Total Synthesis of Amphidinolide E

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Supporting Information:

Part I. References to Total Syntheses of Amphidinolides A, J, K, P, T, W, X and Y

Amphidinolide A: (a) Lam, H. W.; Pattenden, G., *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 508. (b) Maleczka, R. E., Jr.; Terrell, L. R.; Geng, F.; Ward, J. S., III, *Org. Lett.* **2002**, *4*, 2841. (c) Trost, B. M.; Chisholm, J. D.; Wrobleski, S. J.; Jung, M., *J. Am. Chem. Soc.* **2002**, *124*, 12420. (d) Trost, B. M.; Harrington, P. E., *J. Am. Chem. Soc.* **2004**, *126*, 5028. (e) Trost, B. M.; Wrobleski, S. T.; Chisholm, J. D.; Harrington, P. E.; Jung, M., *J. Am. Chem. Soc.* **2005**, *127*, 13589. (f) Trost, B. M.; Harrington, P. E.; Chisholm, J. D.; Wrobleski, S. T., *J. Am. Chem. Soc.* **2005**, *127*, 13598.

Amphidinolide J: Williams, D. R.; Kissel, W. S., *J. Am. Chem. Soc.* **1998**, *120*, 11198.

Amphidinolide K: Williams, D. R.; Meyer, K. G., *J. Am. Chem. Soc.* **2001**, *123*, 765.

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Amphidinolide T: (a) Fürstner, A.; Aissa, C.; Riveiros, R.; Ragot, J., *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 4763. (b) Aiessa, C.; Riveiros, R.; Ragot, J.; Fürstner, A., *J. Am. Chem. Soc.* **2003**, *125*, 15512. (c) Ghosh, A. K.; Liu, C., *J. Am. Chem. Soc.* **2003**, *125*, 2374. (d) Ghosh, A. K.; Liu, C., *Strategies Tactics Org. Synth.* **2004**, *5*, 255. (e) Colby, E. A.; O'Brien, K. C.; Jamison, T. F., *J. Am. Chem. Soc.* **2004**, *126*, 998. (f) Colby, E. A.; O'Brien, K. C.; Jamison, T. F., *J. Am. Chem. Soc.* **2005**, *127*, 4297. (g) O'Brien, K. C.; Colby, E. A.; Jamison, T. F., *Tetrahedron* **2005**, *61*, 6243. (h) Deng, L.-S.; Huang, X.-P.; Zhao, G., *J. Org. Chem.* **2006**, *71*, 4625.

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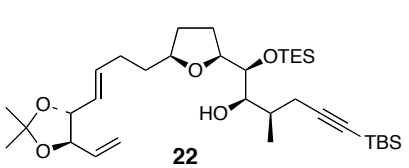
Amphidinolide X: Lepage, O.; Kattnig, E.; Fürstner, A., *J. Am. Chem. Soc.* **2004**, *126*, 15970.

Amphidinolide Y: Fürstner, A.; Kattnig, E.; Lepage, O., *J. Am. Chem. Soc.* **2006**, *128*, 9194**.**

Part II.

Table 1. Summary of Attempted Esterification Reactions of Model Substrates 22-24



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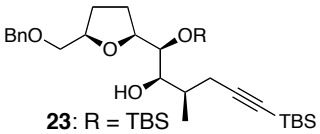

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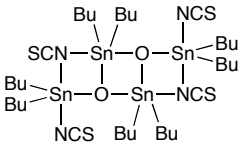
24: R = MOM



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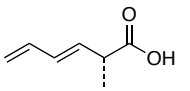

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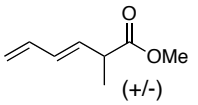

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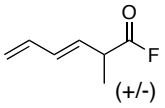

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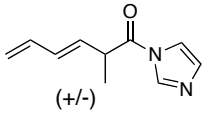

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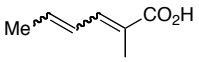
entry	reaction	conditions	results
1	**22** + **26**	2,4,6-trichlorobenzoyl chloride, Et_3N, DMAP, THF, rt to reflux	decomposition of acid
2	**22** + **26**	EDCI•MeI, DMAP, CH_2Cl_2, 0 °C to rt	
3	**23** + **26**	PyBrOP, i-Pr_2NEt, CH_2Cl_2, 0 °C to rt	
4	**23** + **29**	Tol., rt to 100 °C	isolated:
5	**23** + **27**	**25** (10 mol %), Tol., 50 °C	
6	**24** + **26**	DCC, HOBt, THF, rt to 50 °C	
7	**24** + **28**	**24,** $(Bu_3Sn)_2O$, PhH, reflux; then added **28**, CH_2Cl_2	
8	**24** + **28**	**24**, LDA, –78 °C, THF; then **28** or **29**, THF	



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Many conditions were screened to esterify alcohol **22**, or alcohols **23** and **24** (truncated analogs of alcohol **22**) with acid **26** or **27**, **28**, and **29** (Table 1). No more than trace amounts of the corresponding ester could be isolated from all of the reactions in Table 1. Some of the conditions that failed were: the modified Yamaguchi conditions (entry 1), mild peptide coupling conditions (entries 2, 3 and 6), use of Otera's transesterification catalyst **25**[1-3] (entry 5), attempted coupling of the tributyltin ether of **24** with the acyl fluoride **28** (entry 7), and generation of the lithium alkoxide of **24** followed by treatment with acyl fluoride **28** (entry 8). In most cases, large quantities of the fully conjugated, diene migrated acid byproduct **30** were isolated.

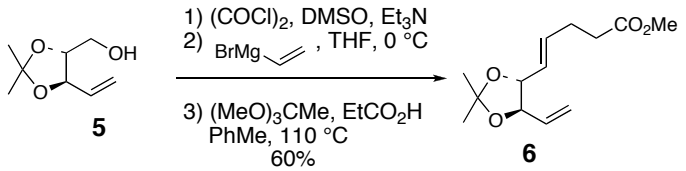
Part III. Experimental Procedures for Total Synthesis of Amphidinolide E

General Experimental Details. All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, diethyl ether, and toluene were purified by passing through a solvent column composed of activated A-1 alumina. Unless indicated otherwise, all reactions were conducted under an atmosphere of argon using flame-dried or oven-dried (170 °C) glassware. Four Å molecular sieves were activated under high vacuum with heat (180 °C) for 12 h and re-activated by thorough flame-drying immediately prior to use.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on commercial instruments at 400 or 500 MHz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 100 and 125 MHz, respectively. The proton signal for residual non-deuterated solvent (7.26 for $CHCl_3$) was used as an internal reference for ^{1}H NMR spectra. For ^{13}C NMR spectra, chemical shifts are reported relative to the 77.2 resonance of $CHCl_3$. Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as films on a Perkin-Elmer Spectrum One FTIR. Opitcal rotations were measured on a Rudolph Autopol IV polarimeter using a quartz cell with 1 mL capacity and a 10 cm path length. Mass spectra were recorded on a ZVG 70-250-S spectrometer manufactured by Micromass Corp. (Manchester, UK).

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates pre-coated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with Hanessian solution (ceric sulfate and ammonium molybdate in aqueous sulfuric acid). Column chromatography was generally performed using Kieselgel 60 (230-400 mesh) silica gel, typically using a 50-100:1 weight ratio of silica gel to crude product.

HPLC purifications were performed by using a HPLC system composed of two Varian Prostar pumps (model 210) connected to normal phase columns. Samples were loaded into the system with a 2 mL Rheodyne 7125 injector and were detected using a Varian Prostar UV and a Varian RI dectector.

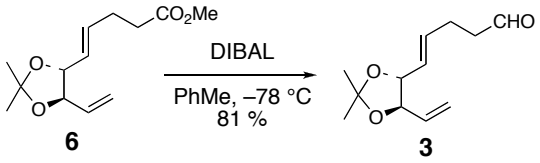


(E)-5-((4R,5R)-2,2-Dimethyl-5-vinyl-[1,3]dioxolan-4-yl)-pent-4-enoic acid methyl ester (6) To a –78 °C solution of $(COCl)_2$ (3.45 mL, 39.4 mmol) in CH_2Cl_2 (80 mL) was added DMSO (3.50 mL, 49.2 mmol) in CH_2Cl_2 (10 mL). The reaction was stirred at –78 °C for 15 min, then alcohol **5**[4] (3.12 g, 19.7 mmol) in CH_2Cl_2 (10 mL) was added. The reaction was stirred for 20 minutes at –78 °C followed by the addition of triethylamine (16.4 mL, 118 mmol). The mixture was allowed to warm to 0 °C. After 30

minutes, the reaction was diluted with Et_2O (300 mL), upon which a white precipitate forms (triethylamine hydrochloride). The slurry was filtered through a 1 inch pad of Celite and concentrated to afford the aldehyde, a yellow oil, which was immediately used in the next reaction.

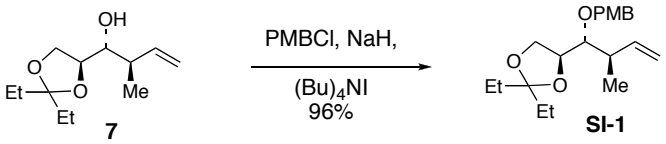
To a 0 °C solution of the crude aldehyde in THF (60 mL) was added vinylmagnesium bromide (60 mL of a 1.0M THF solution, 60 mmol). The reaction was stirred for 2.5 h, and then quenched with saturated aqueous $NaHCO_3$ (50 mL) and extract with Et_2O (20 mL x 3). The organic phase was washed with brine (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a mixture of diastereomeric allylic alcohols as a yellow oil. This oil was used immediately in the next reaction.

To the mixture of diastereomeric allylic alcohols, from the preceeding step, in toluene (66 mL) was added trimethyl orthoacetate (12.5 mL, 98.5 mmol) and propionoic acid (0.3 mL, 3.94 mmol). The reaction was fitted with a condenser and placed in a 110 °C oil bath for 18 h. The solution was then quenched with 3 mL of triethylamine and concentrated. The crude product was purified by flash column chromatography to yield methyl ester **6** (2.83 g, 60% over 3 steps) as a colorless oil: $[\alpha]^{25}_D = -132°$ (*c* 0.99, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 5.74-5.83 (m, 2H), 5.48 (dd, *J* = 6.4, 15.2 Hz, 1H), 5.33 (d, *J* = 17.2 Hz, 1H), 5.24 (d, *J* = 10.4 Hz, 1H), 4.04 (app q, *J* = 6.8 Hz, 2H), 3.67 (s, 3H), 2.36-2.44 (m, 4H), 1.44 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 172. 8, 134.0, 133.7, 126.9, 118.3, 108.7, 82.0, 81.6, 51.3, 33.1, 27.3, 26.8, 26.7; IR (neat) 2987, 2874, 1740, 1437, 1371 cm^{-1}; HRMS (ES+) *m/z* for $C_{12}H_{18}O_3Na$ $[M+Na]^+$ calcd 263.1259, found 263.1255.

