1H), 4.35 (ddd, *J* = 12.9, 7.3, 1.8 Hz, 1H), 4.18 (ddd, *J* = 12.9, 8.5, 1.4 Hz, 1H), 4.02 (m, 2H), 3.26 (app q, *J* = 7.4 Hz, 1H), 2.89 (ddd, *J* = 13.8, 10.4, 5.5 Hz, 1H), 2.70 (ddd, *J* = 13.8, 10.0, 6.1 Hz, 1H), 2.41 (d, *J* = 5.8 Hz, 1H), 2.19 (dddd, *J* = 15.5, 7.3, 3.5, 1.5 Hz, 1H), 2.04 (m,

1H), 1.95 (m, 1H), 1.69 (m, 1H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 141.7, 128.5 (2 peaks), 126.0, 71.1, 70.1, 65.7, 63.0, 36.3, 35.0, 31.8, 25.7, 17.8, -4.2, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{34}NO_5SSi$ [M+H$^+$] 416.1922, found 416.1911.

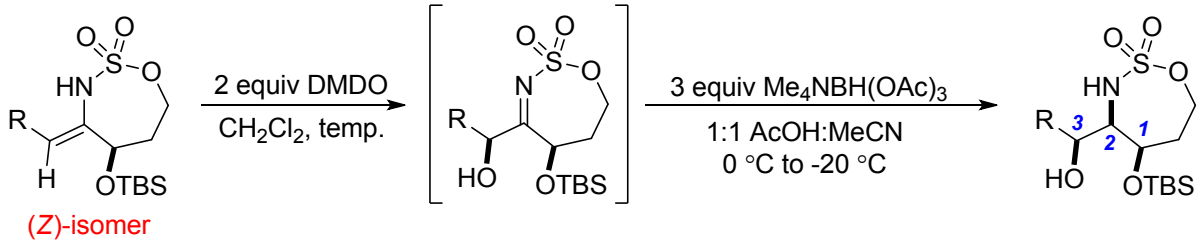



**Compound 39.** The enesulfamate **(*Z*)-14** (0.100 g, 0.220 mmol, 1.0 equiv) was subjected to General Procedure B using 2.0 equiv DMDO at 0 °C over 2 hours. Purification by column chromatography (4% to 20% EtOAc in hexanes) resulted in the isolation of 0.0842 g of the 1,2-*anti*;2,3-*anti* stereotriad **39** (0.178 mmol, 81%), along with 9.4 mg of the 1,2-*anti*;2,3-*syn* stereotriad (0.020 mmol, 9%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.52 (m, 2H), 7.36 (m, 3H), 4.93 (d, *J* = 6.3 Hz, 1H), 4.48 (ddd, *J* = 12.8, 9.1, 2.6 Hz, 1H), 4.10-4.20 (m, 2H), 3.93 (m, 1H), 3.16 (app q, *J* = 6.3 Hz, 1H), 2.22 (ddt, *J* = 15.6, 9.2, 2.6 Hz, 1H), 1.84-1.95 (m, 3H), 1.34 (tdd, *J* = 13.2, 8.9, 4.3 Hz, 1H), 1.00 (td, *J* = 13.2, 4.3 Hz, 1H), 0.88 (s, 9H), 0.71 (td, *J* = 13.2, 4.3 Hz, 1H), 0.30 (s, 3H), 0.29 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 138.7, 133.6, 129.0, 127.9, 72.2, 70.2, 65.0, 63.1, 35.4, 28.2, 25.7, 17.9, 11.0, -3.1, -3.3, -4.3, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{21}H_{43}N_2O_5SSi_2$ [M+$NH_4^+$] 491.2426, found 491.2415.



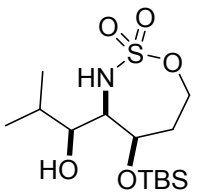
**Compound 40.** The (*E*)-enesulfamate **15** (42.0 mg, 0.114 mmol, 1.0 equiv.) was subjected to General Procedure B using 2.0 equiv of DMDO at 0 °C for 6 h for the oxidation step. Purification by column chromatography (10% to 30% EtOAc in Hexane) yielded 37.5 mg (0.0966 mmol, 85%) of the product **40** as an 8.3:1 mixture of diastereomers. The major diastereomer **40** was obtained in pure form by recrystallization from a hexane/EtOAc mixture (the product is heated in boiling hexane, with EtOAc added gradually until dissolution is complete). Major diastereomer: $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.43 (app d, *J* = 7.2 Hz, 2H), 7.39 (app t, *J* = 7.2 Hz, 2H), 7.33 (app t, *J* = 7.2 Hz, 1H), 5.13 (app dd, *J* = 5.0, 4.0 Hz, 1H), 4.82 (d, *J* = 8.0 Hz, 1H), 4.47 (ddd, *J* = 12.7, 8.5, 1.2 Hz, 1H), 4.16 (ddd, *J* = 12.7, 7.8, 1.3 Hz, 1H), 4.12 (td, *J* = 6.7, 3.0 Hz, 1H), 3.58 (dt, *J* = 8.0, 5.9 Hz, 1H), 2.80 (d, *J* = 4 Hz, 1H), 2.32 (ddt, *J* = 15.5, 8.6, 1.8 Hz, 1H), 2.02 (dtd, *J* = 15.5, 7.1, 1.4 Hz, 1H), 0.87 (s, 9H), 0.04 (s, 3H), -0.03 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 139.6, 128.7, 128.4, 126.7, 72.9, 70.9, 65.4, 64.1, 36.2, 25.7, 17.9, -4.0, -5.0. HRMS (ESI) *m/z* calculated for $C_{17}H_{33}N_2O_5SSi$ [M+$NH_4^+$] 405.1874, found 405.1878.

**XI. Synthesis of 1,2-*syn*:2,3-*syn* stereotriads.**



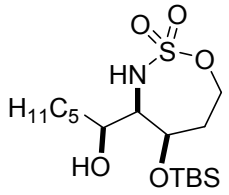

General procedure: The appropriate (*Z*)-enesulfamate is added to a roundbottom flask, either as the neat compound or as a crude stock solution in $CDCl_3$, depending on how it was prepared. (If the latter approach is used, the residual $CDCl_3$ is removed by rotary evaporation prior to the next step.) The flask is cooled to the appropriate temperature (see the individual entries), DMDO

added (2 equiv as a solution in $CH_2Cl_2$), the flask capped and the solution stirred until complete consumption of the starting material is observed by TLC (30% EtOAc/hex, CAM stain). Upon completion, the solution is concentrated under reduced pressure at rt and acetonitrile added to the residue. The resulting solution is cooled to the appropriate temperature (see individual entries) and an equal volume of glacial acetic acid added, followed by $Me_4NBH(OAc)_3$ (3.0 equiv) The reaction is stirred until complete consumption of the starting material is indicated by TLC. The solution is then diluted with $CH_2Cl_2$ and washed with three portions of saturated $NaHCO_3$ and one portion of brine. The organic layer is dried over $Na_2SO_4$ and concentrated under reduced pressure to give a crude oil, which is purified by silica gel chromatography to give the desired 1,2-*syn*:2,3-*syn* stereotriad, in addition to minor diastereomers. The *dr* and yield for the reaction are calculated based on the isolated masses of each diastereomer. As a rule, the isolated *dr* closely matches the *dr* of the crude material, as measured by $^1$H NMR.

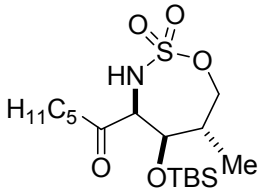



**Compound 41.** The enesulfamate **(*Z*)-5** (0.100 g, 0.298 mmol, 1.0 equiv) was subjected to the general procedure using 4.0 equiv DMDO at -20 °C over 26 h. Reduction at -20 °C and chromatography (4% to 20% EtOAc in hexanes) yielded the desired 1,2-*syn*:2,3-*syn* stereotriad **41** (52.7 mg, 0.149 mmol, 50%) along with the separable 1,2-*anti*:2,3-*anti* stereotriad (18.9 mg, 0.0535 mmol, 18%) and 1,2-*syn*:2,3-*anti* stereotriad (14.7 mg, 0.0417 mmol, 14%). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.42 (d, $J$ = 10.4 Hz, 1H), 4.61 (app t, $J$ = 12.4 Hz, 1H), 4.15-4.22 (m, 2H), 3.40 (dd, $J$ = 10.4, 5.8 Hz, 1H), 3.35 (td, $J$ = 5.8, 2.1 Hz, 1H), 2.42 (br d, $J$ = 2.1 Hz, 1H), 2.17

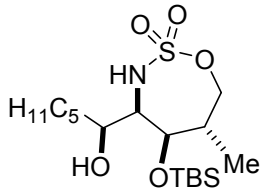
(ddt, $J$ = 15.5, 12.4, 2.7 Hz, 1H), 1.91 (dt, $J$ = 15.5, 3.8 Hz, 1H), 1.82 (m, 1H), 1.03 (d, $J$ = 6.7 Hz, 3H), 0.94 (d, $J$ = 6.7 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 75.8, 69.2, 64.2, 58.4, 37.0, 29.8, 25.7, 19.7, 17.9, 15.8, -4.1, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{35}N_2O_5SSi$ [M+$NH_4^+$] 371.2031, found 371.2036.




**Compound 42.** The enesulfamate **(*Z*)-11** (0.44 mL of a 0.25 M solution in $CDCl_3$, 0.110 mmol, 1.0 equiv) was subjected to the general procedure using 2.0 equiv. DMDO at 0 °C over 1 h. Reduction at 0 °C yielded, after column chromatography (0% to 5% EtOAc in $CH_2Cl_2$), 24.8 mg of the major diastereomer **42** and 5.8 mg of two minor diastereomers in a 1:0.7 ratio. This equates to a combined total of 30.6 mg (0.0801 mmol, 73%) and a 10.1:1.4:1 *dr*. Major diastereomer: $^1$H NMR (500 MHz, $CDCl_3$) δ 5.45 (d, $J$ = 10.6 Hz, 1H), 4.60 (t, $J$ = 12.5 Hz, 1H), 4.22 (bs, 1H), 4.18 (dt, $J$ = 12.5, 2.8 Hz, 1H), 3.57 (m, 1H), 3.25 (dd, $J$ = 10.6, 6.4 Hz, 1H), 2.49 (bs, 1H), 2.16 (ddt, $J$ = 15.0, 12.4, 2.2 Hz, 1H), 1.90 (dt, $J$ = 15.0, 3.0 Hz, 1H), 1.50 (m, 2H), 1.31 (m, 6H), 0.92 (app s, 12H), 0.12 (app s, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 71.3, 68.7, 64.2, 60.8, 37.0, 33.2, 31.8, 25.7, 24.9, 22.5, 17.9, 14.0, -4.0, -4.8. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{39}N_2O_5SSi$ [M+$NH_4^+$] 399.2344, found 399.2327.

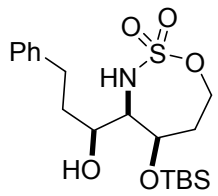


**Compound 60.** The enesulfamate **12** (0.150 g, 0.397 mmol, 1.0 equiv) was dissolved in 4.25 mL of 0.28 M DMDO in dichloromethane (1.19 mmol, 3.0 equiv) at rt. The solution was stirred for 6 h prior to concentration under reduced pressure. The crude residue was dissolved in 4 mL 1,2-dichloroethane, $Al(O^tBu)_3$ (97.8 mg, 0.397 mmol, 1.0 equiv) was added and the solution stirred for 2 h. The reaction mixture was diluted with 20 mL of dichloromethane and 20 mL of saturated Rochelle's salt. After stirring for 15 min, the phases were separated and the aqueous phase extracted with portions of dichloromethane. The combined organic phases were dried with $MgSO_4$, filtered and concentrated. The crude residue was purified by column chromatography (2% to 10% EtOAc in hexanes) to yield 0.105 g of **60** as a colorless oil that solidified upon refrigeration (0.267 mmol, 67%). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.69 (d, $J$ = 10.9 Hz, 1H), 4.68 (d, $J$ = 12.9 Hz, 1H), 4.37 (d, $J$ = 2.9 Hz, 1H), 4.00 (dd, $J$ = 12.9, 2.4 Hz, 1H), 3.82 (d, $J$ = 10.9 Hz, 1H), 2.75 (ddd, $J$ = 18.2, 8.6, 6.4 Hz, 1H), 2.50 (ddd, $J$ = 18.2, 8.6, 6.4 Hz, 1H), 1.90 (qdd, $J$ = 6.9, 2.9, 2.4 Hz, 1H), 1.56 (m, 2H), 1.24-1.38 (m, 4H), 1.15 (d, $J$ = 7.3 Hz, 3H), 0.89 (t, $J$ = 6.9 Hz, 3H), 0.86 (s, 9H), 0.09 (s, 3H), -0.02 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 207.5, 71.8, 68.5, 60.4, 40.6, 39.3, 31.1, 25.7, 22.8, 22.4, 17.8, 13.9, 13.4, -4.7, -5.0. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{39}N_2O_5SSi$ [M+$NH_4^+$] 411.2344, found 411.2346.



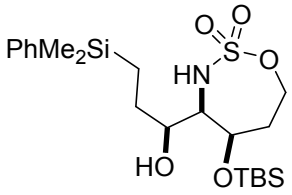

**Compound 61.** Compound **60** (39.5 mg, 0.100 mmol, 1.0 equiv) was dissolved in 1.0 mL of dry MeOH and cooled to -78 °C. Tetrabutylammonium borohydride (77.5 mg, 0.301 mmol, 3.0 equiv) was added in a single portion. After stirring 25 min at -78 °C, the cooling bath was

removed and stirring continued for another 10 min. The reaction was diluted with 10 mL of diethyl ether and quenched with 10 mL of brine. The phases were separated and the aqueous layer extracted with portions of diethyl ether. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated. The crude residue was purified by column chromatography (4% to 20% EtOAc in hexanes) to provide the desired 1,2-*syn*:2,3-*syn* stereotriad **61** (24.5 mg, 0.0620 mmol, 62%) along with the separable 1,2-*anti*;2,3-*syn* stereotriad (10.7 mg, 0.027 mmol, 27%). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.41 (d, *J* = 10.6 Hz, 1H), 4.68 (d, *J* = 12.7 Hz, 1H), 3.97 (dd, *J* = 12.7, 2.6 Hz, 1H), 3.82 (d, *J* = 3.0 Hz, 1H), 3.52 (m, 1H), 3.26 (dd, *J* = 10.6, 7.2 Hz, 1H), 2.45 (s, 1H), 1.89 (qdd, *J* = 7.2, 3.0, 2.6 Hz, 1H), 1.23-1.55 (m, 6H), 1.15 (d, *J* = 7.2 Hz, 3H), 1.86-1.93 (m, 12H), 0.11 (s, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 73.1, 70.7, 68.1, 56.9, 39.6, 33.1, 31.8, 25.7, 24.7, 22.5, 17.9, 14.0, 13.4, -4.1, -4.8. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{41}N_2O_5SSi$ [M+$NH_4^+$] 413.2500, found 413.2504.

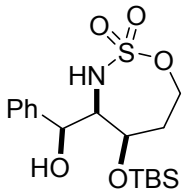



**Compound 43.** The enesulfamate **(*Z*)-13** (0.17 mL of a 0.58 M solution in $CDCl_3$, 0.101 mmol, 1.0 equiv) was subjected to the general procedure using 2.0 equiv. DMDO at 0 °C over 1.5 h. Reduction at 0 °C yielded, after column chromatography (0% to 25% EtOAc in Hexane), 24.0 mg of the major diastereomer **43** and 6.6 mg of two minor diastereomers in a 1.8:1 ratio. This equates to a combined total of 30.6 mg (0.0736 mmol, 73%) and a 10.2:1.8:1 *dr*. Major diastereomer: $^1$H NMR (500 MHz, $CDCl_3$) δ 7.28 (m, 2H), 7.20 (m, 3H), 5.46 (d, *J* = 10.8 Hz, 1H), 4.58 (t, *J* = 12.5 Hz, 1H), 4.16 (m, 2H), 3.56 (m, 1H), 3.25 (dd, *J* = 10.6, 6.4 Hz, 1H), 2.87

(ddd, $J$ = 13.9, 8.6, 6.0, 1H), 2.73 (dt, $J$ = 13.9, 7.9 Hz, 1H), 2.59 (bs, 1H), 2.07 (ddt, $J$ = 15.2, 12.0, 2.7 Hz, 1H), 1.83 (m, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.01 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 141.5, 128.6, 128.5, 126.0, 70.0, 68.4, 64.2, 61.0, 36.9, 35.3, 31.4, 25.7, 17.9, -4.1, -5.0. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{37}N_2O_5SSi$ [M+$NH_4^+$] 433.2187, found 433.2185.

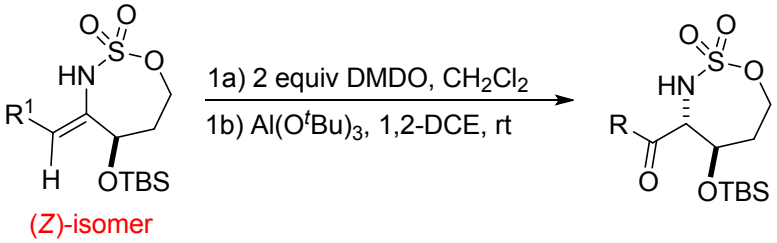



**Compound 44.** Enesulfamate **(*Z*)-14** (50.0 mg, 0.110 mmol, 1.0 equiv) was subjected to the general procedure with 2.0 equiv DMDO at 0 °C over 2.5 hours for the oxidation step. Reduction was carried out at -20 °C, and chromatography (4% to 20% EtOAc in hexanes) yielded the desired 1,2-*syn*:2,3-*syn* stereotriad **44** (29.2 mg, 0.0616 mmol, 56%) along with the separable 1,2-*anti*:2,3-*anti* stereotriad (9.1 mg, 0.0193 mmol, 18%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.35 (m, 3H), 5.38 (d, $J$ = 10.6 Hz, 1H), 4.57 (app t, $J$ = 12.5 Hz, 1H), 4.15 (dt, $J$ = 12.5, 3.2 Hz, 1H), 4.04 (app t, $J$ = 3.2 Hz, 1H), 3.47 (td, $J$ = 6.0, 4.5 Hz, 1H), 3.27 (dd, $J$ = 10.6, 6.0 Hz, 1H), 2.48 (br s, 1H), 2.10 (ddt, $J$ = 15.6, 12.5, 3.2 Hz, 1H), 1.84 (dt, $J$ = 15.6, 3.2 Hz, 1H), 1.60 (tt, $J$ = 12.7, 4.5 Hz, 1H), 1.43 (tdd, $J$ = 12.7, 7.3, 4.5 Hz, 1H), 0.87-0.96 (m, 10H), 0.77 (td, $J$ = 12.7, 4.5 Hz, 1H), 0.29 (s, 3H), 0.28 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 138.7, 133.5, 129.0, 127.8, 73.4, 68.8, 64.2, 59.7, 36.9, 27.3, 25.7, 17.9, 10.8, -3.2, -3.4, -4.1, -5.0. HRMS (ESI) *m*/*z* calculated for $C_{21}H_{43}N_2O_5SSi_2$ [M+$NH_4^+$] 491.2426, found 491.2410.