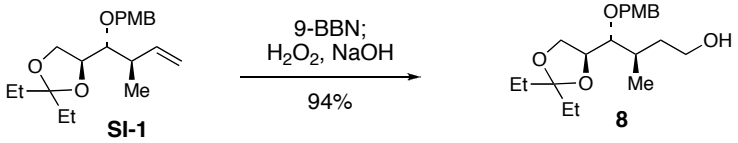


(E)-5-((4R,5R)-2,2-Dimethyl-5-vinyl-[1,3]dioxolan-4-yl)-pent-4-enal (3) To a –78 °C solution of methyl ester **6** (2.25 g, 9.36 mmol) in toluene (31 mL) was added DIBAL (9.36 mL of a 1.0M hexane solution, 9.36 mmol) dropwise such that the internal temperature was below –70 °C. After being stirred for 30 min, the reaction was quenched with saturated aqueous sodium potassium tartrate (Rochelle's salt) (40 mL) and diluted with Et_2O (20 mL). The mixure was stirred at room temperature for 3h and extracted with Et_2O (20 mL x 3). The organic phase was washed with brine (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was purified by flash column chromatography to afford aldehyde **3** (1.59 g, 81%) as a colorless oil: $[\alpha]^{25}_D = -28.7°$ (*c* 1.41, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 9.73 (bs, 1H), 5.70-5.85 (m, 2H), 5.49 (bdd, *J* = 6.0, 15.6 Hz, 1H), 5.34 (d, *J* = 17.2 Hz, 1H), 5.24 (d, *J* = 10.4 Hz, 1H), 4.00-4.10 (m, 2H), 2.52-2.60 (m, 2H), 2.35-2.45 (m, 2H), 1.44 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 201.3, 134.1, 133.8, 127.2, 118.8, 109.0, 82.2, 81.8, 42.8, 27.0, 27.0, 24.7; IR

(neat) 3085, 2987, 2875, 1726, 1379, 1371, 1239 cm^{-1}; HRMS (ES+) *m/z* for $C_{13}H_{20}O_3Na$ $[M+Na]^+$ calcd 233.1154, found 233.1245.

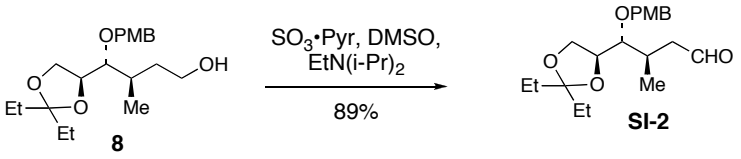


(S)-2,2-Diethyl-4-[(1R,2R)-1-(4-methoxy-benzyloxy)-2-methyl-but-3-enyl]-[1,3]dioxolane (SI-1) To a 0 °C slurry of NaH (1.69 g, 70.6 mmol) and Bu_4NI (1.7 g, 4.7 mmol) in THF (157 mL) was added homoallylic alcohol **7**[5] (10.1 g, 47.0 mmol) followed by PMBCl (6.38 mL, 47. 0 mmol). The reaction was fitted with a condenser and refluxed for 16 h. The reaction was quenched with sat. aq. NH_4Cl (50 mL) and water (50 mL) and extracted with EtOAc (25 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **SI-1** (15.15 g, 96%) as a colorless oil: $[\alpha]^{25}_D = -41°$ (*c* 1.53, $CHCl_3$); ^1H NMR (400MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.86 (ddd, *J* = 8.0, 10.4, 17.2 Hz, 1H), 5.04 (app t, *J* = 17.6 Hz, 2H), 4.60 (AB, *J* = 10.8 Hz, 1H), 4.55 (AB, *J* = 11.2 Hz, 2H), 4.05-4.10 (m, 1H), 4.00 (dd, *J* = 6.0, 7.6 Hz, 1H), 3.81 (s, 3H), 3.77 (d, *J* = 7.6 Hz, 1H), 3.52 (dd, *J* = 3.6, 6.0 Hz, 1H), 2.50-2.54 (m, 1H), 1.57-1.70 (m, 4H), 1.09 (d, *J* = 6.8 Hz, 3H), 0.89 (dt, *J* = 9.6, 7.6 Hz, 6H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.1, 140.1, 130.1, 129.3, 115.0, 113.7, 112.1, 83.1, 77.3, 74.0, 66.9, 55.2, 40.8, 29.7, 29.0, 17.0, 8.2, 8.1; IR (neat) 3073, 2972, 1613, 1514, 1249 cm^{-1}; HRMS (ES+) *m/z* for $C_{20}H_{30}O_4Na$ $[M+Na]^+$ calcd 357.2042, found 357.2044.

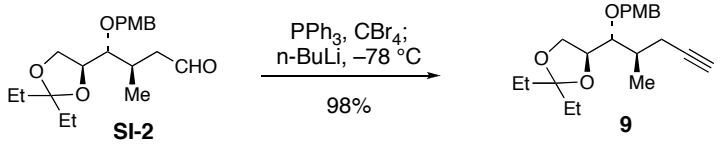


(3R,4R)-4-((S)-2,2-Diethyl-[1,3]dioxolan-4-yl)-4-(4-methoxy-benzyloxy)-3-methyl-butan-1-ol (8) To a solution of **SI-1** (15.1 g, 45.3 mmol) in THF (181 mL) was added 9-BBN (272 mL of a 0.5 M THF solution, 136 mmol). The reaction was fitted with a condenser, refluxed for 3 h, cooled to 0 °C and quenched with water (25 mL). The mixure was then treated with 2N NaOH aq. (227 mL) followed by 30% (w/w) H_2O_2 (46.3 mL) and the biphasic mixture was stirred at room temperature for 17 h. The aqueous phase was extracted with EtOAc (50 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **8** (15.1 g, 94%) as a colorless oil: $[\alpha]^{25}_D = -27°$ (*c* 0.63, $CHCl_3$); ^1H NMR (500MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.56 (s, 2H), 4.16 (app q, *J* = 6.5 Hz, 1H), 4.07 (dd, *J* = 6.0, 8.0 Hz, 1H), 3.80 (s, 3H), 3.75 (app t, *J* = 8.0 Hz, 1H), 3.70-3.76 (m, 1H), 3.60-3.64 (m, 1H), 3.46 (dd, *J* = 4.5, 6.0 Hz, 1H), 2.02-2.07 (m, 1H), 1.95 (dd, *J* = 4.5, 6.0 Hz, 1H),

1.73-1.79 (m, 1H), 1.58-1.67 (m, 4H), 1.03 (d, J = 7.0 Hz, 3H), 0.89 (dt, J = 7.0, 5.5 Hz, 6H); ^{13}C NMR (125MHz, $CDCl_3$) 159.2, 130.3, 129.3, 113.7, 112.6, 83.3, 77.3, 76.3, 67.7, 60.5, 55.2, 34.9, 32.1, 29.7, 29.0, 16.3, 8.2; IR (neat) 3436, 2971, 2881, 1613, 1514, 1249 cm^{-1}; HRMS (ES+) *m/z* for $C_{20}H_{32}O_5Na$ $[M+Na]^+$ calcd 375.2147, found 375.2141.

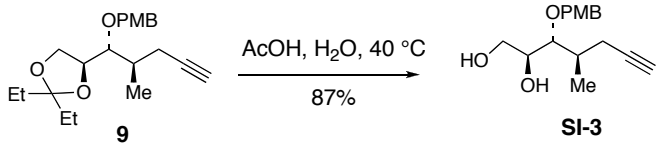


(3R,4R)-4-((S)-2,2-Diethyl-[1,3]dioxolan-4-yl)-4-(4-methoxy-benzyloxy)-3-methyl-butyraldehyde (SI-2) To a 0 °C solution of alcohol **8** (15.0 g, 42.6 mmol) in CH_2Cl_2 (142 mL) was added DMSO (9.1 mL, 128 mmol), i-Pr_2NEt (22.2 mL, 128 mmol) and SO_3·Pyr (20.3 g, 128 mmol). The reaction was stirred at 0 °C for 30 min, then quenched with sat. aq. $Na_2S_2O_3$ (100 mL) and extracted with CH_2Cl_2 (30 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **SI-2** (13.39 g, 89%) as a colorless oil: $[\alpha]^{25}_D$ = –30° (*c* 2.2, $CHCl_3$); ^{1}H NMR (500MHz, $CDCl_3$) 9.73 (app t, J = 2.0 Hz, 1H), 7.23 (d, J = 9.0 Hz, 2H), 6.87 (d, J = 9.0 Hz, 2H), 4.56 (AB, J = 11.0 Hz, 1H), 4.53 (AB, J = 11.0 Hz, 1H), 4.12 (dd, J = 6.5, 13.0 Hz, 1H), 4.06 (dd, J = 6.5, 8.0 Hz, 1H), 3.80 (s, 3H), 3.73 (t, J = 8.0 Hz, 1H), 3.40 (dd, J = 4.5, 6.0 Hz, 1H), 2.65 (ddd, J = 2.0, 6.0, 7.5 Hz, 1H), 2.43-2.48 (m, 1H), 2.37 (ddd, J = 2.0, 7.5, 9.5 Hz, 1H), 1.57-1.67 (m, 4H), 1.06 (d, J = 7.5, Hz, 3H), 0.88 (t, J = 7.0 Hz, 6H); ^{13}C NMR (125MHz, $CDCl_3$) 202.2, 159.2, 130.2, 129.4, 113.7, 113.0, 82.2, 76.1, 73.3, 67.6, 55.2, 47.1, 30.3, 29.7, 28.9, 16.5, 8.2, 8.2; IR (neat) 2971, 2934, 2724, 2721, 1724, 1514, 1249 cm^{-1}; HRMS (ES+) *m/z* for $C_{20}H_{30}O_5Na$ $[M+Na]^+$ calcd 373.1991, found 373.1984.



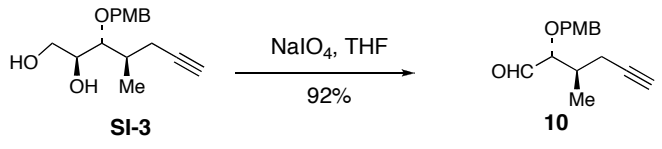
(S)-2,2-Diethyl-4-[(1R,2R)-1-(4-methoxy-benzyloxy)-2-methyl-pent-4-ynyl]-[1,3]dioxolane (9) To a 0 °C solution of PPh_3 (24.9 g, 94.87 mmol) in CH_2Cl_2 (182 mL) was added CBr_4 (15.7 g, 47.4 mmol). The reaction was warmed to room temperture for 30 min and then cooled back to 0 °C. To this mixture was added aldehyde **SI-2** (12.8 g, 36.5 mmol) in CH_2Cl_2 (5 mL). The reaction was stirred for 30 min and then diluted with hexane (400 mL), upon which a white precipitate formed (Ph_3P=O). The slurry was filtered through Celite and concentrated. The residue was dissolve in hexane (300 mL) to precipitate more Ph_3P=O. The slurry was filtered through Celite and again concentrated. The residual oil was dissolved in THF (100 mL), cooled to –78 °C and treated with n-BuLi (32.4 mL of 2.29M hexane solution, 74.3 mmol). The reaction was stirred for 1h and then quenched with sat. aq. NH_4Cl (100 mL)

and extracted with EtOAc (50 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography afforded **9** (11.0 g, 98%) as a colorless oil: $[\alpha]^{25}_D = -7.6°$ (*c* 0.89, $CHCl_3$); ^1H NMR (400MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 4.62 (AB, *J* = 10.8 Hz, 1H), 4.54 (AB, *J* = 11.2 Hz, 1H), 4.17 (dt, *J* = 6.0, 8.0 Hz, 1H), 4.03 (dd, *J* = 6.0, 8.0 Hz, 1H), 3.80 (s, 3H), 3.77 (t, *J* = 8.0 Hz, 1H), 3.57 (t, *J* = 6.0 Hz, 1H), 2.27-2.39 (m, 2H), 1.98 (app t, *J* = 3.2 Hz, 1H), 1.91-1.98 (m, 1H), 1.56-1.71 (m, 4H), 1.10 (d, *J* = 7.2 Hz, 3H), 0.90 (app q, *J* = 7.6 Hz, 6H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.2, 130.5, 129.4, 113.7, 112.8, 83.2, 81.2, 76.5, 73.7, 69.4, 67.0, 55.2, 34.9, 29.7, 29.0, 22.1, 15.7, 8.2, 8.1; IR (neat) 3295, 2971, 1613, 1514 cm^{-1}; HRMS (ES+) *m/z* for $C_{21}H_{30}O_4Na$ $[M+Na]^+$ calcd 369.2042, found 369.2037.