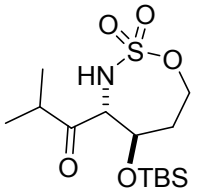

**Compound 45.** The (*E*)-enesulfamate **15** (41.2 mg, 0.111 mmol, 1.0 equiv.) was subjected to the general procedure using 2.0 equiv. DMDO at 0 °C over 18 h. Reduction at -10 °C yielded, after column chromatography (0% to 3% EtOAc in $CH_2Cl_2$), 29.0 mg (0.0747 mmol, 67%) of a colorless oil. This contained the desired product **45** as an 8.7:1 mixture of two diastereomers. The diastereomers were eventually separated by column chromatography using an EtOAc/Hexane gradient (5% to 30%). Major diastereomer: $^1$H NMR (500 MHz, $CDCl_3$) δ 7.39 (m, 5H), 5.66 (d, *J* = 10.7 Hz, 1H), 4.60 (t, *J* = 12.8 Hz, 1H), 4.46 (d, *J* = 9.3 Hz, 1H), 4.17 (dt, *J* = 12.8, 3.1 Hz, 1H), 3.82 (dd, *J* = 3.5, 2.5 Hz, 1H), 3.53 (dd, *J* = 10.7, 9.5, 1H), 3.01 (bs, 1H), 1.96 (ddt, *J* = 15.5, 12.1, 2.7 Hz, 1H), 1.77 (dt, *J* = 15.5, 3.4 Hz, 1H), 0.97 (s, 9H), 0.12 (s, 3H), 0.04 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 138.9, 129.0, 128.9, 127.5, 73.2, 66.6, 64.2, 63.5, 36.6, 25.9, 18.1, -3.7, -4.6. HRMS (ESI) *m/z* calculated for $C_{17}H_{30}NO_5SSi$ [M+H$^+$] 388.1609, found 388.1613.

## XII. Two-pot synthesis of 1,2-*anti*:2,3-*syn* stereotriads.



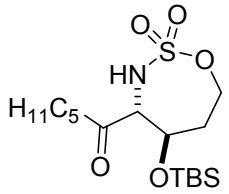

General procedure: The appropriate (*Z*)-enesulfamate is added to a roundbottom flask, either as the neat compound or as a crude stock solution in $CDCl_3$, depending on how it was prepared. (If

the latter approach is used, the residual $CDCl_3$ is removed by rotary evaporation prior to the next step.) The flask is cooled to the appropriate temperature (see the individual entries), DMDO is added (2 equiv as a solution in $CH_2Cl_2$), the flask is capped and the solution is stirred until complete conversion of the starting material is observed by TLC (30% EtOAc/hex, CAM stain). Upon completion, the solution is concentrated at rt under reduced pressure. A portion of 1,2-dichloroethane (0.1 M) is added, followed by 1.0 equiv of $Al(O^tBu)_3$. The suspension is sonicated for 5 min to facilitate dissolution of the aluminum reagent and then stirred at rt until TLC indicates complete consumption of the starting material. The reaction is quenched by the addition of an aqueous solution of Rochelle's salt and the biphasic mixture stirred at rt for 30 min. The reaction is diluted with $CH_2Cl_2$ and the organic layer is washed once with Rochelle's salt and once with brine. The organic layer is dried over $Na_2SO_4$ and concentrated by rotary evaporation to give a crude oil. Purification *via* silica gel chromatography yields the desired 1,2-*anti* α-aminoketone, along with a minor 1,2-syn diastereomer. The yield and *dr* are determined by the isolated masses of the two diastereomers. As a rule, the isolated *dr* closely matches the *dr* of the crude material, as measured by $^1H$ NMR.



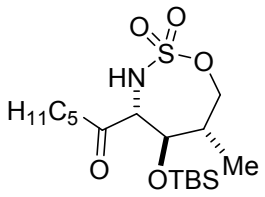

**Compound 48.** The enesulfamate **(*Z*)-5** (0.477 g, 1.42 mmol, 1.0 equiv) was subjected to the general procedure. The oxidation was conducted at 0 °C over 5 h. Purification by column chromatography (4%-20% EtOAc in hexanes) provided 0.267 g of the desired 1,2-*anti* α-aminoketone **48** (0.760 mmol, 54%), along with 89.8 mg of the minor 1,2-*syn* diastereomer

(0.256 mmol, 18%). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.00 (d, *J* = 10.0 Hz, 1H), 4.31-4.34 (m, 2H), 4.21 (app t, *J* = 9.4 Hz, 1H), 3.97 (td, *J* = 9.2, 5.0 Hz, 1H), 2.83 (sep, *J* = 6.9 Hz, 1H), 2.05-2.22 (m, 2H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 9H), 0.06 (s, 3H), -0.03 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 210.4, 72.7, 66.7, 60.0, 41.9, 37.4, 25.6, 17.8, 17.7, 16.4, -4.6, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{33}N_2O_5SSi$ [M+$NH_4^+$] 369.1874, found 369.1857. Minor Isomer: $^1$H NMR (500 MHz, $CDCl_3$) δ 5.76 (d, *J* = 10.8 Hz, 1H), 4.82 (t, *J* = 2.3 Hz, 1H), 4.61 (t, *J* = 12.6 Hz, 1H), 4.21 (dt, *J* = 12.6, 3.2 Hz, 1H), 3.96 (d, *J* = 10.8 Hz, 1H), 3.14 (sep, *J* = 6.8 Hz, 1H), 2.14 (ddt, *J* = 15.4, 12.6, 3.2 Hz, 1H), 1.90 (dt, *J* = 15.4, 3.2 Hz, 1H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.11 (s, 3H), 0.00 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 210.1, 66.3, 64.5, 62.9, 36.9, 36.3, 25.7, 18.1, 17.8, 17.5, -4.6, -4.9. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{33}N_2O_5SSi$ [M+$NH_4^+$] 369.1874, found 369.1874.

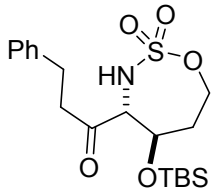



**Compound 49.** The enesulfamate **(*Z*)-11** (0.40 mL of a 0.688 M solution in $CDCl_3$, 0.275 mmol, 1.0 equiv) was subjected to the general procedure and the oxidation occurred at -10 °C over 2.33 h. Purification by column chromatography (0% to 20% EtOAc in hexanes) provided 67.0 mg of the desired 1,2-*anti* α-aminoketone **49** along with 8.5 mg of a 3.3:1 mixture of the two diastereomers, favoring the minor, 1,2-*syn* α-aminoketone. This equates to a total of 75.5 mg (0.199 mmol, 72%) in a 10.6:1 *dr*. Major diastereomer: $^1$H NMR (500 MHz, $CDCl_3$) δ 5.21 (d, *J* = 9.5 Hz, 1H), 4.32 (m, 2H), 4.02 (t, *J* = 9.5 Hz, 1H), 3.93 (td, *J* = 8.8, 5.0 Hz, 1H), 2.67 (t, *J* = 7.5 Hz, 2H), 2.14 (m, 2H), 1.64 (m, 1H), 1.55 (m, 1H), 1.29 (m, 4H), 0.89 (t, *J* = 6.7 Hz, 3H),

0.86 (s, 9H), 0.06 (s, 3H), -0.03 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 207.4, 72.9, 66.7, 62.2, 44.6, 37.4, 31.1, 25.6, 22.5, 22.4, 17.8, 13.9, -4.6, -5.1. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{37}N_2O_5SSi$ [M+$NH_4^+$] 397.2187, found 397.2197.

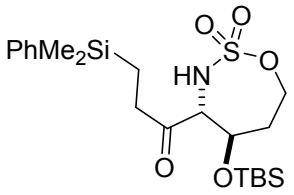



**Compound 50.** The enesulfamate **(*Z*)-12** (0.580 g, 1.0 equiv) was subjected to the general procedure and oxidation occurred at rt over 2 h. Purification by column chromatography (4%-20% EtOAc in hexanes) provided 0.364 g of the desired 1,2-*anti* α-aminoketone **50** (0.925 mmol, 60%). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.70 (d, *J* = 10.7 Hz, 1H), 4.66 (s, 1H), 4.39 (dd, *J* = 12.8, 10.7 Hz, 1H), 3.88 (ddd, *J* = 12.8, 2.7, 0.7 Hz, 1H), 3.77 (d, *J* = 10.7 Hz, 1H), 2.78 (ddd, *J* = 18.3, 9.0, 6.0 Hz, 1H), 2.55 (ddd, *J* = 18.3, 8.5, 5.8 Hz, 1H), 2.14 (m, 1H), 1.57 (m, 1H), 1.18-1.38 (m, 5H), 0.97 (d, *J* = 7.4 Hz, 3H), 0.87-0.91 (m, 12H), 0.14 (s, 3H), -0.10 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 207.7, 70.0, 68.9, 64.9, 40.5, 39.9, 31.1, 26.1, 22.7, 22.4, 18.4, 14.4, 13.9, -4.1, -4.6. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{39}N_2O_5SSi$ [M+$NH_4^+$] 411.2344, found 411.2331.

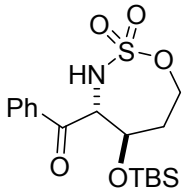



**Compound 51.** The enesulfamate **(*Z*)-13** (0.65 mL of a 0.58M solution in $CDCl_3$, 0.377 mmol, 1.0 equiv) was subjected to the general procedure and the oxidation occurred at 0 °C over 2 h.

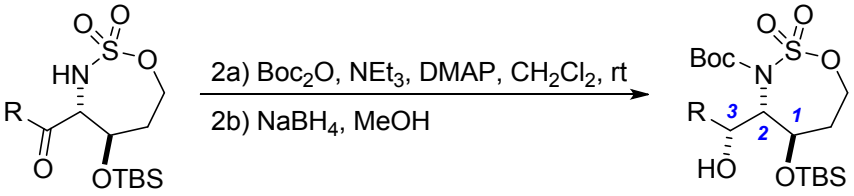
Purification by column chromatography (5% to 20% EtOAc in hexanes) provided 89.8 mg of the desired 1,2-*anti* α-aminoketone **51** along with 8.2 mg of the separable 1,2-*syn* α-aminoketone. This equates to a total of 98.0 mg (0.237 mmol, 63%) in an 11:1 *dr*. Major diastereomer: $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.21 (m, 1H), 7.17 (m, 2H), 5.10 (d, *J* = 9.0 Hz, 1H), 4.32 (m, 2H), 3.99 (t, *J* = 8.8 Hz, 1H), 3.95 (td, *J* = 8.8 Hz, 4.2 Hz, 1H), 3.02 (app td, *J* = 7.4, 1.2 Hz, 2H), 2.96 (m, 1H), 2.86 (m, 1H), 2.18 (app dq, *J* = 15.4, 3.3 Hz, 1H), 2.12 (m, 1H), 0.85 (s, 9H), 0.06 (s, 3H), -0.01 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 206.1, 140.0, 128.6, 128.2, 126.3, 72.8, 66.7, 62.5, 46.0, 37.2, 29.0, 25.6, 17.8, -4.6, -5.0. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{32}NO_5SSi$ [M+H$^+$] 431.2031, found 431.2019.




**Compound 52.** The enesulfamate **(*Z*)-14** (0.100 g, 1.0 equiv) was subjected to the general procedure and the oxidation occurred at 0 °C over 2.5 h. Purification by column chromatography (4%-20% EtOAc in hexanes) provided 53.1 mg of the desired 1,2-*anti* α-aminoketone **52** (0.113 mmol, 51%), along with 7.6 mg (0.0161 mmol, 7%) of the separable 1,2-*syn* α-aminoketone. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.36 (m, 3H), 5.16 (d, *J* = 9.6 Hz, 1H), 4.25-4.34 (m, 2H), 3.99 (app t, *J* = 9.2 Hz, 1H), 3.87 (td, *J* = 9.2, 5.3 Hz, 1H), 2.60 (m, 2H), 2.04-2.16 (m, 2H), 1.08 (m, 1H), 0.92 (m, 1H), 0.80 (s, 9H), 0.29 (s, 6H), 0.02 (s, 3H), -0.10 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 208.0, 137.7, 133.5, 129.2, 127.9, 73.0, 66.7, 61.9, 39.3, 37.4, 25.5, 17.7, 8.5, -3.3, -3.3, -4.7, -5.0. HRMS (ESI) *m*/*z* calculated for $C_{21}H_{41}N_2O_5SSi_2$ [M+$NH_4^+$] 490.2348, found 490.2352.

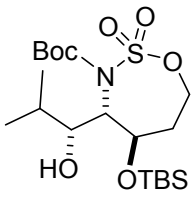



**Compound 53.** The (Z)-enesulfamate **(*Z*)-15** (49.4 mg, 0.134 mmol, 1.0 equiv) was subjected to the general procedure and oxidation occurred at 0 °C over 11 h. Purification by column chromatography (0% to 2% EtOAc in $CH_2Cl_2$) provided 31.3 mg of a white solid. $^1$H NMR analysis showed a 20:1 *dr* in favor of the diastereomer **53**. The mixture was considered pure enough to preclude further purification. $^1$H NMR (500 MHz, $CDCl_3$) δ 8.03 (app d, *J* = 7.3 Hz, 2H), 7.63 (app tt, *J* = 7.3, 0.9 Hz, 1H), 7.50 (app t, *J* = 7.3 Hz, 2H), 5.36 (d, *J* = 9.3 Hz, 1H), 4.99 (t, *J* = 9.3 Hz, 1H), 4.43 (ddd, *J* = 13.0, 10.4, 1.9 Hz, 1H), 4.38 (dt, *J* = 13.0, 3.8 Hz, 1H), 4.02 (td, *J* = 9.3, 4.9 Hz, 1H), 2.25 (m, 2H), 0.60 (s, 9H), -0.04, (s, 3H), -0.34 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 197.1, 135.4, 134.5, 129.5, 128.7, 73.9, 66.9, 58.2, 37.8, 25.3, 17.6, -4.8, -5.5. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{28}NO_5SSi$ [M+H$^+$] 386.1452, found 386.1454.



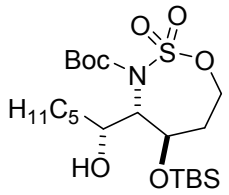

General procedure: The appropriate 1,2-*anti* α-aminoketone is added to a roundbottom flask, followed by $Boc_2O$ (1.2 equiv) and $CH_2Cl_2$ (0.05 – 0.1 M). Triethylamine (1.2 equiv) is added, followed by DMAP (0.1 equiv), and the reaction is stirred at rt until TLC indicates complete consumption of the starting material, generally within 15 min (~30% EtOAc/hex, CAM stain). The solution is passed through a short (~1 inch) silica plug while washing with $CH_2Cl_2$. The resulting solution is concentrated under reduced pressure, the residue dissolved in MeOH (0.05 –

0.1M) and the solution cooled to 0 °C. $NaBH_4$ (5 equiv) is added, and the reaction is monitored by TLC for completion. The reaction is generally complete within 15 min. The reaction is quenched by the addition of a saturated solution of $NH_4Cl$, diluted with EtOAc and the layers separated. The aqueous layer is extracted twice with additional EtOAc. The combined organic layers are washed with brine, dried over $Na_2SO_4$ and concentrated by rotary evaporation to give a crude oil. Purification by silica gel chromatography yields the Boc-protected 1,2-*anti*:2,3-*syn* stereotriad, in addition to the minor 1,2-*anti*:2,3-*anti* product (observed in some cases). Yield and *dr* are determined by the isolated masses of the two diastereomers. As a rule, the isolated *dr* closely matches the *dr* of the crude material, as measured by $^1$H NMR.

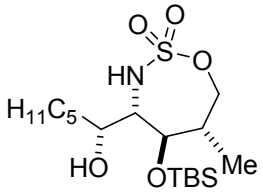



**Compound 54.** Following the general procedure, the ketone **48** (60.0 mg, 1.0 equiv) yielded 57.4 mg of the Boc-protected 1,2-*anti*:2,3-*syn* stereotriad **54** (0.127 mmol, 74%) after chromatography (2% to 10% EtOAc in hexanes) in addition to the separable minor 1,2-*anti*:2,3-*anti* product (10.9 mg, 0.0239 mmol, 14%). $^1$H NMR (500 MHz, $CDCl_3$) δ 4.92 (d, $J$ = 10.0 Hz, 1H), 4.76 (d, $J$ = 9.0 Hz, 1H), 4.36 (ddd, $J$ = 12.3, 5.8, 2.0 Hz, 1H), 4.28 (dd, $J$ = 12.3, 10.0 Hz, 1H), 3.77 (app td, $J$ = 7.9, 5.8 Hz, 1H), 3.54 (dd, $J$ = 9.0, 7.9 Hz, 1H), 2.25 (dt, $J$ = 15.9, 5.8 Hz, 1H), 2.15 (m, 1H), 2.05 (dddd, $J$ = 15.9, 10.0, 7.9, 2.0 Hz, 1H), 1.48 (s, 9H), 1.01 (d, $J$ = 6.7 Hz, 3H), 0.95 (d, $J$ = 6.7 Hz, 3H), 0.90 (s, 9H), 0.09 (5.3, s, 3H), 0.06 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 152.8, 82.5, 79.0, 70.4, 66.2, 58.1, 37.6, 29.5, 27.7, 25.8, 18.6, 17.9, -3.8, -5.1. HRMS (ESI) $m/z$ calculated $C_{19}H_{43}N_2O_7SSi$ [M+$NH_4^+$] 471.2555, found 471.2574. Minor stereoisomer:

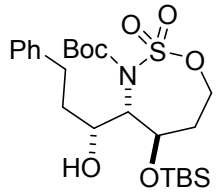
$^1$H NMR (500 MHz, $CDCl_3$) δ 4.92 (app t, *J* = 12.4 Hz, 1H), 4.63 (s, 1H), 4.47 (t, *J* = 4.1 Hz, 1H), 4.33 (dt, *J* = 12.4, 3.3 Hz, 1H), 4.05 (ddd, *J* = 10.7, 5.9, 0.9 Hz, 1H), 2.41 (app t, *J* = 12.4 Hz, 1H), 1.96 (sep, *J* = 6.7 Hz, 1H), 1.71 (br d, *J* = 12.4 Hz, 1H), 1.53 (s, 1H), 1.36 (s, 1H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.86 (d, *J* = 6.7 Hz, 3H), 0.12 (s, 3H), 0.09 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 151.7, 84.8, 74.5, 68.4, 66.2, 62.3, 31.8, 29.0, 27.9, 25.7, 20.2, 17.9, 13.8, -5.1. HRMS (ESI) *m*/*z* calculated $C_{19}H_{39}NO_7SSiNa$ [M+$Na^+$] 476.2109, found 476.2107.