9 **SI-3**

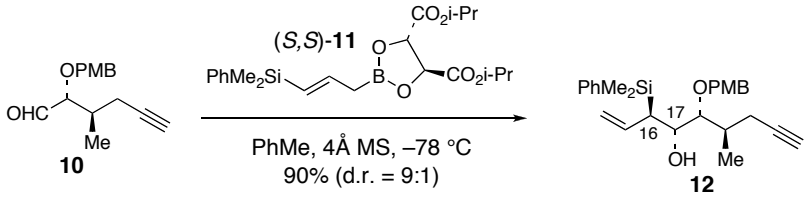
(2S,3R,4R)-3-(4-Methoxy-benzyloxy)-4-methyl-hept-6-yne-1,2-diol (SI-3) To alkyne **9** (4.84 g, 14.0 mmol) was added a 4:1 mixture of AcOH and water (47 mL). The reaction mixture was heated to 40 °C for 6 h and then was diluted with 50 mL of EtOAc. Solid $NaHCO_3$ (20 g) was slowly added portionwise and then the mixture was extracted with EtOAc (25 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford diol **SI-3** (3.39 g, 87%) as a colorless oil: $[\alpha]^{25}_D = +13.6°$ (*c* 0.59, $CHCl_3$); ^1H NMR (400MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 4.64 (AB, *J* = 11.2 Hz, 1H), 4.61 (AB, *J* = 11.2 Hz, 1H), 3.80 (s, 3H), 3.69-3.84 (m, 3H), 3.58 (dd, *J* = 4.4, 7.2 Hz, 1H), 2.33-2.46 (m, 3H), 2.18 (dd, *J* = 4.0, 8.0 Hz, 1H), 2.03 (t, *J* = 2.4 Hz, 1H), 1.96-2.02 (m, 1H), 7.27 (d, *J* = 8.8 Hz, 2H), 1.08 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.4, 130.3, 129.6, 113.9, 83.8, 83.0, 74.8, 71.5, 69.9, 63.3, 55.3, 34.4, 21.9, 16.3; IR (neat) 3413, 3306, 2936, 1612, 1515, 1249 cm^{-1}; HRMS (ES+) *m/z* for $C_{16}H_{22}O_4Na$ $[M+Na]^+$ calcd 301.1416, found 301.1416.



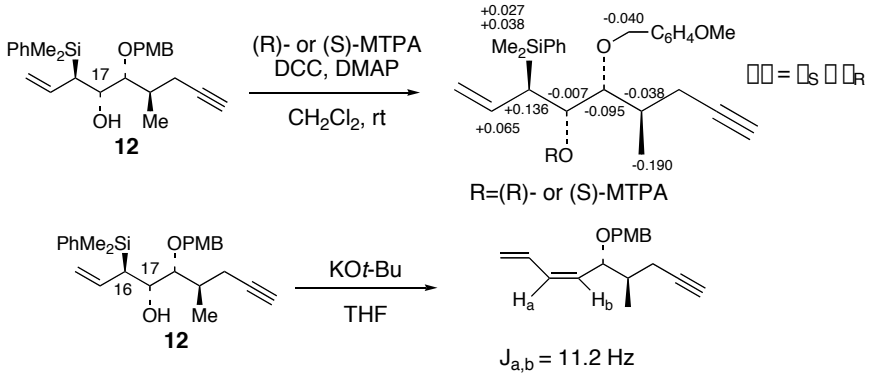
SI-3 **10**

(2R,3R)-2-(4-Methoxy-benzyloxy)-3-methyl-hex-5-ynal (10) To a 0 °C solution of **SI-3** (3.39 g, 12.2 mmol) in THF (20 mL) and pH 7 buffer (20 mL) was added $NaIO_4$ (3.13 g, 14.6 mmol). The reaction was stirred for 4 h, quenched with sat. aq. $Na_2S_2O_3$ (25 mL) and extracted with EtOAc (25 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated to

afford pure **10** (2.76 g, 92%) as a colorless oil: $[\alpha]^{25}_D$ = +80° (*c* 2.26, $CHCl_3$); ^{1}H NMR (500MHz, $CDCl_3$) δ 9.65 (app d, *J* = 3.0 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 4.59 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 3.81 (s, 3H), 3.60 (dd, *J* = 3.0, 10.0 Hz, 1H), 2.34-2.36 (m, 2H), 2.11-2.17 (m, 1H), 1.98 (app t, *J* = 2.5 Hz, 1H), 1.04 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 203.5, 159.5, 129.8, 129.2, 113.8, 85.6, 81.9, 72.8, 70.4, 55.2, 34.0, 21.3, 15.3; IR (neat) 3292, 2967, 2837, 1731, 1515, 1249 cm^{-1}; HRMS (ES+) *m/z* for $C_{15}H_{18}O_3Na$ $[M+Na]^+$ calcd 269.1154, found 269.1147.

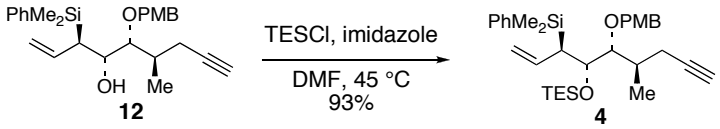


(3R,4S,5R,6R)-3-(Dimethylphenylsilanyl)-5-(4-methoxy-benzyloxy)-6-methyl-non-1-en-8-yn-4-ol (12) To a –78 °C slurry of aldehyde **10** (5.95 g, 24.2 mmol) and 4Å mol. sieves (4.8 g) in toluene (20 mL) was added (*S,S*)-**11**[6] (61 mL of a 1.0M solution in toluene, 60.4 mmol). The reaction was stirred at –78 °C for 18 h and then quenched with 2N NaOH aq. (100 mL). The biphasic mixture was filtered through Celite and extracted with EtOAc (30 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **12** (9.19 g, 90%) as a colorless oil: $[\alpha]^{25}_D$ = –6° (*c* 2.48, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.55-7.57 (m, 2H), 7.34-7.36 (m, 3H), 7.25 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 5.98 (dt, *J* = 10.4, 21.5 Hz, 1H), 5.03 (d, *J* = 10.4 Hz, 1H), 4.85 (d, *J* = 21.5 Hz, 1H), 4.58 (d, *J* = 13.0 Hz, 1H), 4.49 (d, *J* = 13.5 Hz, 1H), 3.81 (s, 3H), 3.73-3.77 (m, 1H), 3.31 (dd, *J* = 3.2, 6.8 Hz, 1H), 2.43 (d, *J* = 4.0 Hz, 1H), 2.08-2.18 (m, 1H), 1.91-1.98 (m, 3H), 1.08 (d, *J* = 7.2 Hz, 3H), 0.39 (s, 3H), 0.34 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.3, 137.9, 134.8, 134.1, 130.4, 129.4, 129.0, 127.6, 114.5, 113.9, 85.5, 83.6, 74.9, 71.1, 69.3, 55.3, 39.2, 34.1, 20.3, 17.9, -3.8, -4.2; IR (neat) 3560, 3304, 2961, 1613, 1514 cm^{-1}; HRMS (ES+) *m/z* for $C_{26}H_{34}O_3SiNa$ $[M+Na]^+$ calcd 445.2175, found 445.2176.

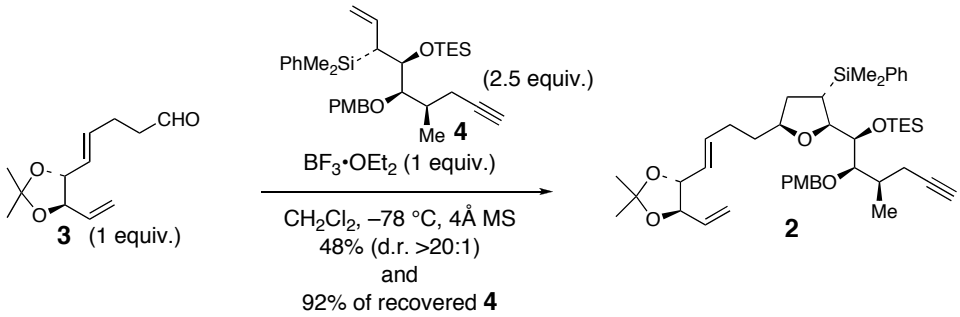


Scheme 1. Absolute and Relative Stereochemical Assignment of **12**

The absolute stereochemistry of the C(17) hydroxyl was confirmed by application of the modified Mosher ester analysis (Scheme 1). In addition, the C(16)-C(17) relative stereochemistry was verified as *anti* by Peterson elimination of **12** to afford the corresponding *Z* diene.



1-[(1R,2S,3R)-3-(Dimethyl-phenyl-silanyl)-1-((R)-1-methyl-but-3-ynyl)-2-triethylsilanyloxy-pent-4-enyloxymethyl]-4-methoxy-benzene (4) To a solution of **12** (1.01 g, 2.39 mmol) in DMF (2.5 mL) was added imidazole (0.50 g, 7.4 mmol) and TESCl (1.21 mL, 7.17 mmol). The reaction was heated to 45 °C for 17 h and then quenched with water (15 mL) and extracted with Et_2O (25 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **4** (1.19 g, 93%) as a colorless oil: $[\alpha]^{25}_D$ = +31° (*c* 1.30, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.49-7.52 (m, 2H), 7.29-7.35 (m, 3H), 7.18 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.12 (dt, *J* = 10.8, 17.2 Hz, 1H), 4.91 (dd, *J* = 10.4, 2.0 Hz, 1H), 4.79 (dd, *J* = 17.2, 1.6 Hz, 1H), 4.30 (AB, *J* = 18.8 Hz, 1H), 4.27 (d, *J* = 12.4 Hz, 1H), 4.50-4.70 (m, 1H), 3.81 (s, 3H), 3.22 (dd, *J* = 3.6, 8.4 Hz, 1H), 2.31-2.36 (m, 2H), 2.19 (dt, *J* = 3.2, 16.8 Hz, 1H), 2.09-2.13 (m, 1H), 1.94 (app t, *J* = 2.4 Hz, 1H), 1.02 (d, *J* = 6.4 Hz, 3H), 0.91 (t, *J* = 8.4 Hz, 9H), 0.50-0.57 (m, 6H), 0.34 (s, 3H), 0.27 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.1, 138.0, 136.5, 134.3, 130.8, 129.3, 128.9, 127.6, 113.6, 113.2, 85.3, 83.4, 72.6, 71.5, 69.5, 55.2, 37.0, 32.9, 22.8, 17.0, 7.1, 5.6, -3.2, -4.2; IR (neat) 3309, 2956, 2877, 1613, 1514, 1248 cm^{-1}; HRMS (ES+) *m/z* for $C_{32}H_{48}O_3Si_2Na$ $[M+Na]^+$ calcd 559.3040, found 559.3044.