**Compound 55.** Following the general procedure, the ketone **49** (31.1 mg, 0.0818 mmol, 1.0 equiv) yielded, after purification by column chromatography (0% to 15% EtOAc/hexane), 30.3 mg (0.0630 mmol, 77%) of **55** as a white solid. $^1$H NMR indicated a single diastereomer was present, in agreement with a $^1$H NMR of the crude material. $^1$H NMR (500 MHz, $CDCl_3$) δ 4.91 (app dd, *J* = 7.5, 6.5 Hz, 1H), 4.87 (d, *J* = 10.6 Hz, 1H), 4.30 (m, 2H), 3.81 (td, *J* = 9.1, 5.1 Hz, 1H), 3.37 (t, *J* = 10.6 Hz, 1H), 2.22 (m, 1H), 2.05 (m, 1H), 1.77 (m, 2H), 1.48 (s, 9H), 1.44-1.22 (m, 6H), 0.89 (m, 12H), 0.07 (s, 3H), 0.05 (m, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 152.2, 82.6, 74.5, 69.7, 66.6, 58.4, 37.8, 31.3, 30.0, 27.7, 25.7, 24.6, 22.4, 17.8, 13.9, -3.9, -5.2. HRMS (ESI) *m*/*z* calculated for $C_{21}H_{47}N_2O_7SSi$ [M+$NH_4^+$] 499.2868, found 499.2885.

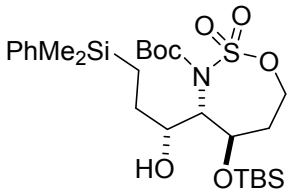


**Compound 56.** This isomer was prepared using an alternative route to the scheme shown above. Starting from ketone **50** (0.0250 g, 0.0635 mmol, 1.0 equiv), the substrate was dissolved in 1.0 mL dry MeOH and cooled to -78 °C. $NaBH_4$ (7.2 mg, 0.191 mmol, 3.0 equiv) was added and the reaction stirred for 1 h before warming to 0 °C. The reaction was quenched with a mixture of saturated $NH_4Cl$ and dichloromethane. The product was extracted with portions of dichloromethane, dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography (5-25% EtOAc in hexanes) isolated the desired 1,2-*syn*:2,3-*anti* stereotriad **56** (17.1 mg, 0.0432 mmol, 68%) along with the separable 1,2-*anti*;2,3-*anti* stereotriad (2.8 mg, 0.0070 mmol, 11%). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.48 (d, $J$ = 10.2 Hz, 1H), 4.40 (dd, $J$ = 12.7, 10.9 Hz, 1H), 3.97 (s, 1H), 3.86 (dd, $J$ = 12.7, 2.3 Hz, 1H), 3.45 (br dd, $J$ = 9.3, 7.8 Hz, 1H), 3.20 (dd, $J$ = 10.2, 9.3 Hz, 1H), 2.46 (br s, 1H), 2.17 (m, 1H), 1.52-1.58 (m, 2H), 1.25-1.45 (m, 6H), 0.94-0.98 (m, 12H), 0.90 (t, $J$ = 6.7 Hz, 3H), 0.14 (s, 3H), 0.11 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 71.6, 69.4, 68.6, 63.1, 40.6, 33.3, 32.0, 26.2, 24.8, 22.5, 18.5, 15.0, 14.0, -3.3, -3.7. HRMS (ESI) *m/z* calculated for $C_{17}H_{38}NO_5SSi$ [M+H$^+$] 396.2235, found 396.2243.

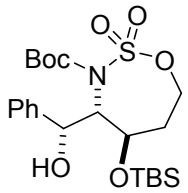



**Compound 57.** Following the general procedure, the ketone **51** (30.7 g, 0.0742 mmol, 1.0 equiv) yielded, after column chromatography (5% to 20% EtOAc/hexane), 29.9 mg (0.0579 mmol, 78%) of **57** as a colorless oil. $^1$H NMR indicated a single diastereomer in both the crude material and the final product. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.26 (m, 4H), 7.18 (m, 1H), 4.96 (d, $J$ =

11.2 Hz, 1H), 4.95 (m, 1H), 4.31 (m, 2H), 3.82 (td, *J* = 9.0, 5.0 Hz, 1H), 3.45 (td, *J* = 10.1, 0.9 Hz, 1H), 2.76 (ddd, *J* = 13.7, 10.8, 5.5 Hz, 1H), 2.60 (ddd, *J* = 13.7, 10.3, 6.4 Hz, 1H), 2.25-2.00 (m, 4H), 1.47 (s, 9H), 0.85 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H). $^{13}$C NMR (125.7 MHz, $CDCl_3$) δ 152.1, 140.6, 128.5, 128.4, 126.0, 82.7, 74.1, 69.6, 66.6, 58.4, 37.8, 32.0, 31.2, 27.7, 25.7, 127.8, -4.0, -5.2. HRMS (ESI) *m*/*z* calculated for $C_{24}H_{45}N_2O_7SSi$ [M+$NH_4^+$] 533.2712, found 533.2717.




**Compound 58.** Following the general procedure, the ketone **52** (29.9 mg, 0.0634 mmol, 1.0 equiv) yielded 27.6 mg (0.0481 mmol, 76%) of the Boc-protected 1,2-*anti*:2,3-*syn* stereotriad **60** after chromatography (2% to 10% EtOAc in hexanes). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.52 (m, 2H), 7.35 (m, 3H), 4.77-4.86 (m, 2H), 4.27-4.32 (m, 2H), 3.80 (td, *J* = 9.1, 4.9 Hz, 1H), 3.52 (td, *J* = 10.4, 0.7 Hz, 1H), 2.21 (m, 1H), 2.04 (m, 1H), 1.77 (m, 2H), 1.45 (s, 9H), 0.80-0.90 (m, 10H), 0.62 (m, 1H), 0.30 (s, 3H), 0.29 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 152.1, 138.5, 133.6, 128.9, 127.8, 82.6, 76.9, 69.6, 66.6, 57.4, 37.9, 27.7, 25.7, 24.4, 17.8, 10.6, -3.2, -3.4, -4.0, -5.2. HRMS (ESI) *m*/*z* calculated $C_{26}H_{51}N_2O_7SSi_2$ [M+$NH_4^+$] 591.3029, found 591.3015.




**Compound 59.** Following the general procedure, the ketone **53** (29.3 mg, 0.0759 mmol, 1.0 equiv) yielded, after column chromatography (0% to 20% EtOAc/hexane), 17.6 mg (0.0361

mmol, 48%) of a white solid containing **59** in a 4:1 *dr*. The diastereomers were separated by column chromatography (0% to 0.5% MeOH/$CH_2Cl_2$). Major diastereomer: $^1$H NMR (500 MHz, $CDCl_3$) δ 7.37 (m, 2H), 7.32 (m, 3H), 5.90 (d, *J* = 2.1 Hz, 1H), 5.00 (d, *J* = 10.2 Hz, 1H), 4.30 (m, 2H), 3.89 (td, *J* = 9.2, 4.8 Hz, 1H), 3.44 (ddd, *J* = 10.2, 9.2, 2.2 Hz, 1H), 2.23 (m, 1H), 2.04 (m, 1H), 1.42 (s, 9H), 0.94 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 151.6, 137.2, 128.6, 128.4, 125.8, 83.2, 75.0, 70.0, 66.3, 62.5, 37.4, 27.6, 25.7, 17.8, -4.0, -5.2. HRMS (ESI) *m*/*z* calculated for $C_{22}H_{41}N_2O_7SSi$ [M+$NH_4^+$] 505.2399, found 505.2376.

## XIII. Rationale for stereochemical outcome in imine/ketone reductions.

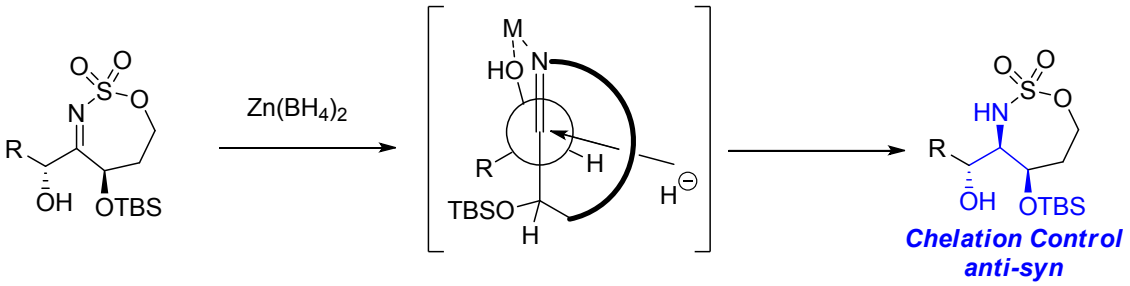



**Figure S1**. Stereochemical model for 1,2-*syn*:2,3-*anti* stereotriad synthesis from 1,3-*anti* imine.

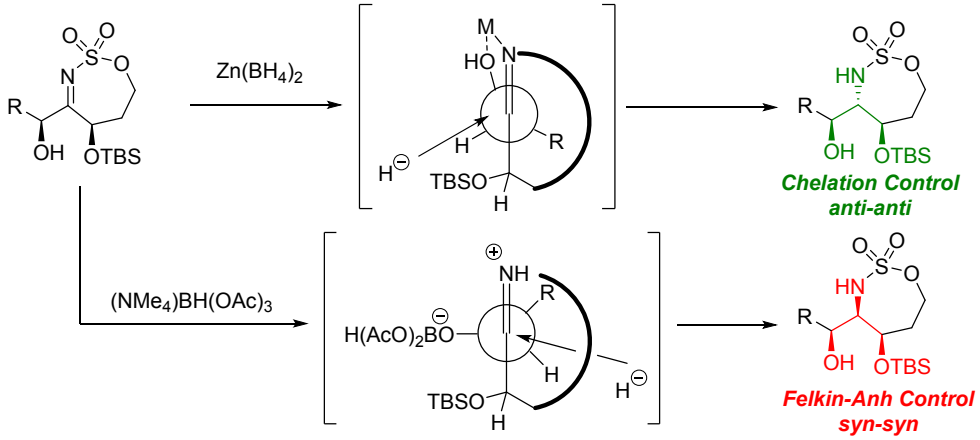



**Figure S2**. Stereochemical model for 1,2-*anti*:2,3-*anti* stereotriad and 1,2-*syn*:2,3-*syn* stereotriad syntheses from a 1,3-*syn* imine.

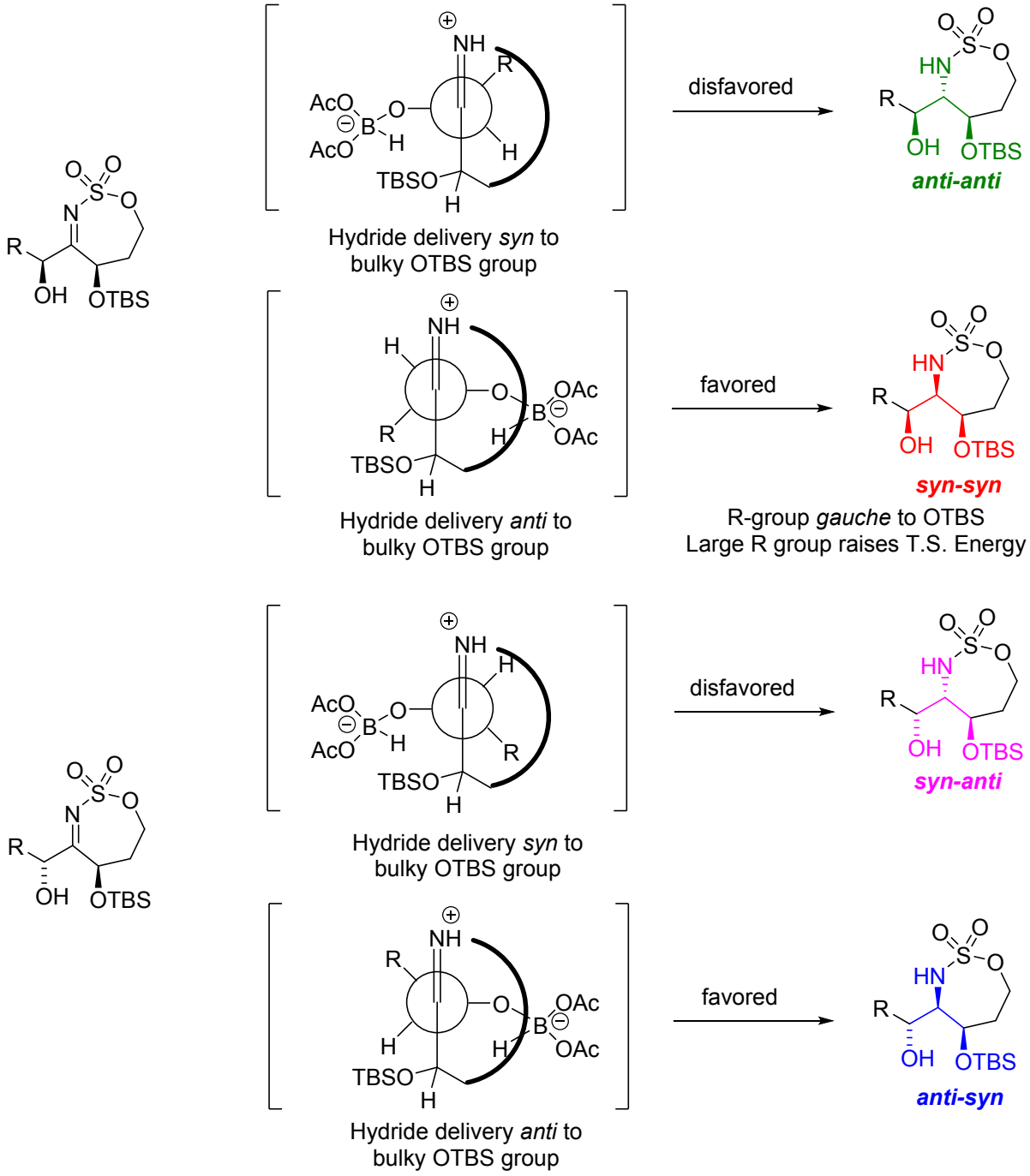



**Figure S3**. Stereochemical models for explaining the unexpected stereoselectivity using $Me_4NBH(OAc)_3$ as the reductant.

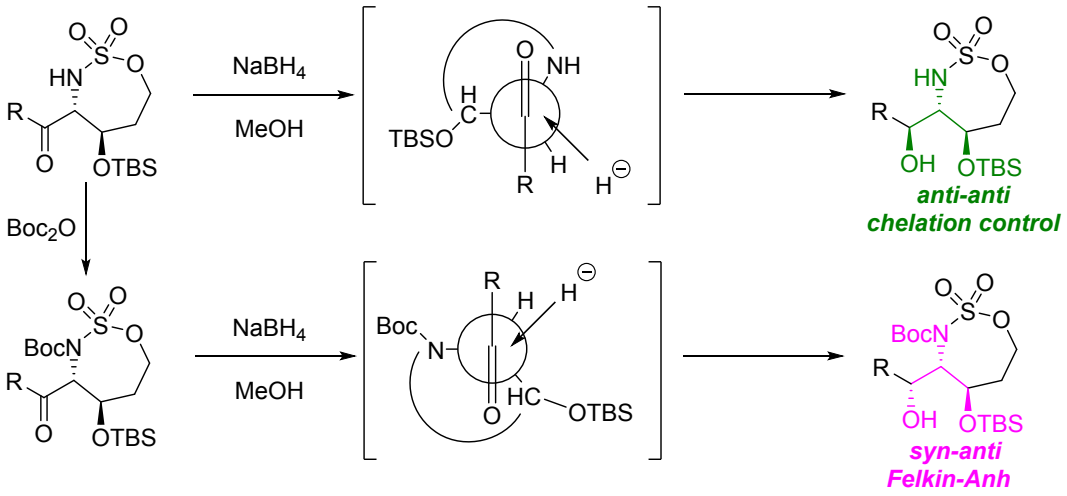



**Figure S4.** Stereochemical model for 1,2-*anti*:2,3-*anti* stereotriad and 1,2-*anti*:2,3-*syn* stereotriad syntheses from 1,2-*anti* ketones.

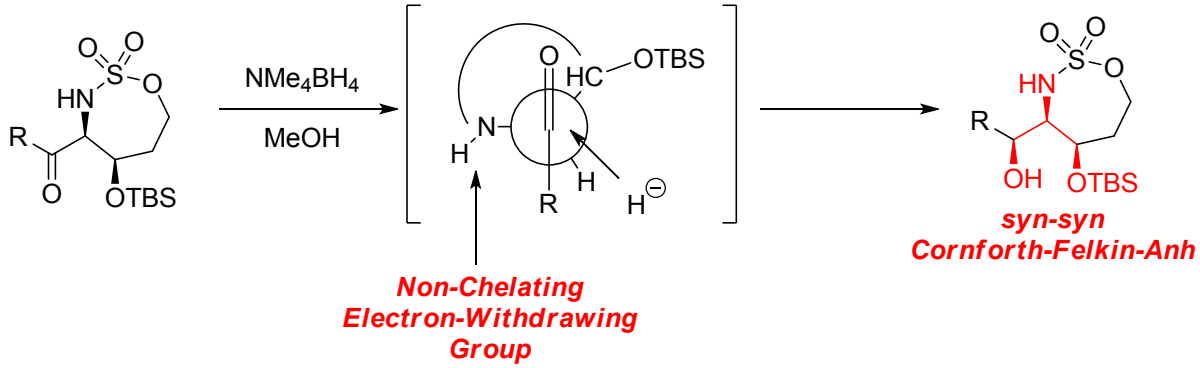
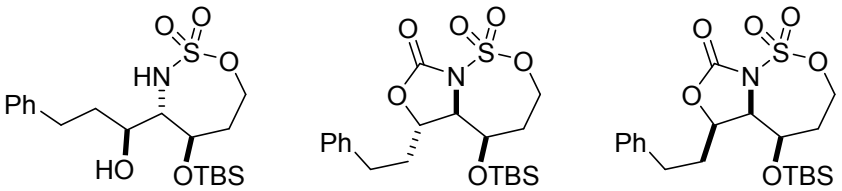



**Figure S5**. Stereochemical model for 1,2-*syn*:2,3-*syn* stereotriad synthesis from a 1,2-*syn* ketone.

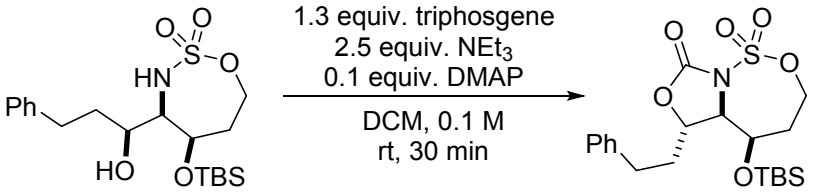
## XIV. Synthesis of crystalline stereotriad derivatives for X-ray analysis.



**38** **S-1 (derived from 43)** **S-2 (derived from 27)**

**Figure S6.** Structures of stereotriads that were crystallized in order to determine relative stereochemistry.

The stereotriads shown in Figure S6 were subjected to X-ray crystallography to confirm the stereochemical outcome of these reactions. (The fourth diastereomer in this series, stereotriad **57**, was not crystallized, as it stereochemistry was inferred by process of elimination.) Stereotriad **38** was crystallized without need for derivitization, but stereotriads **43** and **27** were not crystalline solids at room temperature. It was found that treatment of **43** and **27** with triphosgene under basic conditions yielded the corresponding oxazolidinones, which were readily crystallized to determine their relative stereochemistry. An example procedure for this reaction is given below:




Stereotriad **43** (50.0 mg, 0.120 mmol, 1.0 equiv) was added to a 10-mL roundbottom flask and dissolved in dry $CH_2Cl_2$ (0.1 M). Triethylamine (42 μL, 0.30 mmol, 2.5 equiv) and 4-dimethylaminopyridine (1.5 mg, 0.012 mmol, 0.1 equiv) were added sequentially. In a well-ventilated fume hood, triphosgene (46.3 mg, 0.156 mmol, 1.3 equiv) was carefully added to this solution, and the mixture was stirred at room temperature for 30 min, at which point TLC analysis (30% EtOAc in Hexane) indicated completion of the reaction. The reaction was quenched by the addition of aqueous $NH_4Cl$, and the mixture was transferred to a separatory funnel. The mixture was extracted twice with $CH_2Cl_2$, washed once with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The resulting crude oil was purified by column chromatography (10% to 40% EtOAc in hexane) to give the corresponding oxazolidinone (31.7

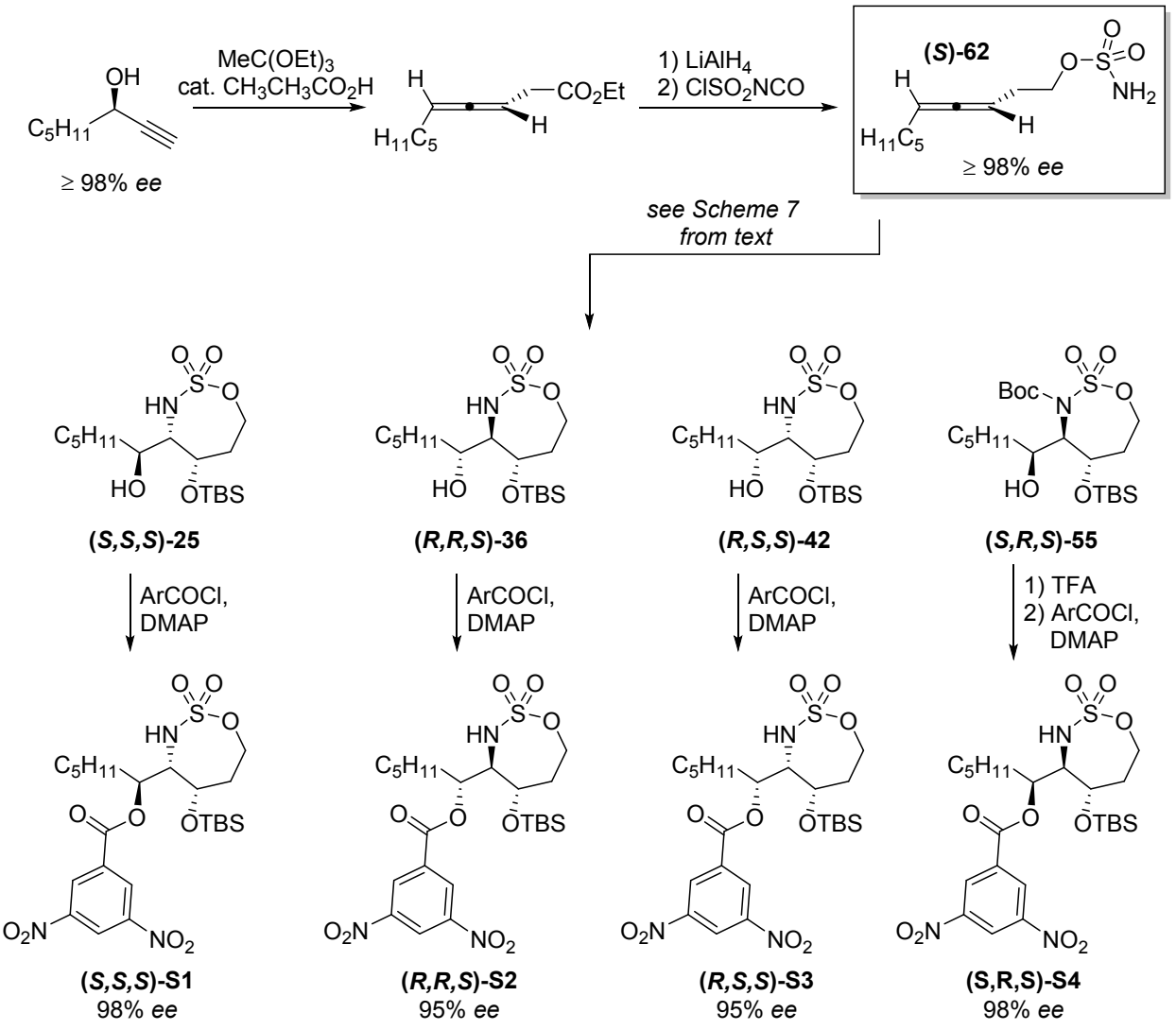
mg, 0.0717 mmol, 60%) as a white solid. In lieu of spectroscopic data, the crystal structure is provided (see additional Supporting Information).

**XV. Transfer of chirality studies**

Transfer-of-chirality experiments were carried out using an enantioenriched homoallenic sulfamate derived from 98+% *ee* (*R*)-(+)-1-octyn-3-ol (Alfa Aesar #L19045) by known methods.[5] The % *ee* of the homoallenic sulfamate could not be readily determined by chiral HPLC, so it was assumed to be ≥98% *ee*.[11] This material was carried through the sequence of steps depicted in Scheme 7 to arrive at enantioenriched triads **(*S,S,S*)-25**, **(*R,R,S*)-36**, **(*R,S,S*)-42**, and **(*S,R,S*)-55**. These compounds were O-benzoylated with 3,5-dinitrobenzoyl chloride as described in the General Procedure below in order to obtain compounds suitable for UV/Vis detection. Compound **(*S,R,S*)-55** decomposed under these conditions and had to be first treated with trifluoroacetic acid in order to cleave the N-Boc group. As seen in Scheme S1, there was minimal erosion of stereochemistry in generating the four stereotriads. The slight erosion observed in compounds **(*R,R,S*)-S2** and **(*R,S,S*)-S3** cannot necessarily be attributed to any one particular step in the stereotriad synthesis, as compound **(*S,R,S*)-S4**, which was derived from the longest sequence of steps from the starting allene, was obtained in an excellent 98% *ee*.

*General procedure for O-benzoylation of O/N/O triads:* The appropriate O/N/O triad (1 equiv) is added to a roundbottom flask and dissolved in dry $CH_2Cl_2$ (0.1 M). 3,5-Dinitrobenzoyl chloride (1.1 equiv) and 4-(dimethylamino)pyridine (1.1 equiv) are added sequentially, and the resulting light yellow solution is stirred at room temperature. The reaction is monitored by TLC (30% EtOAc/hexane, CAM stain). When full consumption of the starting triad is observed, the

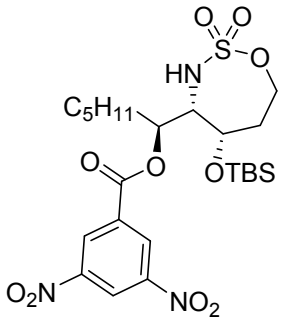
**Scheme S-1. Conversion of enantioenriched homoallenic sulfamate to all four stereotriads with good transfer of chirality.**




reaction is worked up by filtration through a silica plug (~1 in. in height) with 5% EtOAc/DCM. Rotary evaporation yields clean, O-benzoylated product with no trace of competing N-benzoylation or bis-benzoylation. The crude material is generally pure enough for HPLC analysis, but can be further purified by silica gel chromatography if desired (0-30% EtOAc in hexanes). Yields were not recorded for this step, as only an analytical amount of the benzoylated product was needed; however, clean conversion was always observed by NMR.

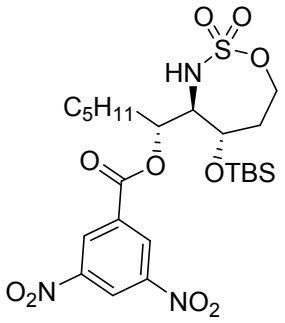
*Example procedure for TFA-mediated Boc deprotection:* The N-Boc protected triad **57** (8.5 mg, 17.6 μmol, 1 equiv.) is added to a 2 mL screw-cap flask and dissolved in a 4:1 mixture of $CH_2Cl_2$/$CF_3CO_2H$. The resulting clear solution is stirred at room temperature for 4 hours, or until TLC analysis (30% EtOAc/hexane, CAM stain) indicates full consumption of the starting material. The reaction mixture is then concentrated by rotary evaporation and any remaining acid residue is removed under vacuum (<1 mmHg). The crude material (4.7 mg, 12.3 μmol, 70%) is then carried on to the benzoylation step without further purification.

*Characterization and HPLC methods for O-benzoylated stereotriads:*

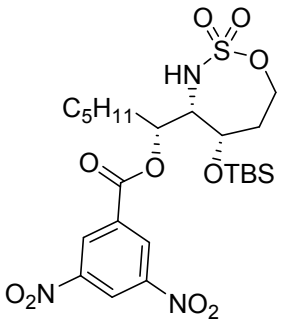



**(*S*,*S*,*S*)-S1.** $^1$H NMR: (500.0 MHz, $CDCl_3$) δ 9.27 (t, *J* = 2.1 Hz, 1H), 9.13 (d, 2.1 Hz, 2H), 5.43 (d, *J* = 11.0 Hz, 1H), 5.11 (ddd, *J* = 9.2, 7.4, 3.4 Hz, 1H), 4.59 (t, *J* = 12.6 Hz, 1H), 4.21 (dt, *J* = 12.6, 3.0 Hz, 1H), 4.16 (t, *J* = 2.6 Hz, 1H), 3.70 (dd, *J* = 10.8, 9.2 Hz, 1H), 2.18 (ddt, *J* = 15.5, 12.7, 2.8 Hz, 1H), 2.03 (m, 1H), 1.92 (dt, *J* = 15.5, 3.5 Hz, 1H), 1.88 (m, 1H), 1.46 (m, 1H), 1.33-1.24 (m, 5H), 0.94 (s, 9H), 0.85 (m, 3H), 0.05 (app s, 6H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 161.8, 148.9, 133.3, 129.3, 122.8, 75.4, 66.2, 64.0, 58.0, 36.6, 31.5, 30.6, 25.8, 24.0, 22.4, 18.0, 13.9, -4.0, -5.0. HRMS (ESI) *m*/*z* calculated $C_{23}H_{41}N_4O_{10}SSi$ [M+$NH_4^+$] 593.2308, found 593.2309. An OJ-H column (4.6 μm diameter x 258 mm) at a temperature of 40 ºC was employed, using 25% isopropanol in hexanes (isocratic) as the eluent and a flow rate of 0.9

mL/min. The enantiomers were detected at 7.88 and 8.99 minutes, with observation at both 215 nm and 225 nm.

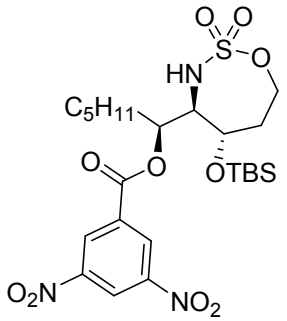



**(*R,R,S*)-S2.** $^{1}$H NMR: (500.0 MHz, $CDCl_3$) δ 9.24 (t, *J* = 2.1 Hz, 1H), 9.17 (d, *J* = 2.1 Hz, 2H), 5.63 (ddd, *J* = 10.6, 4.0, 2.6 Hz, 1H), 5.00 (d, *J* = 9.5 Hz, 1H), 4.37 (ddd, *J* = 13.1, 5.5, 2.9 Hz, 1H), 4.32 (app q, *J* = 13.1 Hz, 1H), 3.90 (td, *J* = 8.7, 4.2 Hz, 1H), 3.69 (td, *J* = 9.1, 4.2 Hz, 1H), 2.24 (dt, *J* = 15.5, 4.3 Hz, 1H), 2.07 (m, 1H), 1.76 (m, 2H), 0.95 (s, 9H), 1.50-1.20 (m, 6H), 0.88 (app t, *J* = 6.6 Hz, 3H), 0.13 (s, 6H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 162.2, 148.7, 133.6, 129.5, 122.6, 74.9, 70.8, 66.3, 60.5, 37.4, 31.6, 28.2, 25.6, 25.4, 22.4, 17.9, 13.9, -3.6, -4.9. HRMS (ESI) *m/z* calculated $C_{23}H_{41}N_4O_{10}SSi$ [M+$NH_4^+$] 593.2308, found 593.2310. An AD-H column (4.6 μm diameter x 258 mm) at a temperature of 40 ºC was employed, using a steady gradient from 5%-30% isopropanol in hexane over 40 minutes and a flow rate of 0.9 mL/min. The enantiomers were detected at 8.18 and 10.06 minutes at both 215 nm and 225 nm.




**(*R,S,S*)-S3.** $^{1}$H NMR: (500.0 MHz, $CDCl_3$) δ 9.23 (t, *J* = 2.1 Hz, 1H), 9.20 (t, *J* = 2.1 Hz, 2H), 5.39 (d, *J* = 10.8 Hz, 1H), 5.23 (ddd, *J* = 12.4, 4.8, 3.8 Hz, 1H), 4.55 (t, *J* = 12.7 Hz, 1H), 4.25 (t,

*J* = 2.7 Hz, 1H), 4.18 (dt, *J* = 12.7, 3.2 Hz, 1H), 3.54 (t, *J* = 10.4 Hz, 1H), 2.18 (ddt, *J* = 15.7, 12.6, 2.7 Hz, 1H), 1.94 (dt, *J* = 15.7, 3.3 Hz, 1H), 1.76 (m, 2H), 1.50-1.18 (m, 6H), 0.98 (s, 9H), 0.88 (app t, *J* = 6.9 Hz, 3H), 0.20 (s, 3H), 0.15 (s, 3H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 162.8, 148.7, 133.6, 129.8, 122.5, 73.9, 66.4, 64.0, 60.3, 36.9, 31.5, 31.2, 25.7, 24.9, 22.4, 18.0, 13.9, -3.9, -4.8. HRMS (ESI) *m*/*z* calculated $C_{23}H_{41}N_4O_{10}SSi$ [M+$NH_4^+$] 593.2308, found 593.2302. An AD-H column (4.6 μm diameter x 258 mm) at a temperature of 40 ºC was employed, using a steady gradient from 5%-30% isopropanol in hexane over 40 minutes and a flow rate of 0.9 mL/min. The enantiomers were detected at 7.72 and 8.87 minutes, with observation at both 215 nm and 225 nm.




**(*S,R,S*)-S4.** $^1$H NMR: (500.0 MHz, $CDCl_3$) δ 9.24 (t, *J* = 1.8 Hz, 1H), 9.15 (d, *J* = 1.8 Hz, 2H), 5.54 (t, *J* = 6.7 Hz, 1H), 5.27 (d, *J* = 10.5 Hz, 1H), 4.39 (m, 2H), 3.89 (td, *J* = 8.4, 4.6 Hz, 1H), 3.55 (t, *J* = 9.7 Hz, 1H), 2.26 (m, 1H), 2.08 (m, 1H), 1.91 (m, 2H), 1.50-1.20 (m, 6H), 0.89 (m, 12H), 0.05 (s, 3H), -0.05 (s, 3H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 161.9, 148.8, 133.6, 129.3, 122.7, 75.2, 70.2, 66.5, 59.3, 37.5, 31.3, 29.7, 25.7, 24.5, 22.4, 17.8, 13.9, -3.7, -4.9. HRMS (ESI) *m*/*z* calculated $C_{23}H_{41}N_4O_{10}SSi$ [M+$NH_4^+$] 593.2308, found 593.2310. An AD-H column (4.6 μm diameter x 258 mm) at a temperature of 40 ºC was employed, using a steady gradient from 5%-30% isopropanol in hexane over 40 minutes and a flow rate of 0.9 mL/min. The enantiomers were detected at 8.30 and 8.92 minutes, with observation at both 215 nm and 225 nm.