(4R,5R)-4-((E)-4-{(2S,4S,5R)-4-(Dimethyl-phenyl-silanyl)-5-[(1S,2R,3R)-2-(4-methoxy-benzyloxy)-3-methyl-1-triethylsilanyloxy-hex-5-ynyl]-tetrahydro-furan-2-yl}-but-1-enyl)-2,2-dimethyl-5-vinyl-[1,3]dioxolane (2) A 25-mL round bottom flask was charged with aldehyde **3** (1.06 g,

5.04 mmol), allylsilane **4** (8.12 g, 15.1 mmol), activated 4 Å molecular sieves (2.0 g) and dichloromethane (10 mL). The slurry was stirred at room temperature for 10 min and then cooled to –78 °C. The cooled reaction was then treated with $BF_3{\cdot}OEt_2$ (0.64 mL, 5.04 mmol, freshly distilled from calcium hydride). The reaction mixture was stirred at –78 °C for 21 h and then quenched with triethylamine (1 mL). The mixture was diluted with sat. aq. $NaHCO_3$ (60 mL) and Et_2O (50 mL) and filtered through Celite. The aqueous phase was extracted with Et_2O (30 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. Purfication of the crude product by flash column chromatography afforded **2** (1.19 g, 48%; (6.27 g of allylsilane **4** was recovered)) as a colorless oil with >20:1 diastereoselectivity: $[\alpha]^{25}_D$ = +23° (*c* 0.76, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.47 (app dd, *J* = 1.6, 7.2 Hz, 2H), 7.29-7.38 (m, 3H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.74-5.82 (m, 2H), 5.41 (b dd, *J* = 7.2, 15.2 Hz, 1H), 5.32 (d, *J* = 17.6 Hz, 1H), 5.22 (d, *J* = 10.4 Hz, 1H), 4.51 (d, *J* = 10.8 Hz, 1H), 4.39 (d, *J* = 10.8 Hz, 1H), 4.05 (app dd, *J* = 6.8, 12.4 Hz, 3H), 3.81 (s, 3H), 3.71 (m, 1H), 3.58 (d, *J* = 5.6 Hz, 1H), 3.32 (app t, *J* = 6.8 Hz, 1H), 2.03-2.34 (m, 5H), 1.94 (t, *J* = 2.4 Hz, 1H), 1.79-1.83 (m, 1H), 1.58-1.69 (m, 3H), 1.44 (s, 3H), 1.43 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.51-0.61 (m, 6H), 0.32 (s, 3H), 0.32 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 158.9, 137.6, 136.4, 134.3, 133.8, 130.9, 129.1, 128.9, 127.8, 125.5, 118.2, 113.2, 108.6, 83.8, 83.2, 82.1, 80.2, 78.5, 77.2, 73.6, 73.1, 69.2, 55.1, 35.2, 34.5. 34.3, 29.3, 27.0, 26.9, 26.2, 22.1, 17.1, 7.1, 5.2, -4.1; IR (neat) 3309, 2955, 2250, 2115, 1614, 1514 cm^{-1}; HRMS (ES+) *m/z* for $C_{44}H_{66}O_6Si_2Na$ $[M+Na]^+$ calcd 769.4296, found 769.4307.

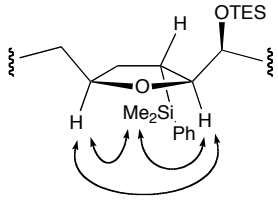
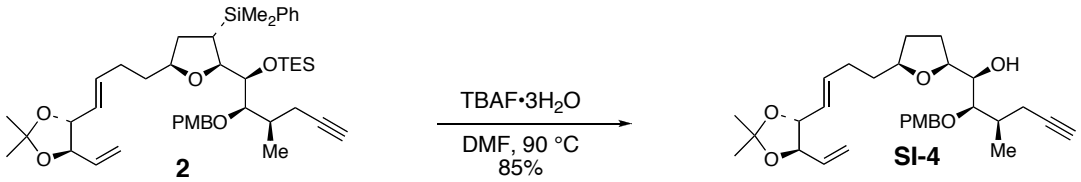


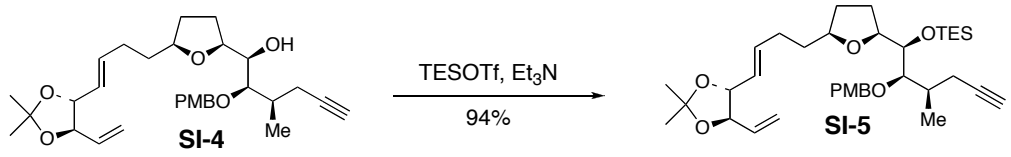
Figure 1. Observed nOe's verifying 2,5-*cis*-THF stereochemistry in **2**.

The 2,5-*cis* relative stereochemistry about the THF ring in [3+2] adduct **2** was confirmed by the observed nOe correlation peaks shown in Figure 1.



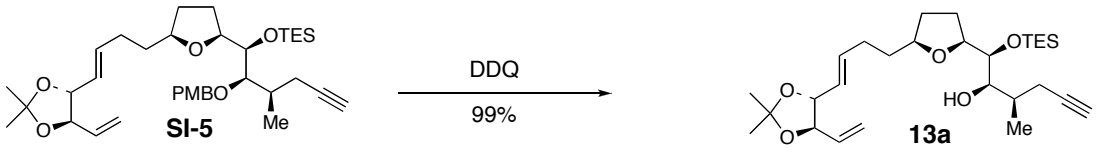
(1R,2R,3R)-1-{(2S,5S)-5-[(E)-4-((4R,5R)-2,2-Dimethyl-5-vinyl-[1,3]dioxolan-4-yl)-but-3-enyl]-tetrahydro-furan-2-yl}-2-(4-methoxy-benzyloxy)-3-methyl-hex-5-yn-1-ol (SI-4) To [3+2]

adduct **2** (1.81 g, 2.42 mmol) in DMF (2.5 mL) was added TBAF•3H_2O (3.82 g, 12.1 mmol, purchased from ACROS). The reaction was fitted with a condenser and placed in a 90 °C oil bath for 72 h. More TBAF•3H_2O (2.0 g, 6.34 mmol) was added to the reaction three times during the 72 h period; at hour 8, hour 32 and hour 56. After 72 h, the reaction was diluted with pH 7 buffer (50 mL) and Et_2O (30 mL). The aqueous phase was extracted with Et_2O (30 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **SI-4** (1.03 g, 85%) as a colorless oil: $[\alpha]^{25}_D$ = +6.4° (*c* 0.39, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) 7.28 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 5.73-5.81 (m, 2H), 5.41 (app bddd, *J* = 1.6, 6.0, 15.6 Hz, 1H), 5.32 (d, *J* = 16.4 Hz, 1H), 5.21 (dd, *J* = 1.2, 10.4 Hz, 1H), 4.58 (app q, *J* = 10.8 Hz, 2H), 4.03 (app q, *J* = 6.8 Hz, 2H), 3.93 (app q, *J* = 7.2 Hz, 1H), 3.85 (quint., *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.45-3.50 (m, 1H), 3.35 (dd, *J* = 2.0, 8.0 Hz, 1H), 5.23 (bd, *J* = 6.8 Hz, 1H), 2.34 (ddq, *J* = 2.4, 6.8, 16.8 Hz, 2H), 2.05-2.24 (m, 3H), 1.99 (t, *J* = 2.4 Hz, 1H), 1.89-1.95 (m, 1H), 1.78-1.86 (m, 1H), 1.64-1.75 (m, 2H), 1.46-1.60 (m, 2H), 1.43 (s, 3H), 1.42 (s, 3H), 1.08 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) 159.2, 135.9, 134.2, 130.4, 129.5, 125.9, 118.4, 113.6, 108.7, 83.1, 82.1, 82.0, 81.6, 80.4, 79.2, 73.5, 73.1, 69.9, 55.1, 35.1, 34.2, 31.0, 29.0, 27.0, 27.0, 21.8, 16.2; IR (neat) 3536, 3296, 2984, 2934, 1613, 1514, 1248 cm^{-1}; HRMS (ES+) *m/z* for $C_{30}H_{42}O_6Na$ $[M+Na]^+$ calcd 521.2879, found 521.2879.

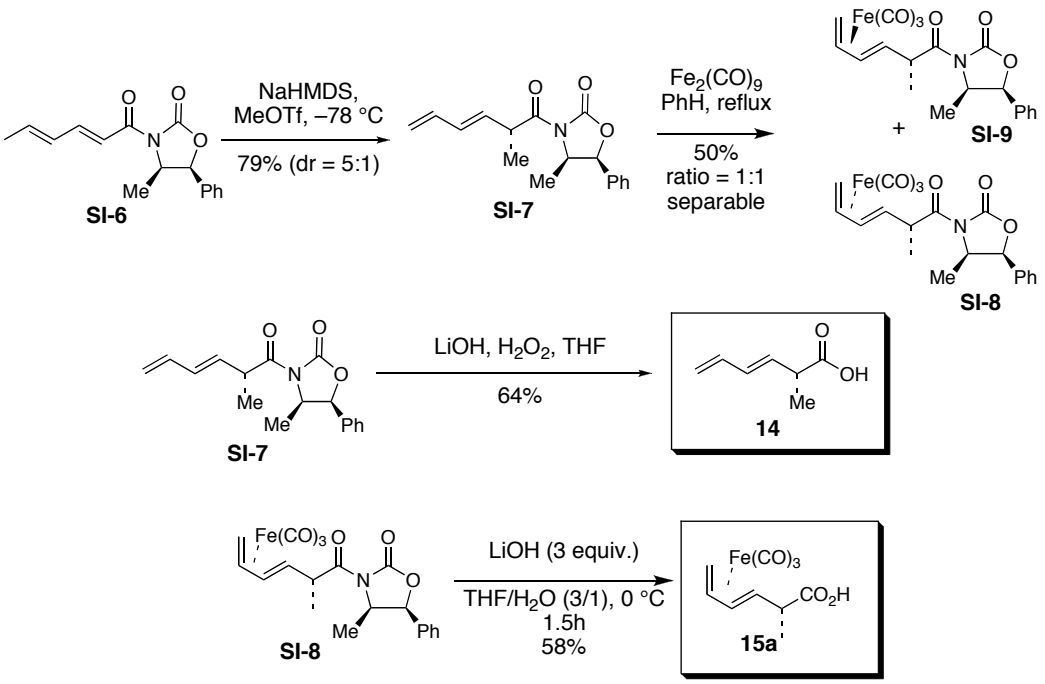


[(1R,2R,3R)-1-{(2S,5S)-5-[(E)-4-((4R,5R)-2,2-Dimethyl-5-vinyl-[1,3]dioxolan-4-yl)-but-3-enyl]-tetrahydro-furan-2-yl}-2-(4-methoxy-benzyloxy)-3-methyl-hex-5-ynyloxy]-triethyl-silane (SI-5) To a 0 °C solution of alcohol **SI-4** (1.2 g, 2.41 mmol) and triethylamine (0.67 mL, 4.82 mmol) in dichloromethane (8 mL) was added TESOTf (0.65 mL, 2.89 mmol). After 5 min the reaction was quenched with sat. aq. $NaHCO_3$ (30 mL) and Et_2O (30 mL). The aqueous phase was extracted with Et_2O (30 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtere and concentrated. The crude product was purified by flash column chromatography to afford **SI-5** (1.39 g, 94%) as a colorless oil: $[\alpha]^{25}_D$ = +11° (*c* 0.36, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 7.25 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.75-5.85 (m, 2H), 5.44 (bdd, *J* = 7.2, 15.2 Hz, 1H), 5.34 (d, *J* = 17.2 Hz, 1H), 5.23 (dd, *J* = 0.8, 10.4 Hz, 1H), 4.55 (s, 2H), 4.05 (app q, *J* = 6.4 Hz, 2H), 3.93 (app q, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 3.75-3.79 (m, 1H), 3.74 (dd, *J* = 3.2, 6.8 Hz, 1H), 3.29 (dd, *J* = 3.2, 8.8 Hz, 1H), 2.28-2.40 (m, 2H), 2.09-2.24 (m, 3H), 1.97 (t, *J* = 2.8 Hz, 1H), 1.79-1.94 (m, 2H), 1.61-1.70 (m, 2H), 1.51-1.59 (m, 2H), 1.45 (s, 3H), 1.44 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.96 (t, *J* = 8.0 Hz, 9H), 0.55-0.72 (m,

6H); ^{13}C NMR (100 MHz, $CDCl_3$) 159.0, 136.3, 134.3, 131.0, 129.0, 125.7, 118.4, 113.6, 108.8, 83.2, 83.1, 82.2, 82.2, 80.4, 78.2, 75.8, 71.9, 69.6, 55.2, 35.3, 33.2, 31.1, 29.2, 27.8, 27.0, 26.9, 22.5, 16.5, 7.0, 5.2; IR (neat) 3308, 2954, 2875, 1612, 1514, 1247, 1057 cm^{-1}; HRMS (ES+) *m/z* for $C_{36}H_{56}O_6SiNa$ $[M+Na]^+$ calcd 635.3744, found 635.3754.

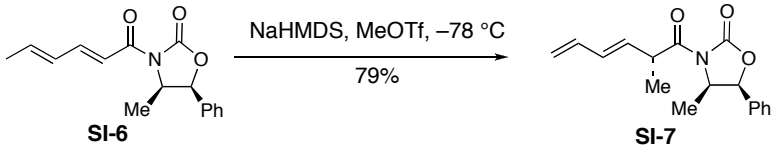


(1S,2R,3R)-1-{(2S,5S)-5-[(E)-4-((4R,5R)-2,2-Dimethyl-5-vinyl-[1,3]dioxolan-4-yl)-but-3-enyl]-tetrahydro-furan-2-yl}-3-methyl-1-triethylsilanyloxy-hex-5-yn-2-ol (13a) To a 0 °C solution of **SI-5** (0.621 g, 1.01 mmol) in dichloromethane (10 mL) and pH 7 buffer (1 mL) was added DDQ (0.46 g, 2.02 mmol). The reaction was stirred for 1 h, and then quenched with sat. aq. $NaHCO_3$ (40 mL) and Et_2O (30 mL). The aqueous phase was extracted with Et_2O (30 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography afforded **13a** (0.49 g, 99%) as a colorless oil: $[]^{25}_D$ = +13° (*c* 0.18, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 5.74-5.83 (m, 2H), 5.43 (app bddd, *J* = 1.2, 6.0, 15.2 Hz, 1H), 5.33 (d, *J* = 17.2 Hz, 1H), 5.23 (dd, *J* = 0.8, 10.4 Hz, 1H), 4.05 (app q, *J* = 6.4 Hz, 2H), 3.76 (m, 2H), 3.67 (d, *J* = 7.2 Hz, 1H), 3.18 (t, *J* = 9.6 Hz, 1H), 2.50 (d, *J* = 9.6 Hz, 1H), 2.48 (dt, *J* = 3.6, 16.4 Hz, 1H), 2.08-2.20 (m, 2H), 1.95 (t, *J* = 2.4 Hz, 1H), 1.84-1.97 (m, 2H), 1.74-1.80 (m, 1H), 1.61-1.66 (m, 1H), 1.59-1.46 (m, 3H), 1.44 (s, 3H), 1.43 (s, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.66 (app dsept., *J* = 7.6, 19.2 6H); ^{13}C NMR (100MHz, $CDCl_3$) 136.2, 134.3, 125.9, 118.5, 108.8, 83.1, 82.2, 82.2, 81.3, 78.7, 74.5, 74.4, 69.3, 35.7, 35.2, 30.8, 29.2, 27.4, 27.1, 27.0, 22.1, 15.7, 7.0, 5.3; IR (neat) 3524, 3310, 2954, 2875, 1379, 1238, 1054 cm^{-1}; HRMS (ES+) *m/z* for $C_{28}H_{48}O_5SiNa$ $[M+Na]^+$ calcd 515.3169, found 515.3171.



Scheme 2. Synthesis of acids **14** and **15a**

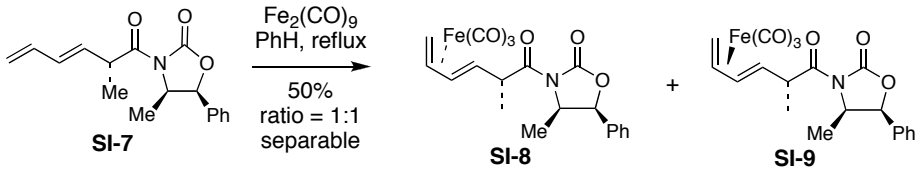
The synthesis of acids **14** and **15a** are shown in Scheme 2. Diastereoselective methylation of oxazolidinone **SI-6**[7] afforded oxazolidinone **SI-7** (79% yield, dr 5:1). Treatment of **SI-7** with diiron nonacarbonyl afforded the diene complexed oxazolidinones **SI-8** and **SI-9** as a 1:1 separable mixture of diastereomers. Hydrolysis of oxazolidinone **SI-7** afforded acid **14** (64% yield). Hydrolysis of iron complexed oxazolidinone **SI-8** afforded acid **15a** (64% yield).



(4R,5S)-4-Methyl-3-((E)-(R)-2-methyl-hexa-3,5-dienoyl)-5-phenyl-oxazolidin-2-one (SI-7)

To a –78 °C solution of oxazolidinone **SI-6**[7] (8.75 g, 32.2 mmol) in THF (90 mL) was added NaHMDS (8.28 g, 45.1 mmol) in THF (10 mL). The reaction was stirred at –78 °C for 1 h and then treated with MeOTf (5.47 mL, 48.4 mmol). After 3 h, the reaction was quenched with sat. aq. NH_4Cl (100 mL) and Et_2O (50 mL). The aqueous phase was extracted with Et_2O (50 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. Analysis of the crude product by ^1H NMR indicated a 5:1 mixture of diastereomers in favor of **SI-7**. The crude product was purified by flash column chromatography in 20% Et_2O/hexane (minor isomer, $R_f = 0.21$; major isomer, $R_f = 0.36$) to afford **SI-7** (7.30 g, 79%) as a colorless oil: $[\alpha]^{25}_D = 27°$ (*c* 0.55, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.44 (m, 3H), 7.30-7.32 (m, 2H), 6.20-6.37 (m, 2H), 5.83 (dd, $J = 8.4, 15.2$ Hz, 1H), 5.66 (d, $J = 7.2$ Hz,

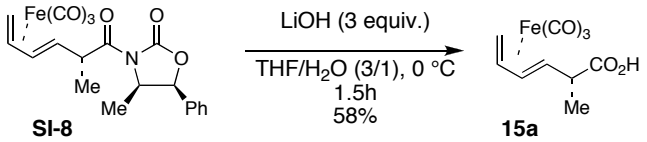
1H), 5.21 (app d, *J* = 17.6 Hz, 1H), 5.09 (app d, *J* = 10.8 Hz, 1H), 4.53 (quint., *J* = 7.6 Hz, 1H), 4.74 (quint., *J* = 6.8 Hz, 1H), 1.33 (d, *J* = 7.2 Hz, 3H), 0.90 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) 174.4, 152.6, 136.5, 133.2, 132.7, 132.6, 128.7, 128.7, 125.6, 117.3, 78.8, 55.1, 40.8, 17.3, 14.5; IR (neat) 2981, 2934, 1782, 1699, 1356, 1197 cm^{-1}; HRMS (ES+) *m/z* for $C_{17}H_{21}NO_4Na$ $[M+Na]^+$ calcd 308.1263, found 308.1262.



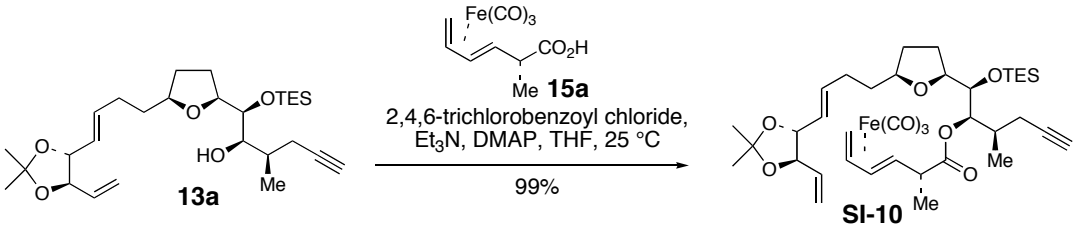
Tricarbonyl[(4R,5S)-4-Methyl-3-((E)-(2S,3R)-2-methyl-hexa-3,5-dienoyl)-5-phenyl-oxazolidin-2-one]iron (SI-8) and Tricarbonyl[(4R,5S)-4-Methyl-3-((E)-(2S,3S)-2-methyl-hexa-3,5-dienoyl)-5-phenyl-oxazolidin-2-one]iron (SI-9) To oxazolidinone **SI-7** (2.0 g, 7.0 mmol) in benzene (23 mL) was added diiron(nonacarbonyl) (3.8 g, 10.5 mmol). The reaction was fitted with a condenser and refluxed for a total of 24 h. Additional diiron(nonacarbonyl) (1.5 g, 4.12 mmol) and benzene (10 mL) was added to the reaction at hour 6 and hour 20. After 24 hours, the reaction was cooled to room temp, filtered through Celite with an Et_2O (25 mL) wash and concentrated to afford a 1:1 mixture of **SI-8** and S**I-9**. The crude product mixture was separated by flash column chromatography (10% Et_2O/hexanes to 40% Et_2O/hexanes with **SI-9** (0.78 g) eluting before **SI-8** (0.71 g), **SI-8** and **SI-9** combined yield of 50%).

Spectroscopic properties of **SI-8** (yellow solid): R_f = 0.33 (30% Et_2O/hexane); $[\alpha]^{25}_D$ = +8° (*c* 0.1, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) 7.36-7.45 (m, 3H), 7.36 (app d, *J* = 6.8 Hz, 2H), 5.71 (d, *J* = 7.2 Hz, 1H), 5.46 (dd, *J* = 4.8, 8.4 Hz, 1H), 5.22-5.27 (m, 1H), 4.76 (quint., *J* = 6.8 Hz, 1H), 3.82-3.40 (m, 1H), 1.78 (app dd, *J* = 1.6, 6.8 Hz, 1H), 1.37 (d, *J* = 6.8 Hz, 3H), 1.15 (app t, *J* = 8.8 Hz, 1H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.39 (app dd, *J* = 2.0, 9.6 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) 210.8, 175.2, 152.9, 133.2, 128.9, 128.8, 125.7, 86.4, 81.9, 78.9, 64.7, 55.1, 41.0, 40.4, 19.9, 14.5; IR (neat) 2984, 2047, 1970, 1779, 1697, 1355 cm^{-1}; HRMS (ES+) *m/z* for $C_{20}H_{19}FeNO_6Na$ $[M+Na]^+$ calcd 448.0459, found 448.0464.

Spectroscopic properties of **SI-9** (yellow solid): R_f = 0.50 (30% Et_2O/hexane); $[\alpha]^{25}_D$ = –83° (*c* 0.1, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) 7.30-7.45 (m, 5H), 5.71 (d, *J* = 7.2 Hz, 1H), 5.28-5.33 (m, 2H), 4.84 (quint., *J* = 6.8 Hz, 1H), 3.65-3.78 (m, 1H), 1.40 (d, *J* = 6.8 Hz, 3H), 1.36 (app dd, *J* = 7.6, 10.0 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.45 (app dd, *J* = 2.8, 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) 211.4, 174.6, 152.6, 133.2, 128.7, 125.6, 87.1, 82.7, 79.2, 62.9, 55.4, 43.4, 40.4, 26.3, 22.3, 14.3; IR (neat) 2977, 2046, 1978, 1782, 1700, 1342 cm^{-1}; HRMS (ES+) *m/z* for $C_{20}H_{19}FeNO_6Na$ $[M+Na]^+$ calcd 448.0459, found 448.0462.