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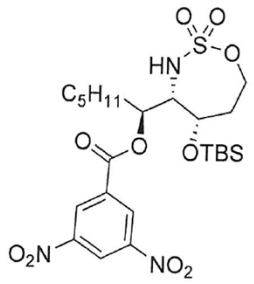

(enantioenriched)

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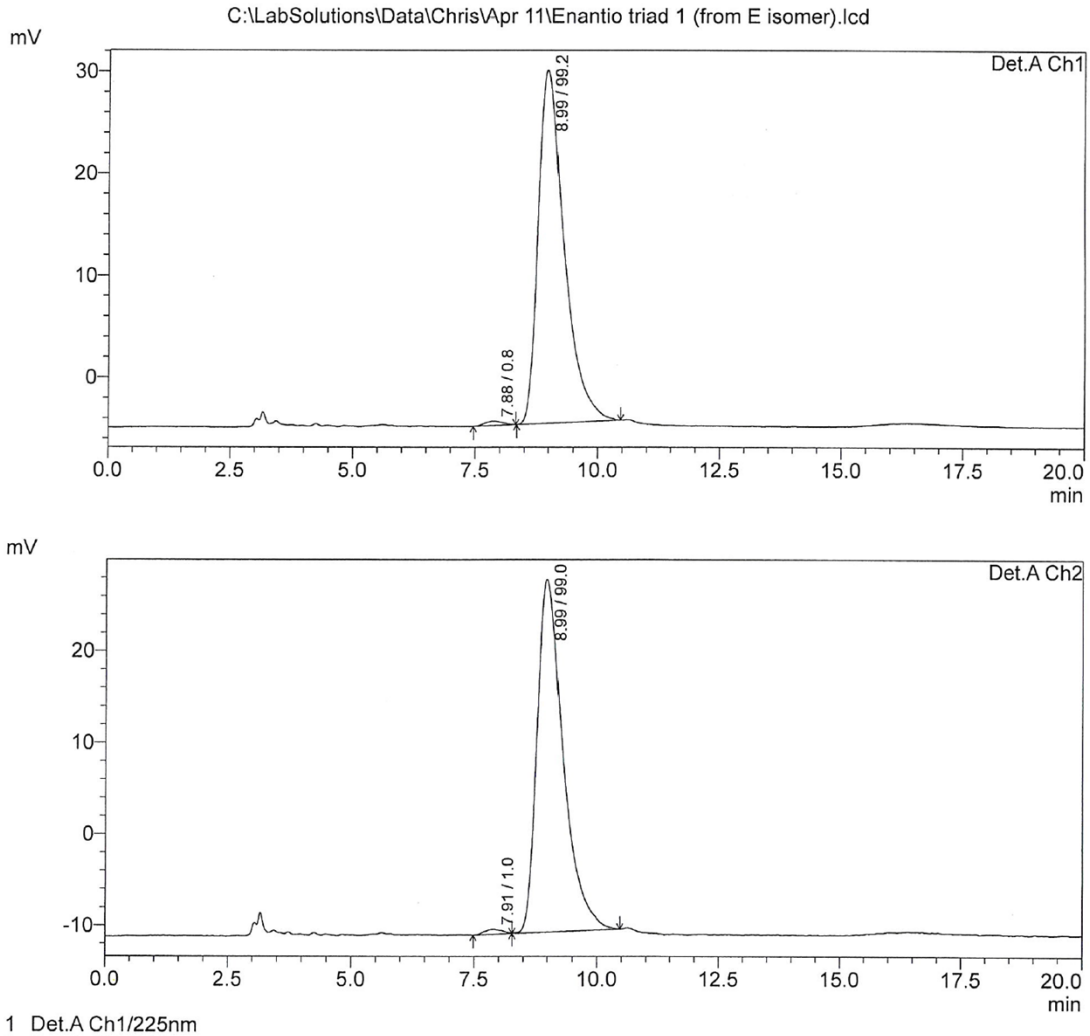


1 Det.A Ch1/225nm
2 Det.A Ch2/215nm

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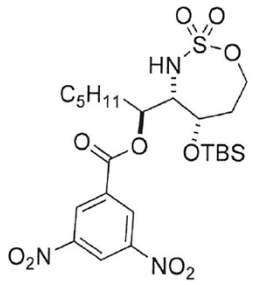

(racemic)

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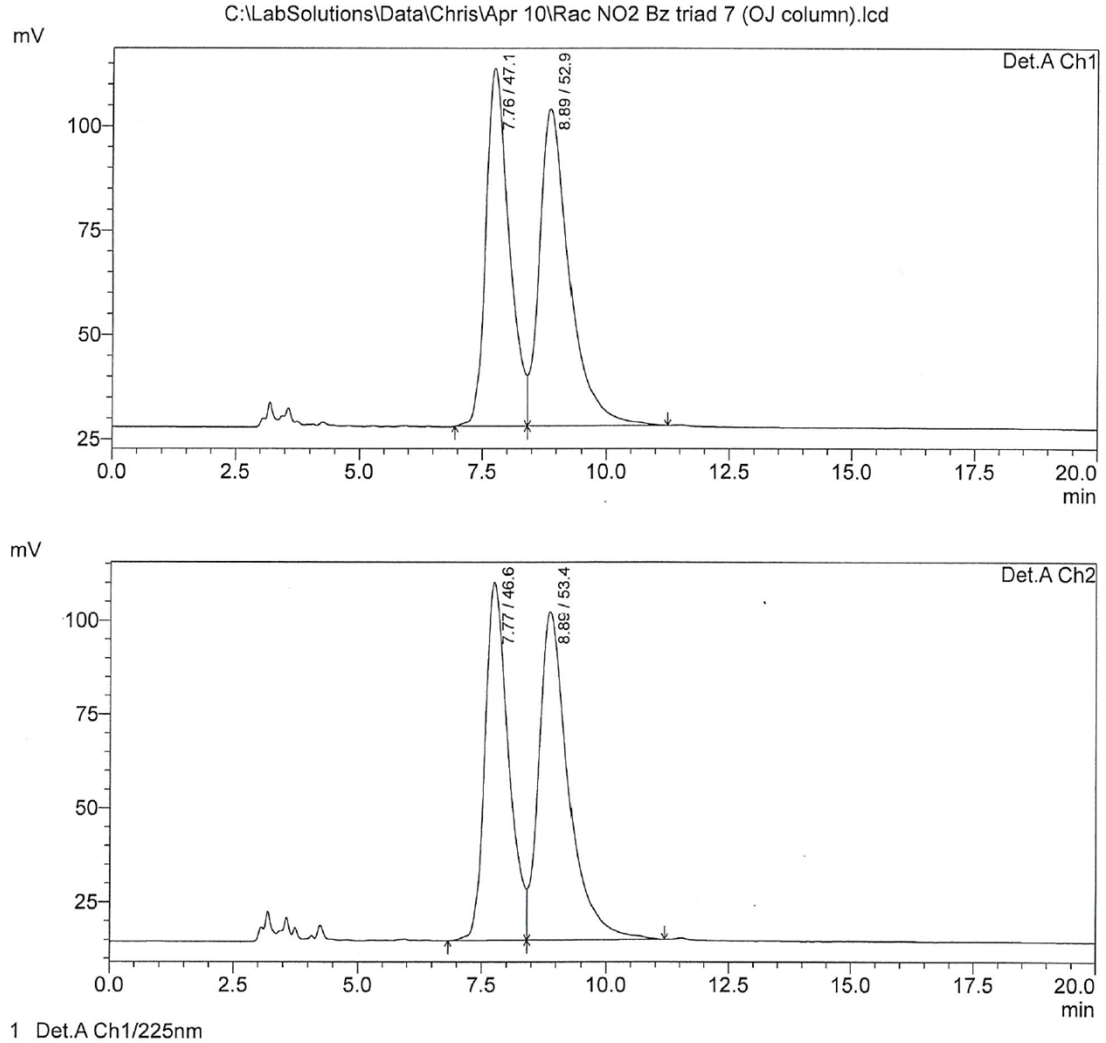


1 Det.A Ch1/225nm
2 Det.A Ch2/215nm

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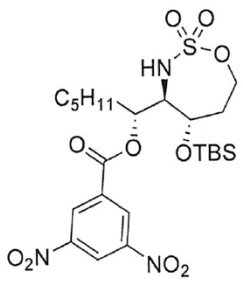

(enantioenriched)

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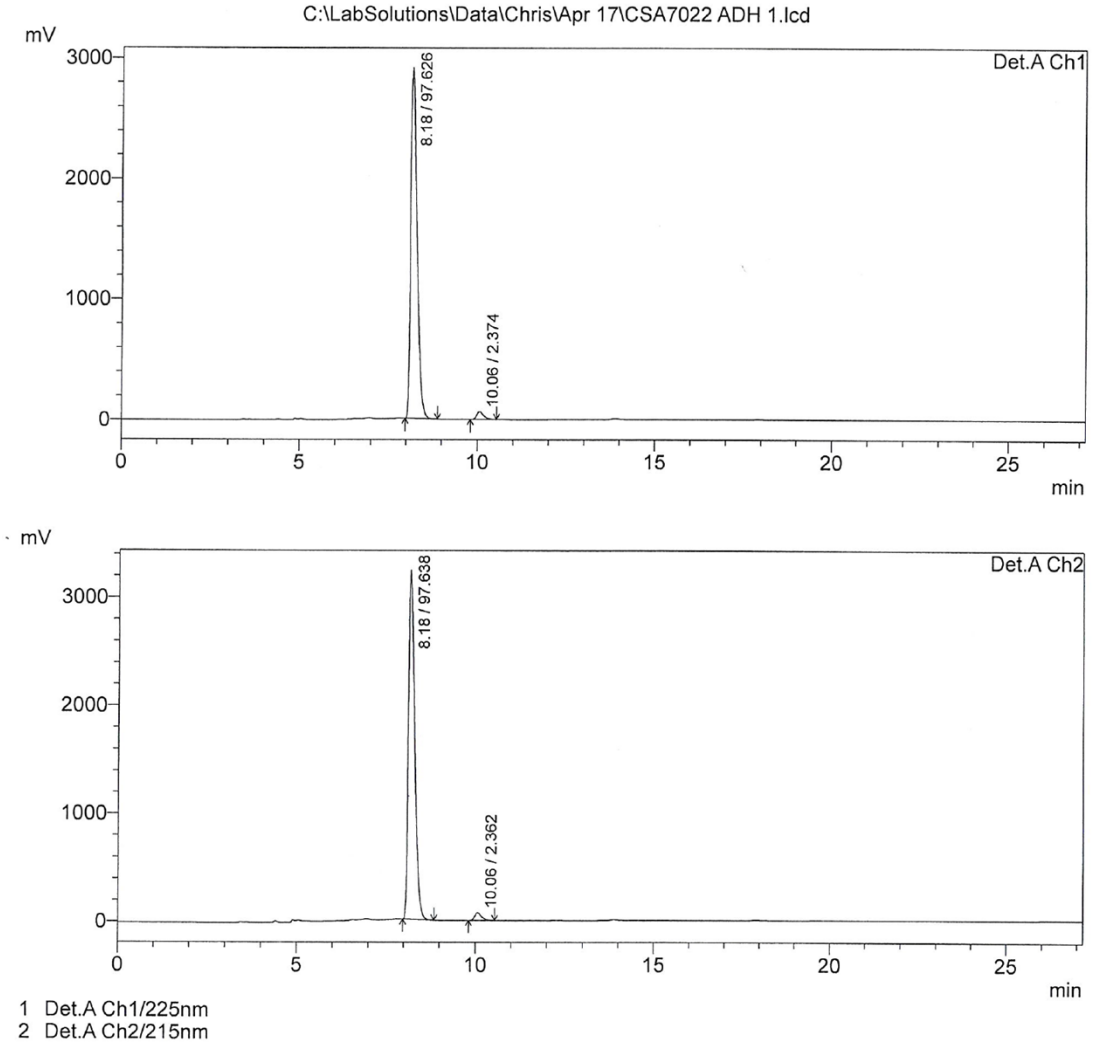


1 Det.A Ch1/225nm
2 Det.A Ch2/215nm

C:\LabSolutions\Data\Chris\Apr 17 night\CSA7014 ADH run 2.lcd

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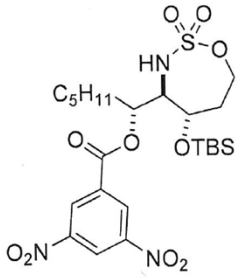
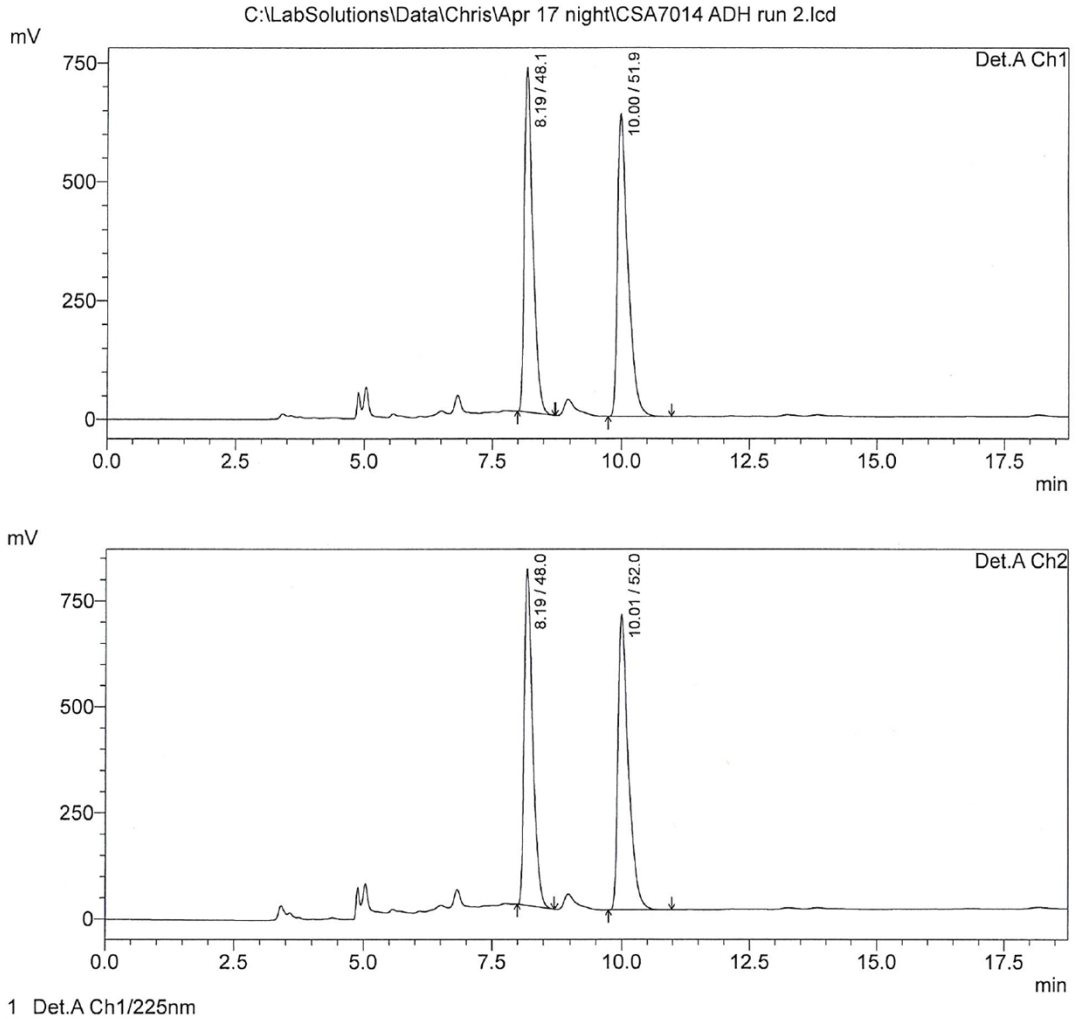


(racemic)

**<Chromatogram>**




1 Det.A Ch1/225nm
2 Det.A Ch2/215nm

C:\LabSolutions\Data\Chris\Apr 17 night\CSA7023 ADH run 2.lcd

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| Injection Volume | : 5 uL |
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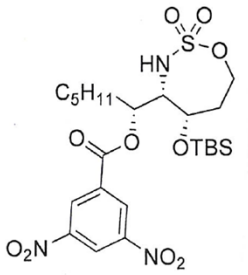
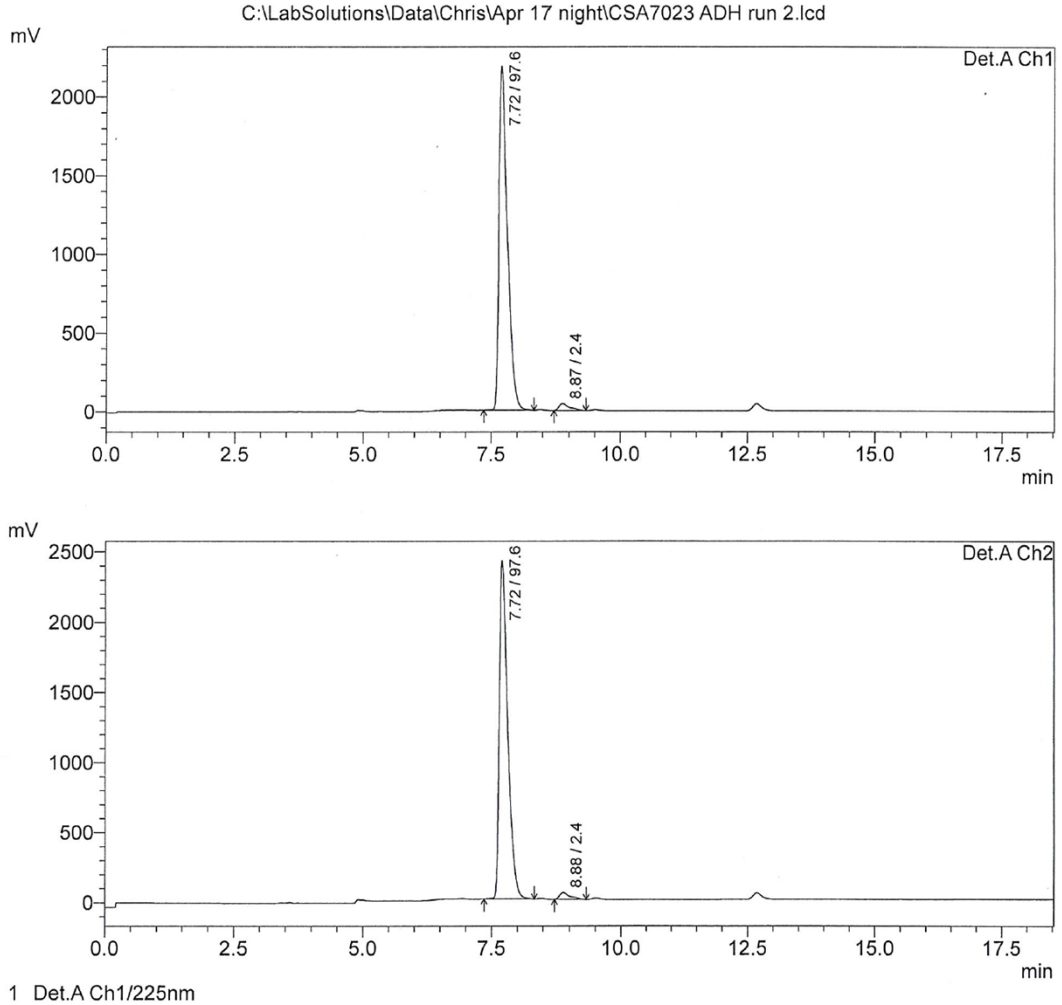