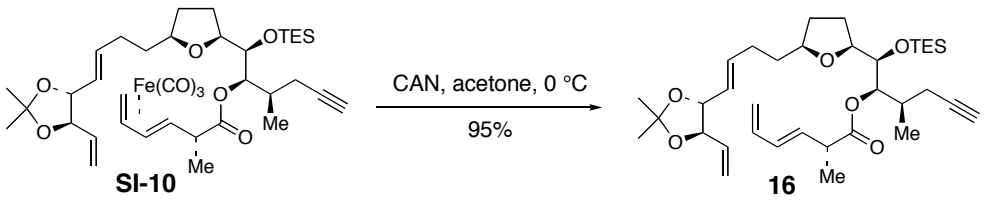


Tricarbonyl[(E)-(2S,3R)-2-Methyl-hexa-3,5-dienoic acid]iron (15a) To a 0 °C solution of oxazolidinone **SI-8** (1.15 g, 2.70 mmol) in THF (21 mL) and water (7 mL) was added LiOH (0.194 g, 8.11 mmol). The reaction was stirred for 1.5 h and then quenched with 1M HCl (25 mL) and Et_2O (25 mL). The aqueous phase was extracted with Et_2O (25 mL x 3). The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. The crude carboxylic acid was purified by flash column chromatography to afford **15a** (0.423 g, 58%) as a yellow solid: $[\alpha]^{25}_D$ = +11° (*c* 0.1, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 10.40 (bs, 1H), 5.38-5.44 (m, 1H), 5.25-5.30 (m, 1H), 2.32 (bs, 1H), 1.81 (d, *J* = 6.4 Hz, 1H), 1.35 (d, *J* = 6.4 Hz, 3H), 0.94 (app t, *J* = 9.2 Hz, 1H), 0.38 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.1, 181.1, 87.1, 82.3, 63.1, 44.0, 40.5, 19.0; IR (neat) 2983, 2049, 1971, 1705 cm^{-1}; HRMS (EI+) *m/z* for $C_9H_{10}FeO_4$ $[M-CO]^+$ calcd 237.9928, found 237.9918. The spectroscopic data obtained for **15a** are fully consistent with data for racemic **15a** previously published by Donaldson.[8]

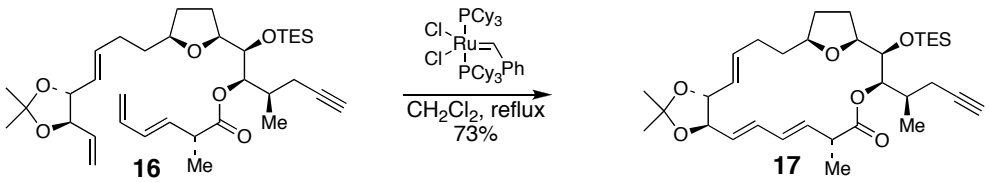


Tricarbonyl[(E)-(2S,3R)-2-Methyl-hexa-3,5-dienoic acid (1R,2R)-1-((R)-{(2S,5S)-5-[(E)-4-((4R,5R)-2,2-dimethyl-5-vinyl-[1,3]dioxolan-4-yl)-but-3-enyl]-tetrahydro-furan-2-yl}-triethylsilanyloxy-methyl)-2-methyl-pent-4-ynyl ester]iron (SI-10). To 0 °C solution of **13a** (120 mg, 0.244 mmol), **15a** (105 mg, 0.390 mmol), triethylamine (0.12 mL, 0.854 mmol), and DMAP (30 mg, 0.244 mmol) in THF (0.5 mL) was added 2,4,6-trichlorobenzoyl chloride (61 μL, 0.390 mmol). The redish brown solution was stirred at 0 °C for 1 h and allowed to warm to room temperature over another 1 h. After complete consumption of **13a** was observed by TLC analysis, the reaction was quenched with sat. aq. $NaHCO_3$ (30 mL) and Et_2O (30 mL). The aqueous phase was extracted with Et_2O (25 mL x 3). The organic phase was washed with sat. aq. NH_4Cl, brine, dried over anhydrous $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography afforded **SI-10** (179 mg, 99%) as a colorless oil: $[\alpha]^{25}_D$ = +13° (*c* 0.18, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 5.74-5.81 (m, 2H), 5.43 (app dd, *J* = 4.8, 8.4 Hz, 2H), 5.33 (d, *J* = 16.8 Hz, 1H), 5.21-5.26 (m, 1H), 5.22 (d, *J* = 11.6 Hz, 1H), 4.69 (dd, *J* = 1.2, 9.2 Hz, 1H), 4.04 (app q, *J* = 6.8 Hz, 2H), 3.72 (quint., *J* = 5.6, 1H), 3.67 (dd, *J* = 1.6, 7.6 Hz, 1H), 3.60 (app q, *J* = 8.0 Hz, 1H), 1.99-2.32 (m, 7H), 1.94 (t, *J* = 2.8 Hz, 1H), 1.73-1.88 (m,

3H), 1.50-1.66 (m, 2H), 1.38-1.48 (m, 1H), 1.44 (s, 3H), 1.43 (s, 3H), 1.31 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.97 (app d, *J* = 8.0 Hz, 1H), 0.59-0.76 (m, 6H), 0.32 (bdd, *J* = 1.6, 9.2 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) 211.2, 173.7, 136.1, 134.3, 126.0, 118.5, 108.9, 87.5, 82.2, 82.2, 82.2, 80.7, 78.5, 77.4, 77.2, 75.4, 69.7, 63.9, 44.5, 40.4, 35.2, 33.3, 30.9, 29.2, 27.8, 27.1, 26.9, 22.3, 19.2, 16.1, 7.1, 5.4; IR (neat) 3310, 2049, 1978, 1732, 1238, 1170 cm^{-1}; HRMS (ES+) *m/z* for $C_{38}H_{56}FeO_9SiNa$ $[M+Na]^+$ calcd 763.2941, found 763.2944.

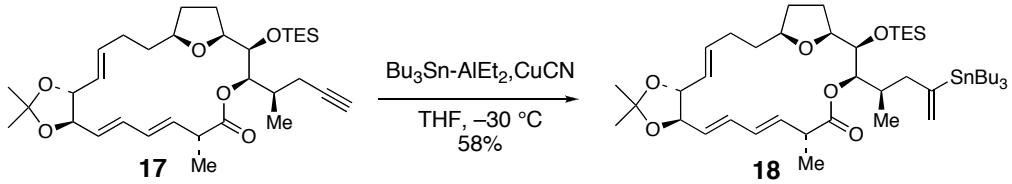


(E)-(R)-2-Methyl-hexa-3,5-dienoic acid (1R,2R)-1-((R)-{(2S,5S)-5-[(E)-4-((4R,5R)-2,2-dimethyl-5-vinyl-[1,3]dioxolan-4-yl)-but-3-enyl]-tetrahydro-furan-2-yl}-triethylsilanyloxy-methyl)-2-methyl-pent-4-ynyl ester (16) To a 0 °C solution of **SI-10** (45 mg, 0.061 mmol) in acetone (1 mL) was added cerium ammonium nitrate (CAN) (67 mg, 0.122 mmol). The reaction was stirred for 1h, then quenched with triethylamine (1 mL) and diluted with sat. aq. $NaHCO_3$ (30 mL) and Et_2O (30 mL). The aqueous phase was extracted with Et_2O (20 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **16** (35 mg, 95%) as a colorless oil: $[\alpha]^{25}_D$ = –1.0° (*c* 0.10, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) 6.29 (dt, *J* = 10.0, 16.8, 1H), 6.15 (dd, *J* = 10.4, 15.2 Hz, 1H), 5.72-5.82 (m, 3H), 5.42 (bdd, *J* = 1.6, 6.0, 15.6 Hz, 1H), 5.32 (d, *J* = 16.4 Hz, 1H), 5.22 (dd, *J* = 1.2, 10.4 Hz, 1H), 5.17 (d, *J* = 17.6, 1H), 5.06 (d, *J* = 10.0 Hz, 1H), 4.70 (dd, *J* = 2.0, 8.8 Hz, 1H), 4.04 (app q, *J* = 7.2 Hz, 2H), 3.71 (quint., *J* = 5.6 Hz, 1H), 3.67 (dd, *J* = 2.0, 7.2 Hz, 1H), 3.59 (q, *J* = 6.4 Hz, 1H), 3.21 (quint., *J* = 7.2 Hz, 1H), 1.98-2.36 (m, 5H), 1.94 (t, *J* = 2.4 Hz, 1H), 1.74-1.88 (m, 2H), 1.57-1.66 (m, 1H), 1.46-1.56 (m, 1H), 1.43 (s, 3H), 1.42 (s, 3H), 1.36-1.45 (m, 2H), 1.29 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.4 Hz, 3H), 0.95 (t, *J* = 6.8 Hz, 9H), 0.57-0.72 (m, 6H); ^{13}C NMR (100MHz, $CDCl_3$) 173.7, 136.3, 136.2, 134.3, 132.5, 132.3, 125.8, 118.5, 117.0, 108.8, 82.4, 82.2, 82.2, 80.4, 78.4, 77.4, 75.3, 69.6, 42.8, 35.2, 33.3, 30.9, 29.2, 27.0, 26.9, 22.2, 17.0, 16.1, 7.0, 5.3; IR (neat) 3310, 2953, 2876, 1733, 1378, 1239 cm^{-1}; HRMS (ES+) *m/z* for $C_{35}H_{56}O_6SiNa$ $[M+Na]^+$ calcd 623.3744, found 623.3748.



(4E,11E,13E)-(1S,6R,10R,15R,18R,19R,20S)-8,8,15-Trimethyl-18-((R)-1-methyl-but-3-ynyl)-19-triethylsilanyloxy-7,9,17,23-tetraoxa-tricyclo[18.2.1.0^{6,10}]tricosa-4,11,13-trien-16-one (17)

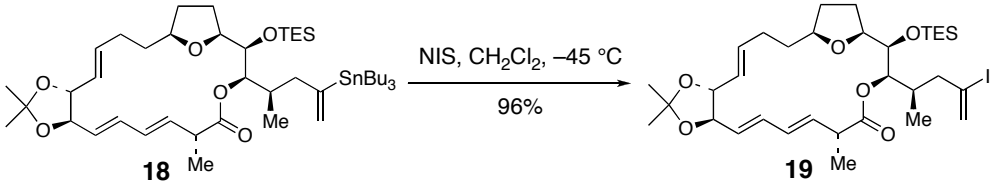
To polyene **16** (63 mg, 0.105 mmol) in dichloromethane (105 mL) was added Grubbs' first generation catalyst (17 mg, 0.021 mmol) in dichloromethane (2 mL). The reaction was fitted with a condenser, refluxed for 12 h and condensed. The crude product was purified by flash column chromatography to afford **17** (44 mg, 73%) as a colorless oil. In addition, an inseparable mixture of products thought to arrive by eneyne metathesis (4 mg, 10%) was also isolated. Spectroscopic data for **17**: $[\alpha]^{25}_{D}$ = –34° (*c* 0.21, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 6.15-6.26 (m, 2H), 5.72 (ddd, *J* = 3.6, 9.6, 15.2 Hz, 1H), 5.49-5.57 (m, 2H), 5.33 (app dd, *J* = 8.4, 15.6 Hz, 1H), 4.55 (app dd, *J* = 1.6, 9.6 Hz, 1H), 4.02 (app dt, *J* = 8.4, 26.0 Hz, 2H), 3.71 (app dd, *J* = 1.6, 8.4 Hz, 1H), 3.20-3.35 (m, 3H), 2.19-2.36 (m, 3H), 1.82-2.03 (m, 3H), 1.95 (t, *J* = 2.8 Hz, 1H), 1.62-1.70 (m, 1H), 1.50-1.59 (m, 1H), 1.38-1.49 (m, 1H), 1.43 (s, 3H), 1.42 (s, 3H), 1.23 (d, *J* = 6.8 Hz, 3H), 1.15-1.28 (m, 2H), 1.06 (d, *J* = 6.4 Hz, 3H), 0.96 (t, *J* = 7.6 Hz, 9H), 0.57-0.73 (m, 6H); ^{13}C NMR (100MHz, $CDCl_3$) δ 174.2, 138.4, 135.5, 131.3, 127.6, 125.7, 109.0, 83.0, 82.9, 82.3, 79.9, 78.5, 77.2, 75.1, 69.3, 44.2, 33.2, 32.0, 29.6, 28.6, 27.2, 27.1, 27.0, 22.5, 16.9, 15.6, 7.1, 5.6; IR (neat) 3310, 2950, 2874, 1732, 1378, 1237, 1170, 1053 cm^{-1}; HRMS (ES+) *m/z* for $C_{33}H_{52}O_6SiNa$ $[M+Na]^+$ calcd 595.3431, found 595.3442.



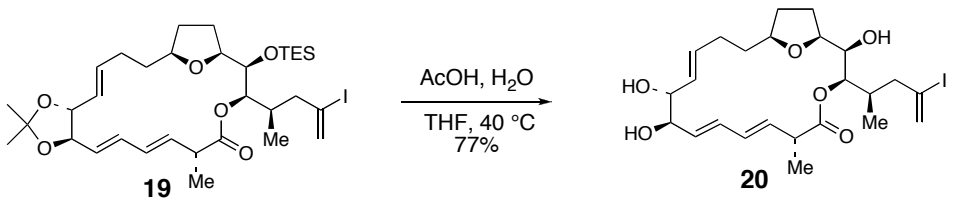
(4E,11E,13E)-(1S,6R,10R,15R,18R,19R,20S)-8,8,15-Trimethyl-18-((R)-1-methyl-3-tributylstannanyl-but-3-enyl)-19-triethylsilanyloxy-7,9,17,23-tetraoxa-tricyclo[18.2.1.0^{6,10}]tricosa-4,11,13-trien-16-one (18) To a 0 °C solution of *i*-Pr_2NH (0.45 mL, 3.2 mmol) in THF (3 mL) was added n-BuLi (1.30 mL of a 2.31M solution in hexanes, 3.0 mmol). The reaction was allowed to stir for 30 min and then cooled to –30 °C. To this mixture was added Bu_3SnH (0.80 mL, 3.0 mmol). After 1h, Et_2AlCl (1.7 mL of a 1.8M solution in toluene, 3.0 mmol) was added. The reaction was stirred at –30 °C for another 1.5 h and then used immediately in the stannylalumination-protonylysis of **17**.

To a –30 °C solution of **17** (44 mg, 0.077 mmol) in THF (1 mL) was added Bu_3Sn-$AlEt_2$ (1.1 mL of the 0.41M solution from above, 0.45 mmol), followed by CuCN (2 mg, 0.022 mmol). The bright orange solution was stirred for 1 h at –30 °C, then quenched with sat. aq. NH_4Cl (20 mL) and Et_2O (20 mL). This mixture was stirred vigorously at room temp for 15 min. The aqueous phase was extracted with Et_2O (10 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography afforded **18** (38 mg, 58%) as a colorless oil: $[\alpha]^{25}_{D}$ = –34.5° (*c* 0.11, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 6.15-6.26 (m, 2H),

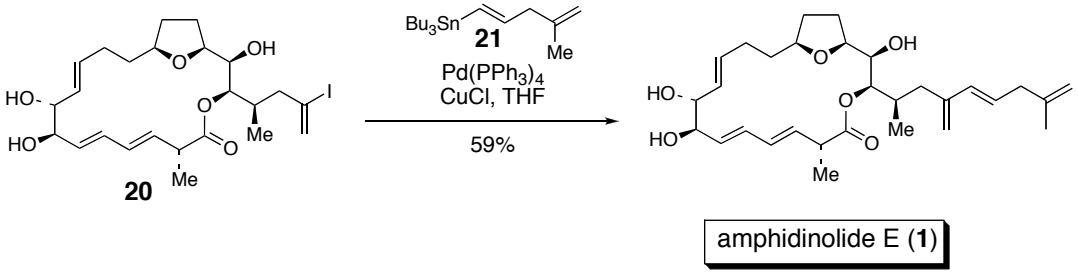
5.72 (app ddd, J = 3.6, 9.6, 15.2 Hz, 1H), 5.63 (app t, $^3J_{Sn\text{-}H}$ = 70 Hz, 1H), 5.50-5.90 (m, 2H), 5.34 (dd, J = 8.8,15.2 Hz, 1H), 5.14 (dt, J = 2.4 Hz, $^3J_{Sn\text{-}H}$ = 31.6 Hz, 1H), 4.50 (d, J = 10.0 Hz, 1H), 4.02 (app dt, J = 8.8, 24.0 Hz, 2H), 3.75 (d, J = 8.8 Hz, 1H), 3.15-3.35 (m, 3H), 2.33 (d, J = 13.2 Hz, 2H), 1.82-2.06 (m, 4H), 1.60-1.70 (m, 1H), 1.40-1.57 (m, 8H), 1.44 (s, 3H), 1.43 (s, 3H), 1.25-1.36 (m, 7H), 1.22 (d, J = 6.8 Hz, 3H), 1.18-1.24 (m, 2H), 0.96 (t, J = 8.0 Hz, 9H), 0.93-0.99 (m, 1H), 0.85-0.93 (m, 14H), 0.81 (d, J = 6.4 Hz, 3H), 0.55-0.72 (m, 6H); ^{13}C NMR (100MHz, $CDCl_3$) 174.2, 154.1, 138.5, 136.0, 135.8, 131.1, 127.5, 126.7, 125.7, 109.0, 83.1, 82.4, 80.1, 79.6, 77.2, 75.0, 45.4, 44.4, 33.0, 32.1, 29.7, 29.2, 29.1, 28.5, 27.4, 27.2, 27.1, 16.9, 14.8, 13.7, 9.6, 7.2, 5.7; IR (neat) 2954, 2931, 2873, 1732, 1237, 1170, 1053 cm^{-1}; HRMS (ES+) *m/z* for $C_{45}H_{80}O_6SiSnNa$ $[M+Na]^+$ calcd 887.4644, found 887.4655.



(4E,11E,13E)-(1S,6R,10R,15R,18R,19R,20S)-18-((R)-3-Iodo-1-methyl-but-3-enyl)-8,8,15-trimethyl-19-triethylsilanyloxy-7,9,17,23-tetraoxa-tricyclo[18.2.1.0^{6,10}]tricosa-4,11,13-trien-16-one (19) To a –45 °C solution of stannane **18** (121 mg, 0.140 mmol) in dichloromethane (2 mL) was added NIS (38 mg, 0.17 mmol). The reaction was stirred at –45 °C for 2 h and then quenched with sat. aq. $Na_2S_2O_3$ (30 mL) and extracted with Et_2O (20 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **19** (94 mg, 96%) as a colorless oil: $[\alpha]^{25}_D$ = –63° (*c* 0.13, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) 6.15-6.28 (m, 2H), 6.04 (s, 1H), 5.73 (s, 1H), 5.72 (ddd, J = 4.0, 10.4, 14.8 Hz, 1H), 5.53 (app dt, J = 9.2, 14.4 Hz, 2H), 5.33 (dd, J = 8.8, 15.2 Hz, 1H), 4.56 (d, J = 10.0 Hz, 1H), 4.02 (app dt, J = 8.8, 28.4 Hz, 2H), 3.73 (d, J = 8.8 Hz, 1H), 3.20-3.37 (m, 3H), 2.28-2.48 (m, 3H), 2.00 (dd, J = 10.0, 13.6 Hz, 3H), 1.82-1.95 (m, 2H), 1.62-1.70 (m, 1H), 1.49-1.58 (m, 1H), 1.43 (s, 3H), 1.42 (s, 3H), 1.31-1.46 (m, 2H), 1.22 (d, J = 6.8 Hz, 3H), 1.16-1.20 (m, 1H), 0.98 (t, J = 8.0 Hz, 9H), 0.85 (d, J = 6.4 Hz, 3H), 0.56-0.75 (m, 6H); ^{13}C NMR (100MHz, $CDCl_3$) 174.4, 138.3, 135.9, 135.5, 131.3, 127.7, 127.1, 125.7, 111.4, 109.0, 83.1, 82.3, 80.0, 78.6, 77.2, 75.0, 48.0, 44.1, 32.7, 32.0, 29.5, 28.5, 27.2, 27.0, 16.9, 14.5, 7.2, 5.7; IR (neat) 2950, 2874, 1731, 1378, 1237, 1170, 1053 cm^{-1}; HRMS (ES+) *m/z* for $C_{33}H_{53}IO_6SiNa$ $[M+Na]^+$ calcd 723.2554, found 723.2559.



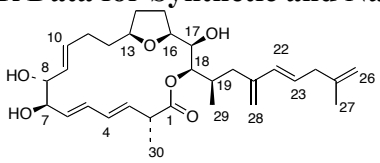
(7E,9E,13E)-(1S,2R,3R,6R,11R,12R,17S)-2,11,12-Trihydroxy-3-((R)-3-iodo-1-methyl-but-3-enyl)-6-methyl-4,20-dioxa-bicyclo[15.2.1]icosa-7,9,13-trien-5-one (20). A solution of vinyl iodide **19** (15 mg, 0.021 mmol) in a mixture of AcOH, THF and water (4/1/1) (0.5 mL) was heated to 40 °C for 6h. The mixture was then carefully poured into a separatory funnel containing Et_2O (20 mL) and sat. aq. $NaHCO_3$ (40 mL). The aqueous phase was extracted with Et_2O (10 mL x 3). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography to afford **20** (9 mg, 77%) as a colorless oil: $[\alpha]^{25}_D = -14.2°$ (*c* 0.12, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) δ 6.10-6.28 (m, 2H), 6.05 (s, 1H), 5.74 (s, 1H), 5.50-5.69 (m, 3H), 5.26 (dd, *J* = 8.0, 15.2 Hz, 1H), 4.68 (d, *J* = 9.2 Hz, 1H), 3.91 (app dt, *J* = 8.8, 28.8 Hz, 2H), 3.68-3.74 (m, 1H), 3.55 (app q, *J* = 7.6 Hz, 1H), 3.36-3.44 (m, 1H), 3.22-3.31 (m, 1H), 3.35-2.57 (m, 4H), 2.23-2.31 (m, 1H), 2.05 (dd, *J* = 10.0, 14.0 Hz, 1H), 1.72-1.93 (m, 3H), 1.29-1.62 (m, 5H), 1.25 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 174.4, 135.0, 134.9, 134.1, 131.5, 129.5, 127.3, 110.7, 79.8, 78.1, 77.6, 77.2, 77.1, 76.6, 73.3, 48.4, 44.0, 33.2, 32.5, 29.9, 29.0, 27.1, 17.5, 14.7; IR (neat) 3428, 2932, 2873, 1729, 1167, 990 cm^{-1}; HRMS (ES+) *m/z* for $C_{24}H_{35}IO_6Na$ $[M+Na]^+$ calcd 569.1376, found 569.1369.



Amphidinolide E (1) To a slurry of vinyl iodide **20** (20 mg, 0.037 mmol) and CuCl (20 mg, 0.201 mmol) in THF (0.5 mL) was added vinylstannane **21**[9] (68 mg, 0.183 mmol), followed by $Pd(PPh_3)_4$ (8.5 mg, 0.00732 mmol) in THF (0.5 mL). The reaction was stirred at room temp for 16 h, and then diluted with Et_2O (30 mL), filtered through Celite and concentrated. The crude product was purified by flash column chromatography using 10% methanol/chloroform to afford material that was still contaminated with an organotin impurity. The stannane impurity was removed by hplc purification with 100% ethyl acetate eluent on a normal phase, Varian Dynamax Microsorb 60-8 Si, 250 x 21.4 mm column. The retention time for amphidinolide E was 9.5 min. The flow rate was 18 mL/min.