(enantioenriched)

**<Chromatogram>**




1 Det.A Ch1/225nm
2 Det.A Ch2/215nm

C:\LabSolutions\Data\Chris\Apr 17 night\CSA7013 ADH run 2.lcd

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| Sample ID | : |
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| Vail # | : 65 |
| Injection Volume | : 5 uL |
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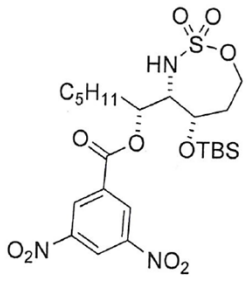
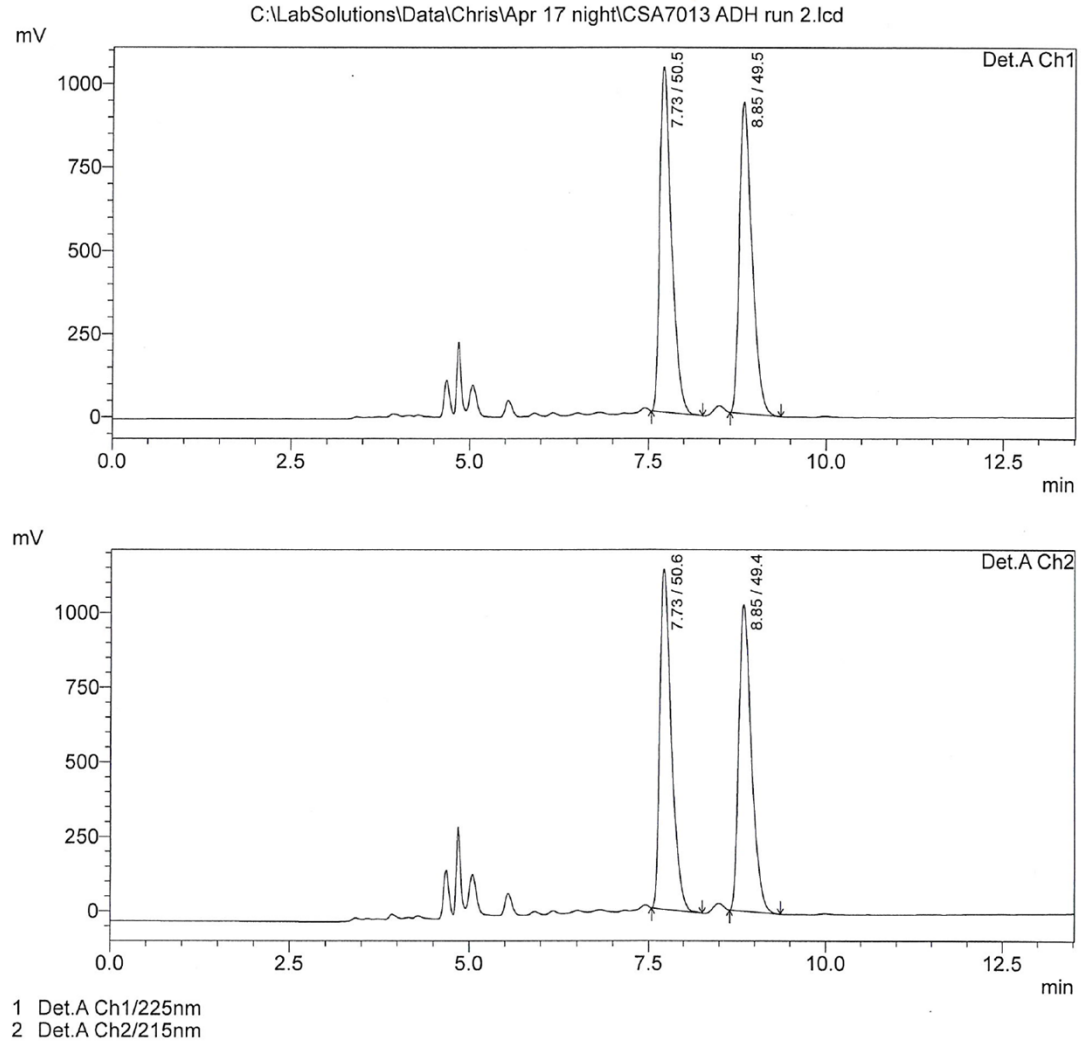



(racemic)

**<Chromatogram>**




1 Det.A Ch1/225nm
2 Det.A Ch2/215nm

C:\LabSolutions\Data\Chris\Apr 17\CSA7021 ADH 1.lcd

| | |
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| Sample ID | : |
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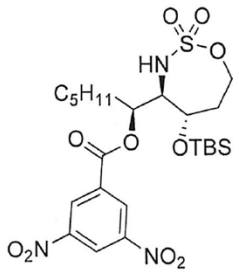
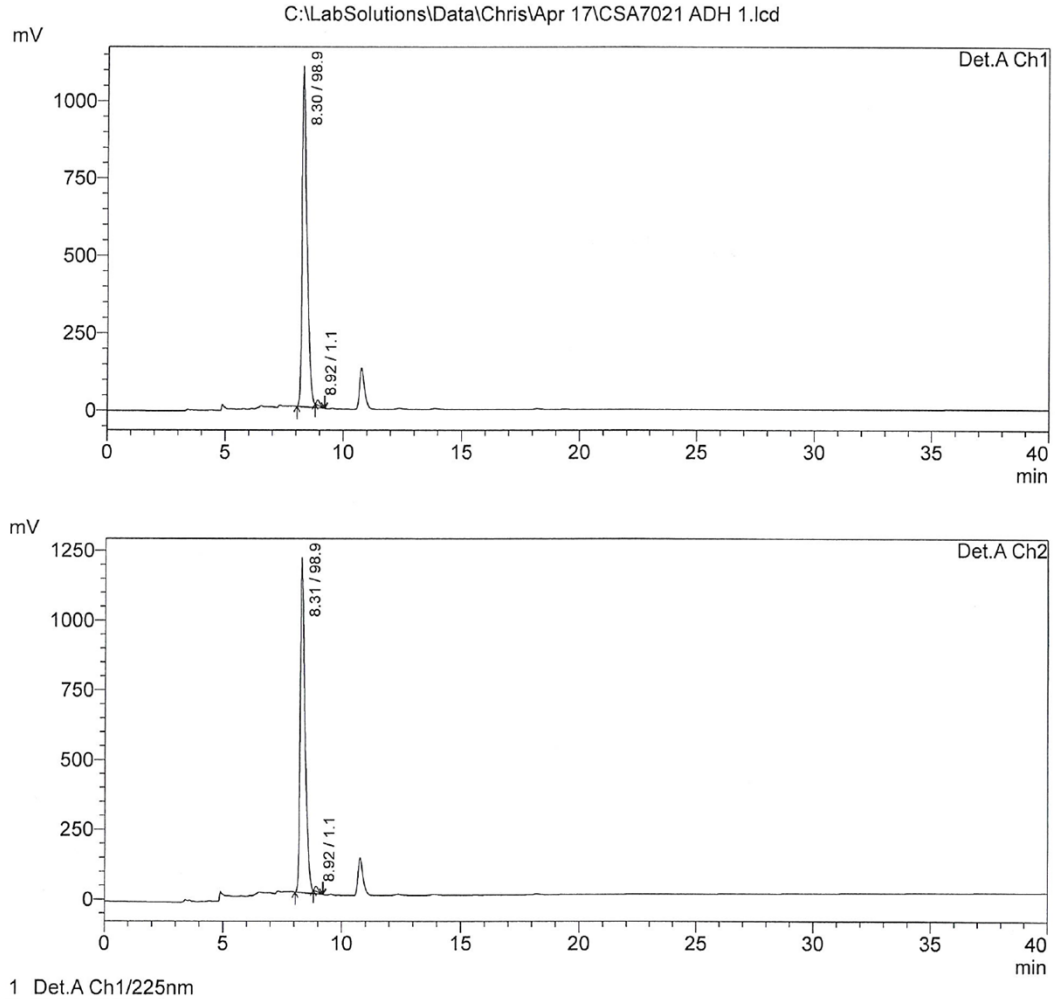



(enantioenriched)

**<Chromatogram>**




1 Det.A Ch1/225nm
2 Det.A Ch2/215nm

C:\LabSolutions\Data\Chris\Apr 17 night\CSA7018 ADH run2 (different pre run).lcd

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| Sample ID | : |
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| Vail # | : 69 |
| Injection Volume | : 5 uL |
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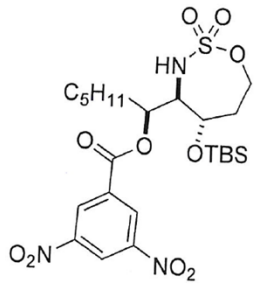

(racemic)

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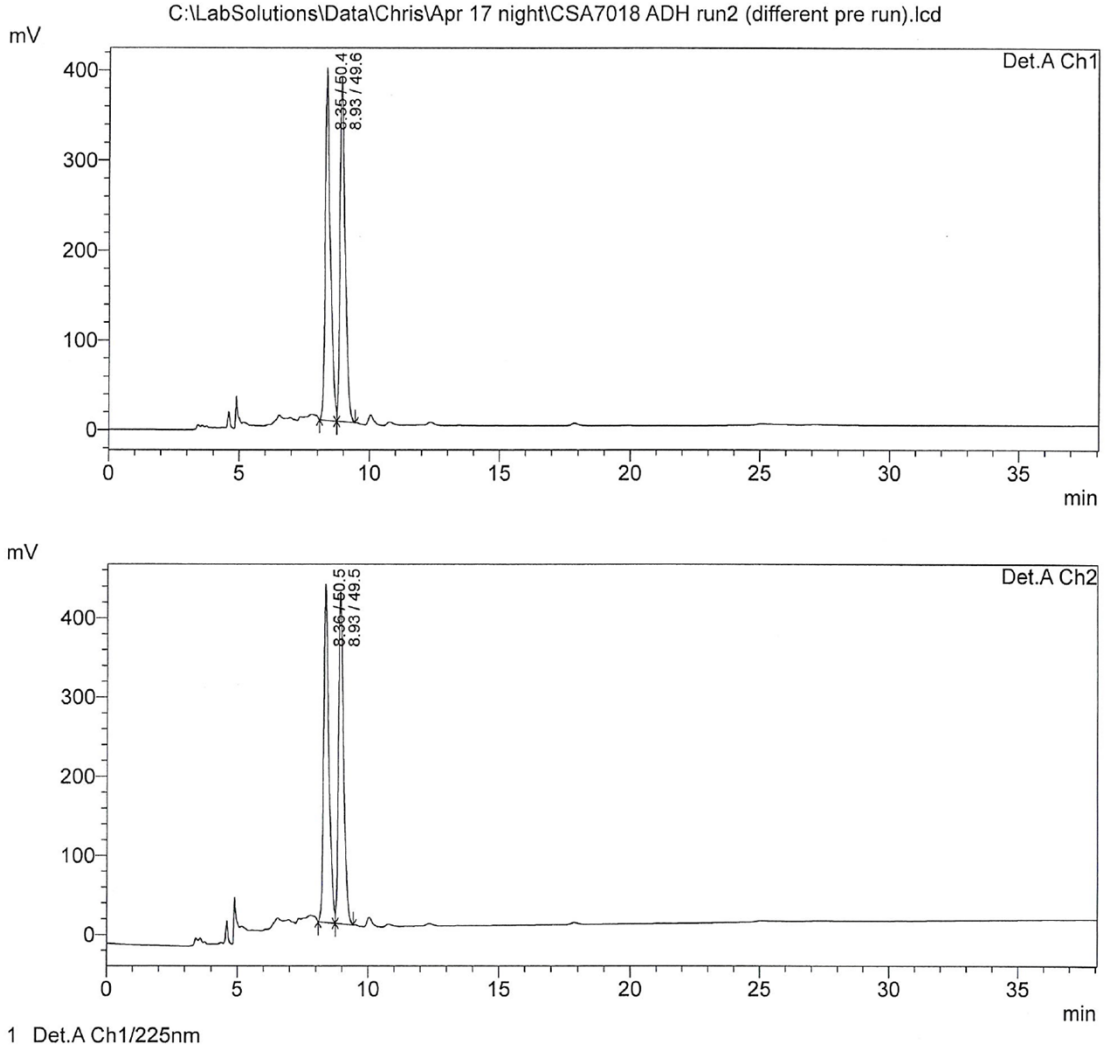
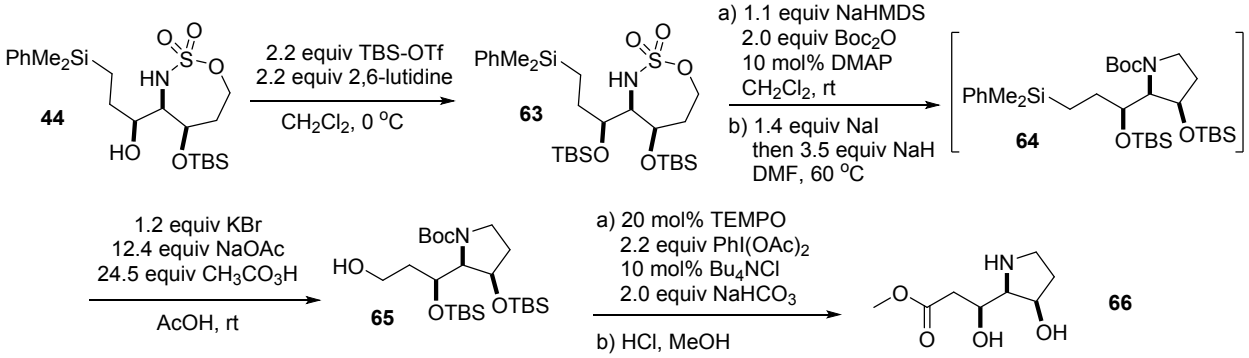



1 Det.A Ch1/225nm
2 Det.A Ch2/215nm

**XVI. Total synthesis of (±)-detoxinine methyl ester.**




**Compound 63.** The 1,2-*syn*:2,3-*syn* stereotriad **44** (0.722 g, 1.52 mmol, 1.0 equiv) was dissolved in 5.0 mL of dry dichloromethane. The solution was cooled to 0 °C and 0.387 mL of 2,6-lutidine (3.34 mmol, 2.2 equiv) and 0.768 mL of TBSOTf (3.34 mmol, 2.2 equiv) were added. The reaction mixture was stirred for 25 min, diluted with 20 mL dichloromethane and quenched with 30 mL of water. The phases were separated and the aqueous phase extracted with dichloromethane (2 x 15 mL). The combined organic fractions were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (2% to 10% EtOAc in hexanes) on silica gel. The product **63** (0.761 g, 1.29 mmol, 85%) was isolated as a white solid. $^1$H NMR: (500.0 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.35 (m, 3H), 5.21 (d, *J* = 10.6 Hz, 1H), 4.52 (t, *J* = 12.4 Hz, 1H), 4.14 (t, *J* = 3.1 Hz, 1H), 4.10 (dt, *J* = 12.4, 3.1 Hz, 1H), 3.61 (ddd, *J* = 8.0, 5.8, 2.8 Hz, 1H), 3.32 (dd, *J* = 10.6, 8.0 Hz, 1H), 1.99 (ddt, *J* = 15.7, 12.4, 3.1 Hz, 1H), 1.83 (dt, *J* = 15.7, 3.1 Hz, 1H), 1.50 (tdd, J = 14.0, 3.7, 2.8 Hz, 1H), 1.34 (tdd, *J* = 14.0, 5.8, 4.2 Hz, ), 0.90 (s, 9H), 0.86 (s, 9H), 0.80 (td, *J* = 14.0, 3.7 Hz, 1H), 0.72 (td, *J* = 14.0, 4.2 Hz, 1H), 0.27 (s, 3H), 0.26 (s, 3H), 0.09 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), -0.06 (s, 3H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 138.6, 133.5, 129.0, 127.9, 72.9, 66.1, 63.9,

59.8, 37.1, 27.0, 25.8, 25.8, 18.0, 17.9, 10.0, -2.9, -3.5, -3.8, -4.2, -4.6, -4.8. HMRS (ESI) *m/z* calculated for $C_{27}H_{54}NO_5SSi_3$ $[M + H]^+$ 588.3026, found 588.3032.

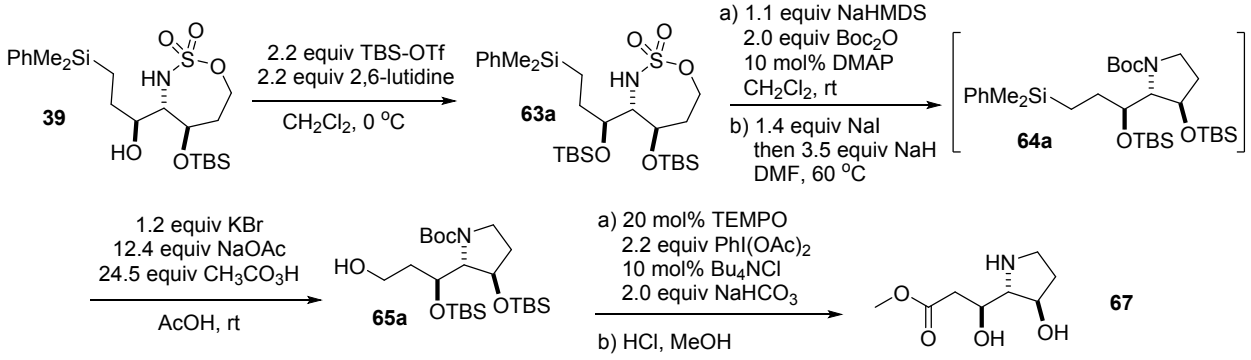
**Compound 65.** The sulfamate **63** (0.689 g, 1.17 mmol, 1.0 equiv) was dissolved in 6.0 mL of dry dichloromethane. The solution was cooled to 0 °C and DMAP was added (14.3 mg, 0.117 mmol, 10 mol%), followed by dropwise addition of NaHMDS (1.30 mL of 1.0 M solution in THF, 1.30 mmol, 1.1 equiv). After completion of the addition, $Boc_2O$ was added (0.511 g, 2.34 mmol, 2.0 equiv). The solution was warmed to rt and allowed to stir for 3.5 h. The solution containing the protected sulfamate was concentrated under reduced pressure to a tan syrup. The material was redissolved in 5.9 mL of dry DMF and 0.246 g NaI (1.64 mmol, 1.4 equiv) was added. The thick solution was warmed to 45 °C and stirred for 15 min prior to the cautious addition of NaH (0.164 g of 60% wt suspension in mineral oil, 4.10 mmol, 3.5 equiv). The solution was then warmed to 60 °C and stirred for 10 h. The reaction mixture was cooled and cautiously quenched with 50 mL of water. The mixture was extracted with diethyl ether (4 x 50 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residual HMDS was removed from the crude residue by flash chromatography (5% EtOAc in hexanes) to yield oil **64** of sufficient purity for the Fleming-Tamao oxidation.

The crude pyrrolidine **64** was dissolved in 8.7 ml of glacial acetic acid containing KBr (0.164 g, 1.38 mmol, 1.2 equiv) and NaOAc (0.292 g, 3.56 mmol, 3.1 equiv). Peroxyacetic acid (1.47 mL of 32% wt in acetic acid, 7.01 mmol, 6.1 equiv) was added dropwise with ice bath cooling to control the exotherm. After stirring for 5 min, a second portion of NaOAc was added (0.876 g, 10.7 mmol, 9.3 equiv), followed by a second portion of peroxyacetic acid (4.45 mL, 21.2 mmol, 18.4 equiv). The solution was stirred at rt for 2 h before dilution with 100 mL diethyl ether and

100 mL of water containing 11.7 g sodium thiosulfate pentahydrate. The phases were separated, and the aqueous phase extracted with diethyl ether (3 x 50 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ before drying with $MgSO_4$. The crude residue was purified by column chromatography (4% to 20% EtOAc in hexanes) to yield **65** as a colorless oil (0.386 g, 0.788 mmol, 67% from sulfamate). $^1$H NMR: (500.0 MHz, toluene-$d_8$, 60 °C) δ 4.44 (ddd, *J* = 9.2, 3.5, 2.8 Hz, 1H), 4.37 (m, 1H), 4.13 (app q, *J* = 9.2 Hz, 1H), 3.92 (m, 1H), 3.71 (m, 1H), 3.45 (td, *J* = 10.3, 3.1 Hz, 1H), 3.35 (m, 1H), 3.15 (m, 1H), 2.21 (m, 1H), 2.00-2.10 (m, 1H), 1.70-1.85 (m, 2H), 1.43 (s, 9H), 0.95 (s, 9H), 0.91 (s, 9H), 0.15 (s, 3H), 0.10 (s, 3H), 0.03 (s, 3H), 0.00 (s, 3H). $^{13}$C NMR: (125.7 MHz, toluene-$d_8$) δ 156.2, 79.4, 72.0, 71.1, 61.2, 60.0, 44.8, 38.5, 32.2, 28.4, 26.1, 26.0, 18.3, 18.2, -3.7, -4.2, -4.9, -5.0. HMRS (ESI) *m/z* calculated for $C_{24}H_{52}NO_5Si_2$ $[M + H]^+$ 490.3379, found 490.3372.

**Compound 66.** A 5 mL round bottom flask equipped with a magnetic stir bar was charged with **64** (91.5 mg, 0.187 mmol), sodium bicarbonate (31.4 mg, 0.374 mmol, 2.0 equiv), $Bu_4NCl$ (5.2 mg, 0.0187 mmol, 10 mol%), and 1.10 mL 1:1 $CH_3CN$:$H_2O$. The mixture was stirred vigorously, and TEMPO (5.8 mg, 0.0374, 20 mol%) was added, followed by $PhI(OAc)_2$ (0.130 g, 0.411 mmol, 2.20 equiv). After stirring under nitrogen for 24 hours, the reaction was diluted with 5 mL $CH_2Cl_2$ and 5 mL of 0.2 M HCl. The phases were separated, and the aqueous phase extracted with $CH_2Cl_2$ (4 x 5 mL). The combined organic fractions were dried with $MgSO_4$ and concentrated to a crude oil. The oil was treated with 5.60 mL of 0.5 M HCl in methanol (prepared by reaction of TMS-Cl in methanol) and stirred for 1 hour. Concentration by rotary evaporation afforded a crude oil. Non-polar organics were removed by column chromatography (10% $CH_3CN$ in $CH_2Cl_2$, then 10% MeOH in $CH_3CN$) yielding crude white solid **66** that was

triturated with cold $CH_3CN$ and isolated by filtration (26.9 mg, 0.142 mmol, 76%). $^1$H NMR: (500.0 MHz, $D_2O$) δ 4.51 (t, *J* = 3.3 Hz, 1H), 4.40 (ddd, *J* = 9.9, 9.2, 3.2 Hz, 1H), 3.73 (s, 3H), 3.40-3.58 (m, 3H), 2.84 (dd, *J* = 15.8, 3.2 Hz, 1H), 2.63 (dd, *J* = 15.8, 9.2 Hz, 1H), 2.23 (dtd, *J* = 14.3, 10.1, 3.3 Hz, 1H), 2.12 (ddd, *J* = 14.3, 7.8, 3.0 Hz, 1H). $^{13}$C NMR: (125.7 MHz, $D_2O$) δ 173.2, 69.3, 68.0, 64.9, 52.5, 42.9, 39.1, 33.1. HMRS (ESI) *m/z* calculated for $C_8H_{16}NO_4$ [M + H]$^+$ 190.1074, found 190.1079.




**Compound 63a.** The 1,2-*anti*:2,3-*anti* stereotriad **39** (0.150 g, 0.317 mmol, 1.0 equiv) was dissolved in 3.1 mL of dry dichloromethane. The solution was cooled to 0 °C and 0.0806 mL of 2,6-lutidine (0.696 mmol, 2.2 equiv) and 0.160 mL of TBSOTf (0.696 mmol, 2.2 equiv) were added. The reaction mixture was stirred for 25 min, diluted with 10 mL dichloromethane and quenched with 10 mL of water. The phases were separated and the aqueous phase extracted with dichloromethane (2 x 15 mL). The combined organic fractions were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (2% to 10% EtOAc in hexanes) on silica gel. The product **63a** (0.165 g, 0.281 mmol, 89%) was isolated as a white solid. $^1$H NMR: (500.0 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.34 (m, 3H), 4.77 (d, *J* = 6.0 Hz, 1H), 4.43 (ddd, *J* = 12.4, 8.8, 1.3 Hz, 1H), 4.18 (ddd, *J* = 12.4, 7.3, 1.8 Hz, 1H), 4.05-4.10 (m, 2H), 3.27 (app q, *J* = 6.0 Hz, 1H), 2.13 (ddt, *J* = 15.6, 8.8, 2.1 Hz, 1H), 1.90 (m, 1H), 1.65 (m, 1H), 1.52 (m, 1H), 0.87 (s, 9H), 0.86 (s, 9H), 0.77 (td, *J* = 14.0, 4.2

Hz, 1H), 0.67 (td, $J$ = 14.0, 3.9 Hz, 1H), 0.27 (s, 3H), 0.26 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), -0.00 (s, 3H), -0.01 (s, 3H); $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 138.8, 133.6, 129.0, 127.8, 71.7, 69.7, 65.3, 62.0, 35.5, 26.3, 25.8, 25.7, 18.0, 17.9, 9.7, -3.2, -3.2, -4.0, -4.2, -4.6, -4.9. HMRS (ESI) *m/z* calculated for $C_{27}H_{54}NO_5SSi_3$ $[M + NH_4]^+$ 605.3291, found 605.3307.

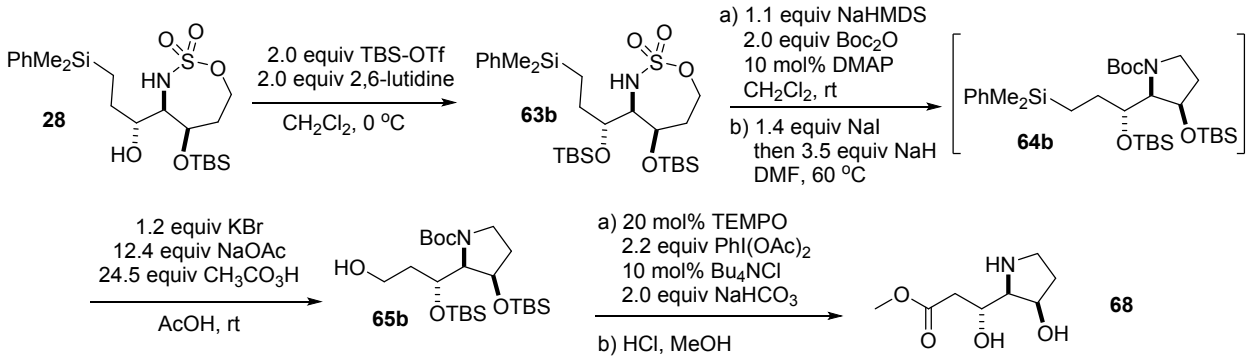
**Compound 65a.** The sulfamate **63a** (0.144 g, 0.246 mmol, 1.0 equiv) was dissolved in 1.5 mL of dry dichloromethane. The solution was cooled to 0 °C and DMAP was added (3.0 mg, 0.0246 mmol, 10 mol%), followed by dropwise addition of NaHMDS (0.271 mL of 1.0 M solution in THF, 0.271 mmol, 1.1 equiv). After completion of the addition, $Boc_2O$ was added (0.107 g, 0.492 mmol, 2.0 equiv). The solution was warmed to rt and allowed to stir for 50 minutes. The solution containing the protected sulfamate was concentrated under reduced pressure to a tan syrup. The material was redissolved in 1.3 mL of dry DMF and 0.0516 g NaI (0.344 mmol, 1.4 equiv) was added. The thick solution was warmed to 45 °C and stirred for 15 min prior to the cautious addition of NaH (0.0344 g of 60% wt suspension in mineral oil, 0.861 mmol, 3.5 equiv). The solution was then warmed to 60 °C and stirred for 10 h. The reaction mixture was cooled and cautiously quenched with 10 mL of water. The mixture was extracted with diethyl ether (4 x 10 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residual HMDS was removed from the crude residue by flash chromatography (5% EtOAc in hexanes) to yield 0.0983 g of oil **64a** of sufficient purity for the Fleming-Tamao oxidation.

The crude pyrrolidine **64a** was dissolved in 1.2 ml of glacial acetic acid containing KBr (0.0231 g, 0.194 mmol, 1.2 equiv) and NaOAc (0.0411 g, 0.501 mmol, 3.1 equiv). Peroxyacetic acid (0.207 mL of 32% wt in acetic acid, 0.986 mmol, 6.1 equiv) was added dropwise with ice bath cooling to control the exotherm. After stirring for 5 min, a second portion of NaOAc was

added (0.123 g, 1.50 mmol, 9.3 equiv), followed by a second portion of peroxyacetic acid (0.625 mL, 2.97 mmol, 18.4 equiv). The solution was stirred at rt for 2 h before dilution with 10 mL diethyl ether and 12 mL of water containing 1.62 g sodium thiosulfate pentahydrate. The phases were separated, and the aqueous phase extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ before drying with $MgSO_4$. The crude residue was purified by column chromatography (4% to 20% EtOAc in hexanes) to yield **65a** as a colorless oil (0.0698 g, 0.142 mmol, 58% from sulfamate). (Note: This spectrum is complicated by the presence of two rotamers in the product structure. However, the rotamers are fairly well resolved for this compound). $^1$H NMR: (500.0 MHz, $CDCl_3$) δ 4.45 (br s, 1H), 4.17 (m, 1H), 3.80 (dt, *J* = 10.8, 6.7 Hz, 0.6H), 3.68-3.75 (m, 2H), 3.58 (app q, *J* = 8.7 Hz, 0.4H), 3.42-3.50 (m, 1H), 3.25-3.33 (m, 1H), 2.80 (br s, 0.4H), 2.04 (m, 1H), 1.64-1.85 (m, 3.6H), 1.43-1.49 (2 x s, 9H), 0.87 (s, 9H), 0.86 (s, 9H), -0.05-0.07 (overlapping s, 12H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 155.2, 154.8, 79.5, 79.4, 72.6, 71.8, 70.2, 69.6, 69.5, 69.2, 59.6, 59.5, 45.2, 45.0, 38.2, 37.8, 34.1, 33.5, 28.6, 28.5, 25.9, 25.8, 25.7, 25.6, 17.9 x 2, 17.8, 17.8, -4.4, -4.5, -4.6, -4.7 x 2, -4.8, -4.9, -5.0. HMRS (ESI) *m/z* calculated for $C_{24}H_{52}NO_5Si_2$ $[M + H]^+$ 490.3379, found 490.3273.

**Compound 67.** A 5 mL round bottom flask equipped with a magnetic stir bar was charged with **65a** (65.0 mg, 0.133 mmol), sodium bicarbonate (22.3 mg, 0.266 mmol, 2.0 equiv), $Bu_4NCl$ (3.7 mg, 0.0133 mmol, 10 mol%), and 0.78 mL 1:1 $CH_3CN$:$H_2O$. The mixture was stirred vigorously, and TEMPO (4.2 mg, 0.0266, 20 mol%) was added, followed by $PhI(OAc)_2$ (92.4 mg, 0.293 mmol, 2.20 equiv). After stirring under nitrogen for 24 hours, the reaction was diluted with 4 mL $CH_2Cl_2$ and 4 mL of 0.2 M HCl. The phases were separated, and the aqueous phase

extracted with $CH_2Cl_2$ (4 x 5 mL). The combined organic fractions were dried with $MgSO_4$ and concentrated to a crude oil. The oil was treated with 4.0 mL of 0.5 M HCl in methanol (prepared by reaction of TMS-Cl in methanol) and stirred for 1 hour. Concentration by rotary evaporation afforded a crude oil. Non-polar organics were removed by column chromatography (10% $CH_3CN$ in $CH_2Cl_2$, then 10% MeOH in $CH_3CN$) yielding crude white solid **67** that was purified by trituration with cold $CH_2Cl_2$ (23.9 mg, 0.126 mmol, 95%). $^1$H NMR: (500.0 MHz, $D_2O$) δ 4.59 (ddd, *J* = 6.0, 4.8, 4.2 Hz, 1H), 4.46 (dt, *J* = 8.7, 4.2 Hz, 1H), 3.75 (s, 3H), 3.58 (t, *J* = 4.2 Hz, 1H), 3.41-3.52 (m, 2H), 2.81 (dd, *J* = 16.2, 4.2 Hz, 1H), 2.76 (dd, *J* = 16.2, 8.7 Hz, 1H), 2.29 (ddt, *J* = 13.0, 6.9, 6.0 Hz, 1H), 2.04 (dddd, *J* = 13.0, 11.5, 5.9, 4.8 Hz, 1H); $^{13}$C NMR: (125.7 MHz, D2O) δ 173.0, 69.1, 68.3, 64.8, 52.5, 44.5, 38.4, 33.0. HMRS (ESI) *m/z* calculated for $C_8H_{16}NO_4$ $[M + H]^+$ 190.1074, found 190.1078.




**Compound 63b.** The 1,2-*anti*:2,3-*anti* stereotriad **28** (0.260 g, 0.549 mmol, 1.0 equiv) was dissolved in 5.0 mL of dry dichloromethane. The solution was cooled to 0 °C and 0.127 mL of 2,6-lutidine (1.10 mmol, 2.0 equiv) and 0.252 mL of TBSOTf (1.10 mmol, 2.0 equiv) were added. The reaction mixture was stirred for 25 min, diluted with 10 mL dichloromethane and quenched with 10 mL of water. The phases were separated and the aqueous phase extracted with dichloromethane (2 x 15 mL). The combined organic fractions were dried with $MgSO_4$, filtered,

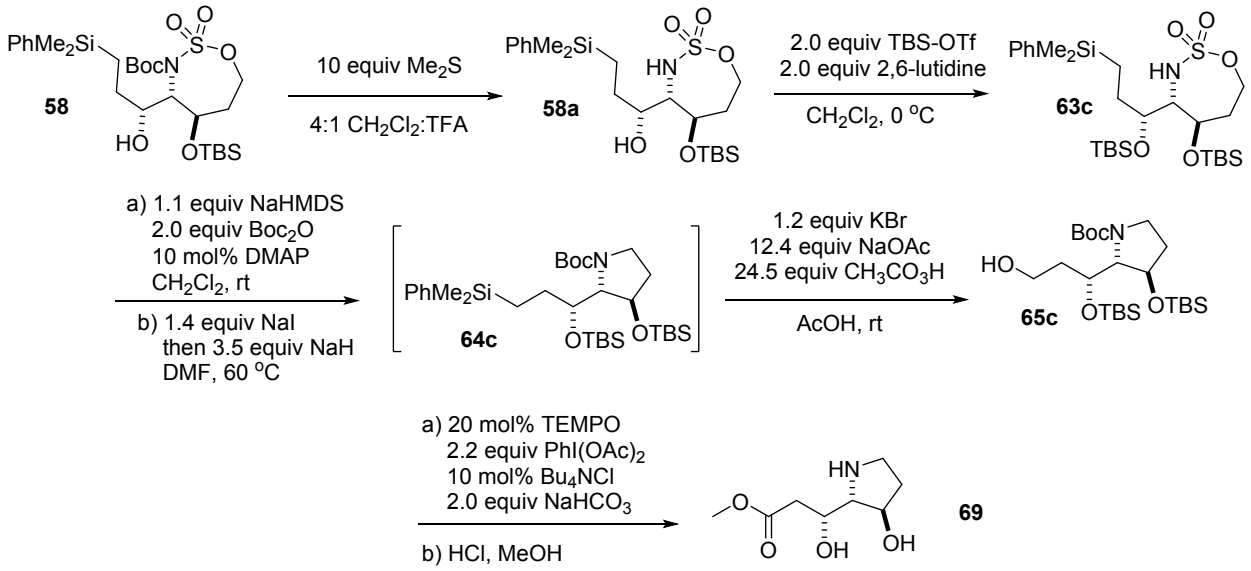
and concentrated under reduced pressure. The crude residue was purified by column chromatography (3% to 15% EtOAc in hexanes) on silica gel. The product **63b** (0.313 g, 0.532 mmol, 97%) was isolated as a clear, colorless oil. $^{1}$H NMR: (500.0 MHz, $CDCl_3$) δ 7.54 (m, 2H), 7.34 (m, 3H), 5.24 (d, *J* = 11.0 Hz, 1H), 11.2 (t, *J* = 12.5 Hz, 1H), 4.39 (dd, *J* = 3.3, 2.4 Hz, 1H), 4.14 (dt, *J* = 12.5, 3.1 Hz, 1H), 3.65 (ddd, *J* = 9.3, 3.9, 2.7 Hz, 1H), 3.33 (dd, *J* = 11.0, 9.3 Hz, 1H), 2.07 (dddd, *J* = 15.6, 12.5, 3.1, 2.4 Hz, 1H), 1.89 (ddd, *J* = 15.6, 3.3, 3.1 Hz, 1H), 1.77 (tdd, *J* = 14.0, 3.5, 2.7 Hz, 1H), 1.55 (tt, *J* = 14.0, 3.9 Hz, 1H), 1.03 (td, *J* = 14.0, 3.9 Hz, 1H), 0.90 (s, 9H), 0.86 (s, 9H), 0.75 (td, *J* = 14.0, 3.5 Hz, 1H), 0.28 (s, 3H), 0.27 (s, 3H), 0.10 (s, 3H), 0.10 (s, 3H), 0.02 (s, 3H), -0.03 (s, 3H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 139.1, 133.7, 128.8, 127.7, 71.5, 66.5, 63.8, 58.8, 36.6, 27.3, 25.9, 25.8, 18.1, 18.1, 6.5, -3.3, -3.3, -3.3, -3.8, -4.5, -4.6. HMRS (ESI) *m/z* calculated for $C_{27}H_{54}NO_5SSi_3$ $[M + NH_4]^+$ 605.3291, found 605.3282.

**Compound 65b.** The sulfamate **63b** (0.298 g, 0.507 mmol, 1.0 equiv) was dissolved in 2.6 mL of dry dichloromethane. The solution was cooled to 0 °C and DMAP was added (6.2 mg, 0.0507 mmol, 10 mol%), followed by dropwise addition of NaHMDS (0.557 mL of 1.0 M solution in THF, 0.557 mmol, 1.1 equiv). After completion of the addition, $Boc_2O$ was added (0.220 g, 1.01 mmol, 2.0 equiv). The solution was warmed to rt and allowed to stir for 4 hours. The solution containing the protected sulfamate was concentrated under reduced pressure to a tan syrup. The material was redissolved in 2.5 mL of dry DMF and 0.106 g NaI (0.709 mmol, 1.4 equiv) was added. The thick solution was warmed to 45 °C and stirred for 15 min prior to the cautious addition of NaH (0.071 g of 60% wt suspension in mineral oil, 1.77 mmol, 3.5 equiv). The solution was then warmed to 60 °C and stirred for 10 h. The reaction mixture was cooled and cautiously quenched with 10 mL of water. The mixture was extracted with diethyl ether (4 x 15

mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residual HMDS was removed from the crude residue by flash chromatography (5% EtOAc in hexanes) to yield 0.198 g of oil **64b** of sufficient purity for the Fleming-Tamao oxidation.

The crude pyrrolidine **64b** was dissolved in 2.4 ml of glacial acetic acid containing KBr (0.0463 g, 0.389 mmol, 1.2 equiv) and NaOAc (0.0820 g, 1.00 mmol, 3.1 equiv). Peroxyacetic acid (0.416 mL of 32% wt in acetic acid, 1.98 mmol, 6.1 equiv) was added dropwise with ice bath cooling to control the exotherm. After stirring for 5 min, a second portion of NaOAc was added (0.246 g, 3.01 mmol, 9.3 equiv), followed by a second portion of peroxyacetic acid (1.26 mL, 5.96 mmol, 18.4 equiv). The solution was stirred at rt for 2 h before dilution with 20 mL diethyl ether and 25 mL of water containing 3.60 g sodium thiosulfate pentahydrate. The phases were separated, and the aqueous phase extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ before drying with $MgSO_4$. The crude residue was purified by column chromatography (6% to 30% EtOAc in hexanes) to yield **65b** as a colorless oil (0.0707 g, 0.144 mmol, 28% from sulfamate). (Note: This spectrum is complicated by the presence of two rotamers in the product structure. However, the rotamers are fairly well resolved for this compound). $^1$H NMR: (500.0 MHz, $CDCl_3$) δ 4.41 (dt, $J$ = 10.5, 7.4 Hz, 1H), 4.28 (m, 1H), 3.62-9.95 (m, 3H), 3.38 (t, $J$ = 10.2 Hz, 1H), 3.20 (m, 1H), 2.12-2.38 (m, 2H), 1.83-1.95 (m, 2H), 1.46 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.01-0.09 (overlapping s, 12H). $^{13}$C NMR (Major Rotamer): (125.7 MHz, $CDCl_3$) δ 154.6, 79.4, 72.8, 71.7, 60.5, 59.7, 43.3, 37.3, 32.9, 28.5, 25.9, 25.8, 17.9, 17.8, -4.6, -4.7, -5.0, -5.0. HMRS (ESI) *m/z* calculated for $C_{24}H_{52}NO_5Si_2$ $[M + H]^+$ 490.3379, found 490.3382.

**Compound 68.** A 5 mL round bottom flask equipped with a magnetic stir bar was charged with **65b** (67.3 mg, 0.137 mmol), sodium bicarbonate (23.1 mg, 0.274 mmol, 2.0 equiv), $Bu_4NCl$ (3.8 mg, 0.0137 mmol, 10 mol%), and 0.80 mL 1:1 $CH_3CN$:$H_2O$. The mixture was stirred vigorously, and TEMPO (4.3 mg, 0.0274, 20 mol%) was added, followed by $PhI(OAc)_2$ (95.3 mg, 0.302 mmol, 2.20 equiv). After stirring under nitrogen for 36 hours, the reaction was diluted with 4 mL $CH_2Cl_2$ and 4 mL of 0.2 M HCl. The phases were separated, and the aqueous phase extracted with $CH_2Cl_2$ (4 x 5 mL). The combined organic fractions were dried with $MgSO_4$ and concentrated to a crude oil. The oil was treated with 4.5 mL of 0.5 M HCl in methanol (prepared by reaction of TMS-Cl in methanol) and stirred for 1 hour. Concentration by rotary evaporation afforded a crude oil. Non-polar organics were removed by column chromatography (10% $CH_3CN$ in $CH_2Cl_2$, then 10% MeOH in $CH_3CN$) yielding crude white solid **68** that was purified by trituration with cold $CH_2Cl_2$ (16.3 mg, 0.0861 mmol, 63%). $^1$H NMR: (500.0 MHz, $D_2O$) δ 4.69 (t, *J* = 1.5 Hz, 1H), 4.49 (td, *J* = 8.6, 3.7 Hz, 1H), 3.76 (s, 3H), 3.46-3.64 (m, 3H), 2.84 (dd, *J* = 15.9, 3.7 Hz, 1H), 2.75 (dd, *J* = 15.9, 8.6 Hz, 1H), 2.23 (dtd, *J* = 13.7, 10.1, 3.9 Hz, 1H), 2.14 (ddd, *J* = 13.7, 6.9, 1.5 Hz, 1H). $^{13}$C NMR: (125.7 MHz, $D_2O$) δ 173.1, 69.7, 66.0, 64.0, 52.5, 43.9, 39.1, 32.4. HMRS (ESI) *m/z* calculated for $C_8H_{16}NO_4$ $[M + H]^+$ 190.1074, found 190.1071.




**Compound 58a.** The 1,2-*anti*:2,3-*syn* stereotriad **58** (0.104 g, 0.181 mmol, 1.0 equiv) was dissolved in 1.8 mL of dry dichloromethane. Dimethyl sulfide (0.112 g, 1.81 mmol, 10 equiv) was added to the solution. The solution was cooled to 0 °C and 0.45 mL of TFA was added. The reaction mixture was stirred for 60 min at 0 °C and 2 hours at room temperature. The reaction was diluted with 30 mL dichloromethane and quenched with saturated aqueous $NaHCO_3$. The phases were separated and the organic phase dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (6% to 30% EtOAc in hexanes) on silica gel. The product **58a** (0.0580 g, 0.122 mmol, 68%) was isolated as a clear, colorless oil. $^1$H NMR: (500.0 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.36 (m, 3H), 5.00 (br s, 1H), 4.22-4.33 (m, 2H), 3.94 (td, *J* = 6.7, 1.9 Hz, 1H), 3.86 (td, *J* = 8.9, 4.6 Hz, 1H), 3.25 (td, *J* = 9.7, 2.0 Hz, 1H), 2.11 (dtd, *J* = 15.7, 4.5, 2.0 Hz, 1H), 1.99 (dddd, *J* = 15.7, 9.7, 8.9, 4.0 Hz, 1H), 1.60-1.70 (m, 2H), 1.54 (tdd, *J* = 13.0, 6.7, 4.6 Hz, ), 0.88 (s, 9H), 0.79 (td, *J* = 13.0, 4.7 Hz, 1H), 0.70 (td, *J* = 13.0, 4.5 Hz, 1H), 0.30 (s, 3H), 0.30 (s, 3H), 0.07 (s, 3H), 0.07 (s, 3H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 138.63, 133.57, 129.02, 127.85, 70.66, 69.93, 66.60, 59.73,

37.43, 28.12, 25.67, 17.87, 11.09, -3.17, -3.31, -4.36, -4.96. HMRS (ESI) *m/z* calculated for $C_{21}H_{43}N_2O_5SSi_2$ $[M + NH_4]^+$ 491.2426, found 491.2427.

**Compound 63c.** The 1,2-*anti*:2,3-*syn* stereotriad **58a** (0.140 g, 0.295 mmol, 1.0 equiv) was dissolved in 2.95 mL of dry dichloromethane. The solution was cooled to 0 °C and 0.069 mL of 2,6-lutidine (0.591 mmol, 2.0 equiv) and 0.136 mL of TBSOTf (0.591 mmol, 2.0 equiv) were added. The reaction mixture was stirred for 25 min, diluted with 10 mL dichloromethane and quenched with 10 mL of water. The phases were separated and the aqueous phase extracted with dichloromethane (2 x 15 mL). The combined organic fractions were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (2% to 10% EtOAc in hexanes) on silica gel. The product **63c** (0.138 g, 0.235 mmol, 80%) was isolated as a clear, colorless oil. $^1$H NMR: (500.0 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.34 (m, 3H), 4.81 (d, *J* = 8.9 Hz, 1H), 4.40 (dd, *J* = 12.6, 6.5 Hz, 1H), 4.25 (dd, *J* = 12.6, 9.6 Hz, 1H), 3.94 (td, *J* = 7.7, 4.4 Hz, 1H), 3.88 (dd, *J* = 10.5, 4.2 Hz, 1H), 3.47 (dd, *J* = 8.9, 7.7 Hz, 1H), 2.21 (ddd, *J* = 15.8, 6.5, 4.2 Hz, 1H), 2.05 (ddd, *J* = 15.8, 10.5, 9.6 Hz, 1H), 1.66 (tdd, *J* = 13.6, 7.7, 4.9 Hz, 1H), 1.41 (tt, *J* = 13.6, 3.4 Hz, 1H), 0.88 (s, 9H), 0.84 (s, 9H), 0.79 (td, *J* = 13.6, 4.9 Hz, 1H), 0.47 (td, *J* = 13.6, 3.3 Hz, 1H), 0.29 (s, 3H), 0.28 (s, 3H), 0.07 (s, 6H), -0.01 (s, 3H), -0.03 (s, 3H). 13C NMR: (125.7 MHz, CDCl3) delta 138.5, 133.5, 129.0, 127.8, 73.7, 71.5, 66.1, 58.9, 37.5, 28.5, 25.9, 25.7, 18.0, 17.9, 10.9, -3.1, -3.4, -3.5, -3.6, -4.3, -4.7. HMRS (ESI) *m/z* calculated for $C_{27}H_{57}N_2O_5SSi_3$ $[M + NH_4]^+$ 605.3291, found 605.3293.

**Compound 65c.** The sulfamate **63c** (0.124 g, 0.212 mmol, 1.0 equiv) was dissolved in 2.1 mL of dry dichloromethane. The solution was cooled to 0 °C and DMAP was added (2.6 mg, 0.0212

mmol, 10 mol%), followed by dropwise addition of NaHMDS (0.233 mL of 1.0 M solution in THF, 0.233 mmol, 1.1 equiv). After completion of the addition, $Boc_2O$ was added (0.0925 g, 0.424 mmol, 2.0 equiv). The solution was warmed to rt and allowed to stir for 60 minutes. The solution containing the protected sulfamate was concentrated under reduced pressure to a tan syrup. The material was redissolved in 2.1 mL of dry DMF and 0.0445 g NaI (0.297 mmol, 1.4 equiv) was added. The thick solution was warmed to 45 °C and stirred for 25 min prior to the cautious addition of NaH (0.0300 g of 60% wt suspension in mineral oil, 0.742 mmol, 3.5 equiv). The solution was then warmed to 60 °C and stirred for 5 h. The reaction mixture was cooled and cautiously quenched with 10 mL of brine. The mixture was extracted with diethyl ether (4 x 10 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residual HMDS was removed from the crude residue by flash chromatography (5% EtOAc in hexanes) to yield 0.0926 g of oil **64c** of sufficient purity for the Fleming-Tamao oxidation.

The crude pyrrolidine **64c** was dissolved in 1.1 ml of glacial acetic acid containing KBr (0.0218 g, 0.183 mmol, 1.2 equiv) and NaOAc (0.0387 g, 0.472 mmol, 3.1 equiv). Peroxyacetic acid (0.195 mL of 32% wt in acetic acid, 0.929 mmol, 6.1 equiv) was added dropwise with ice bath cooling to control the exotherm. After stirring for 5 min, a second portion of NaOAc was added (0.116 g, 1.42 mmol, 9.3 equiv), followed by a second portion of peroxyacetic acid (0.589 mL, 2.80 mmol, 18.4 equiv). The solution was stirred at rt for 2 h before dilution with 10 mL diethyl ether and 12 mL of water containing 1.62 g sodium thiosulfate pentahydrate. The phases were separated, and the aqueous phase extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ before drying with $MgSO_4$. The crude residue was purified by column chromatography (4% to 20% EtOAc in hexanes) to yield **65c** as a white solid (0.0577 g, 0.118 mmol, 56% from sulfamate). (Note: This spectrum is

complicated by the presence of two rotamers in the product structure) $^{1}$H NMR: (500.0 MHz, $CDCl_3$) δ 4.30-4.42 (2 s, 1H), 4.05-4.18 (m, 1H), 3.30-3.95 (m, 5H), 2.62 (br s, 0.29H), 1.80-2.10 (m, 0.71 H), 1.69-1.80 (m, 1H), 1.45-1.65 (m, 12H), 0.85-0.93 (2 s, 18H), 0.05-0.15 (3 s, 12H). $^{13}$C NMR: (125.7 MHz, $CDCl_3$) δ 155.8, 155.3, 79.8, 79.3, 73.3, 72.9, 70.8, 70.7, 68.8, 68.8, 60.7, 60.5, 45.9, 45.4, 35.9, 35.2, 34.1, 33.3, 28.7, 28.5, 26.0, 25.7, 17.9, 17.8, -3.5, -4.0, -4.2, -4.4, -4.6, -4.6, -4.9, -5.2. HMRS (ESI) *m/z* calculated for $C_{24}H_{52}NO_5Si_2$ $[M + H]^+$ 490.3379, found 490.3378.

**Compound 69.** A 10 mL round bottom flask equipped with a magnetic stir bar was charged with **65c** (55.0 mg, 0.112 mmol), sodium bicarbonate (18.8 mg, 0.224 mmol, 2.0 equiv), $Bu_4NCl$ (1.5 mg, 0.0056 mmol, 5 mol%), and 0.56 mL 1:1 $CH_3CN$:$H_2O$. The mixture was stirred vigorously, and TEMPO (3.5 mg, 0.0224 mmol, 20 mol%) was added, followed by $PhI(OAc)_2$ (77.7 mg, 0.246 mmol, 2.20 equiv). After stirring under nitrogen for 36 hours, 0.25 mL dichloromethane was added with an additional 0.90 mg TEMPO (0.00576 mmol, 5 mol%) and 19.4 mg $PhI(OAc)_2$ (0.0615 mmol, 0.55 equiv). After an additional 24 hours the reaction was diluted with 4 mL $CH_2Cl_2$ and 4 mL of 0.2 M HCl. The phases were separated, and the aqueous phase extracted with $CH_2Cl_2$ (4 x 5 mL). The combined organic fractions were dried with $MgSO_4$ and concentrated to a crude oil. The oil was treated with 3.4 mL of 0.5 M HCl in methanol (prepared by reaction of TMS-Cl in methanol) and stirred for 1 hour. Concentration by rotary evaporation afforded a crude oil. Non-polar organics were removed by column chromatography (10% $CH_3CN$ in $CH_2Cl_2$, then 10% MeOH in $CH_3CN$) yielding crude white solid **69** that was purified by trituration with cold $CH_2Cl_2$ (19.6 mg, 0.104 mmol, 92%). $^{1}$H NMR: (500.0 MHz, $D_2O$) δ 4.40 (dt, *J* = 6.0, 4.6 Hz, 1H), 4.26 (ddd, *J* = 8.9, 7.8, 3.8 Hz, 1H),

3.75 (s, 3H), 3.42-3.54 (m, 3H), 2.86 (dd, $J$ = 16.2, 3.8 Hz, 1H), 2.67 (dd, $J$ = 16.2, 8.9 Hz, 1H), 2.32 (dtd, $J$ = 14.2, 8.2, 6.0 Hz, 1H), 2.06 (dddd, $J$ = 14.2, 8.0, 5.2, 4.6 Hz, 1H). $^{13}$C NMR: (125.7 MHz, $D_2O$) δ 173.0, 71.3, 69.1, 65.1, 52.5, 43.7, 39.1, 32.1. HMRS (ESI) *m/z* calculated for $C_8H_{16}NO_4$ $[M + H]^+$ 190.1074, found 190.1080.

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11. In a previous publication from our group (see ref. 3c in the text), it was demonstrated that this homoallenic sulfamate could be generated in >98% *ee* from the same enantioenriched starting material and by the same sequence of transformations employed here. However, the HPLC conditions used previously were found to no longer separate the allene enantiomers, likely due to slight degradation of the HPLC since this previous publication.