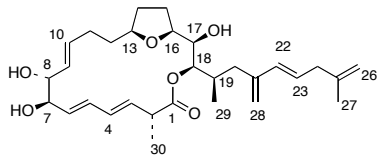
Amphidinolide E was detected using UV absorbtion (= 254 nm and 280 nm) and RI detection. Using the above conditions 10.6 mg (59%) of pure amphidinolide E was isolated: $[\alpha]^{25}_{D} = -86°$ (*c* 0.08, $CHCl_3$); ^{1}H NMR (400MHz, $CDCl_3$) 6.10-6.28 (m, 2H) (H4 and H5), 6.05 (d, *J* = 15.2 Hz, 1H) (H22), 5.58-5.75 (m, 3H) (H3, H10, H23), 5.27 (dd, *J* = 7.6, 14.4 Hz, 1H) (H9), 4.98 (s, 1H) (H29), 4.87 (s, 1H) (H29), 4.75 (s, 1H) (H26), 4.71 (s, 1H) (H26), 4.66 (d, *J* = 9.2 Hz, 1H) (H18), 3.95 (t, *J* = 8.4 Hz, 1H) (H8), 3.89 (t, *J* = 8.8 Hz, 1H) (H7), 3.68-3.74 (m, 1H) (H17), 3.52-3.60 (m, 1H) (H16), 3.36-3.45 (m, 1H) (H13), 3.21-3.30 (m, 1H) (H2), 2.71-2.84 (m, 2H) (H24), 2.20-2.45 (m, 6H) (H20a, H19, H11a and –OH x 3), 1.75-1.94 (m, 3H) (H11b, H12a, H20b), 1.72 (s, 3H) (H27), 1.51-1.68 (m, 1H) (H15a, overlapping w/ water), 1.21-1.51 (m, 4H) (H12b, H14a, H14b, H15b), 1.25 (d, *J* = 6.8 Hz, 3H) (H30), 0.92 (d, *J* = 6.8 Hz, 3H) (H29); ^{13}C NMR (100MHz, $CDCl_3$) 174.4, 144.4, 144.0, 135.1, 135.0, 134.1, 133.3, 131.4, 131.4, 129.4, 127.9, 115.7, 110.7, 79.9, 78.3, 78.0, 77.6, 76.7 (overlapping w/ chloroform), 73.2, 44.1, 41.2, 36.0, 32.6, 32.3, 29.9, 28.9, 27.1, 22.5, 17.5, 15.3; IR (neat) 3439, 2929, 1731, 1454, 1168, 990 cm^{-1}; HRMS (ES+) *m/z* for $C_{30}H_{44}O_6Na$ $[M+Na]^+$ calcd 523.3036, found 523.3038.

Comparison of ^{1}H NMR Data for Synthetic and Natural Amphidinolide E



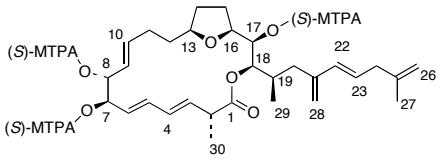
Position	Natural (Kobayashi, 600 MHz)[10]	Synthetic (Roush, 400 MHz)
1	----	----
2	3.26 (1H, dq, J = 10.0, 6.8 Hz)	3.26 (1H, m)
3	5.59 (1H, dd, J = 14.0, 10.0)	5.59 (1H, m) *H3, H10 & H23 overlap*
4	6.20 (1H, dd, J = 14.0, 10.6)	6.20 (1H, m) *H4 and H5 overlap*
5	6.16 (1H, dd, J = 14.5, 10.6)	6.16 (1H, m) *H4 and H5 overlap*
6	5.53 (1H, dd, J = 14.5, 8.5)	5.53 (1H, dd, J = 14.8, 8.8)
7	3.88 (1H, t, J = 8.5)	3.89 (1H, t, J = 8.8)
8	3.95 (1H, t, J = 8.5)	3.95 (1H, t, J = 8.4)
9	5.27 (1H, dd, J = 15.6, 8.5)	5.27 (1H, dd, J = 14.4, 7.6)
10	5.64 (1H, m)	5.64 (1H, m) *H3, H10 & H23 overlap*
11a	2.23 (1H, m)	2.25 (1H, m) *H11a & H19 overlap*
11b	1.82 (1H, m)	1.82 (1H, m)
12a	1.76 (1H, m)	1.76 (1H, m)
12b	1.48 (1H, m)	1.48 (1H, m)
13	3.41 (1H, m)	3.40 (1H, m)
14a	1.40 (1H, m)	1.40 (1H, m)
14b	1.25 (1H, m)	1.25 (1H, m)
15a	1.58 (1H, m)	1.58 (1H, m) *overlapping w/ water*
15b	1.33 (1H, m)	1.33 (1H, m)
16	3.56 (1H, dt, J = 7.5, 7.1)	3.56 (1H, m)
17	3.72 (1H, dt, J = 7.5, 4.5)	3.72 (1H, m)
18	4.66 (1H, d, J = 8.3)	4.66 (1H, d, J = 9.2)
19	2.25 (1H, m)	2.26 (1H, m) *H11a & H19 overlap*
20a	2.40 (1H, d, J = 13.4)	2.40 (1H, d, J = 14.0)
20b	1.79 (1H, m)	1.79 (1H, m)
21	----	----
22	6.05 (1H, d, J = 15.9)	6.05 (1H, d, J = 15.2)
23	5.71 (1H, dt, J = 15.9, 6.8)	5.71 (1H, m) *H3, H10 & H23 overlap*
24	2.78 (2H, br d, J = 6.8)	2.78 (2H, m)
25	----	----
26a	4.75 (1H, s)	4.75 (1H, s)
26b	4.71 (1H, s)	4.71 (1H, s)
27	1.72 (3H, s)	1.72 (3H, s)
28a	4.98 (1H, s)	4.98 (1H, s)
28b	4.87 (1H, s)	4.87 (1H, s)
29	0.92 (3H, d, J = 6.6)	0.92 (3H, d, J = 6.8)
30	1.25 (3H, d, J = 6.8)	1.25 (3H, d, J = 6.8)

Comparison of ^{13}C NMR Data for Synthetic and Natural Amphidinolide E



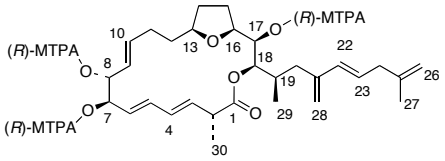
Position	Natural (Kobayashi)[10]	Synthetic (Roush)
1	174.42 ppm	174.4
2	44.06	44.1
3	135.14	135.1
4	134.93	135.0
5	134.15	134.1
6	133.34	133.3
7	79.86	79.9
8	78.27	78.3
9	131.40	131.4
10	131.37	131.4
11	41.26	41.3
12	36.07	36.0
13	78.04	78.0
14	32.60	32.6
15	29.94	29.9
16	77.58	77.6
17	76.68	76.7 *under* $CDCl_3$
18	73.20	73.2
19	32.34	32.3
20	28.95	29.0
21	144.68	144.7
22	129.41	129.4
23	127.93	127.9
24	27.14	27.1
25	144.00	144.0
26	115.70	115.8
27	22.53	22.5
28	110.71	110.7
29	17.52	17.5
30	15.36	15.3

Comparison of ^{1}H NMR Data for (S)-MTPA Mosher Triesters of Amphidinolide E



Position	Natural (Kobayashi, 600 MHz)[11]	Synthetic (Roush, 400 MHz)
1	----	----
2	3.24 (1H, m)	3.24 (1H, m)
3	5.67 (1H, m)	5.67 (1H, m)
4	6.17 (1H, dd, J = 10.4, 15.3)	6.17 (1H, dd, J = 10.4, 14.4)
5	6.40 (1H, dd, J = 10.8, 15.3)	6.40 (1H, dd, J = 11.2, 15.2)
6	5.39 (1H, dd, J = 9.3, 15.3)	5.39 (1H, m)
7	5.60 (1H, brt, J = 9.3)	5.60 (1H, m)
8	5.65 (1H, m)	5.65 (1H, m)
9	5.21 (1H, dd, J = 7.4, 15.6)	5.21 (1H, dd, J = 7.2, 15.6)
10	5.75 (1H, dt, J = 15.6, 7.1)	5.75 (1H, m)
11a	2.28 (1H, m)	2.26 (1H, m)
11b	2.00 (1H, m)	2.01 (1H, m)
12a	1.56 (1H, m)	1.56 (1H, m)
12b	1.72 (1H, m)	1.72 (1H, m)
13	3.31 (1H, m)	3.31 (1H, m)
14a	1.35 (1H, m)	1.35 (1H, m)
14b	1.79 (1H, m)	1.79 (1H, m)
15a	1.45 (1H, m)	1.45 (1H, m)
15b	1.67 (1H, m)	1.67 (1H, m)
16	3.64 (1H, dt, J = 6.7, 9.3)	3.64 (1H, m)
17	5.38 (1H, d, J = 9.3)	5.38 (1H, m)
18	4.78 (1H, d, J = 10.4)	4.78 (1H, d, J =9.6)
19	1.81 (1H, m)	1.81 (1H, m)
20a	1.74 (1H, m)	1.74 (1H, m)
20b	2.25 (1H, m)	2.25 (1H, m)
21	----	----
22	5.96 (1H, d, J = 16.0)	5.96 (1H, d, J = 15.2)
23	5.54 (1H, dt, J = 16.0, 7.1)	5.54 (1H, m)
24	2.71 (2H, brt, J = 7.1)	2.72 (2H, bs)
25	----	----
26a	4.67 (1H, brs)	4.67 (1H, brs)
26b	4.74 (1H, brs)	4.74 (1H, brs)
27	1.70 (3H, s)	1.70 (3H, s)
28a	4.72 (1H, brs)	4.72 (1H, brs)
28b	4.93 (1H, brs)	4.93 (1H, brs)
29	0.86 (3H, d, J = 6.7)	0.86 (3H, d, J = 6.4)
30	1.25 (3H, d, J = 6.7)	1.25 (3H, d, J = 6.7)
OMe (3x)	3.34(3H, s), 3.39(3H, s), 3.56(3H, s)	3.35(3H, s), 3.39(3H, s), 3.58(3H, s)
Ph groups	7.31-7.47 (14H, m)	7.30-7.47 (14H, m)
Ph groups	7.64 (1H, d, J = 7.8)	7.64 (1H, d, J = 7.6)

Comparison of ^{1}H NMR Data for (R)-MTPA Mosher Triesters of Amphidinolide E



Position	Natural (Kobayashi, 600 MHz)[11]	Synthetic (Roush, 400 MHz)
1	----	----
2	3.26 (1H, m)	3.26 (1H, m)
3	5.64 (1H, m)	5.64 (1H, m)
4	6.15 (1H, dd, J = 10.8, 15.3)	6.15 (1H, dd, J = 10.4, 15.2)
5	6.35 (1H, dd, J = 10.4, 15.3)	6.36 (1H, dd, J = 10.8, 14.8)
6	5.28 (1H, dd, J = 9.3, 15.3)	5.28 (1H, dd, J = 8.8, 14.8)
7	5.52 (1H, brt, J = 9.3)	5.52 (1H, brt, J = 9.2)
8	5.58 (1H, m)	5.58 (1H, m)
9	5.05 (1H, dd, J = 7.1, 15.6)	5.05 (1H, dd, J = 6.4, 15.6)
10	5.45 (1H, dt, J = 15.6, 7.1)	5.45 (1H, m)
11a	1.82 (1H, m)	1.82 (1H, m)
11b	2.09 (1H, m)	2.09 (1H, m)
12a	1.41 (1H, m)	1.41 (1H, m)
12b	1.58 (1H, m)	1.58 (1H, m)
13	3.17 (1H, m)	3.17 (1H, m)
14a	1.29 (1H, m)	1.29 (1H, m)
14b	1.71 (1H, m)	1.71 (1H, m)
15a	1.41 (1H, m)	1.41 (1H, m)
15b	1.63 (1H, m)	1.63 (1H, m)
16	3.46 (1H, m)	3.46 (1H, m)
17	5.36 (1H, d, J = 9.3)	5.36 (1H, d, J = 9.6)
18	4.81 (1H, d, J = 10.4)	4.81 (1H, d, J = 10.4)
19	2.00 (1H, m)	2.00 (1H, m)
20a	1.80 (1H, dd, J = 10.4, 13.8)	1.80 (1H, m)
20b	2.33 (1H, dd, J = 3.4, 13.4)	2.33 (1H, app d, J = 14.4)
21	----	----
22	6.03 (1H, d, J = 15.6)	6.03 (1H, d, J = 16.4)
23	5.61 (1H, m)	5.61 (1H, m)
24	2.72 (2H, m)	2.72 (2H, d, 7.2)
25	----	----
26a	4.67 (1H, brs)	4.67 (1H, brs)
26b	4.73 (1H, brs)	4.73 (1H, brs)
27	1.69 (3H, s)	1.69 (3H, s)
28a	4.82 (1H, s)	4.82 (1H, s)
28b	4.99 (1H, brs)	4.98 (1H, brs)
29	0.90 (3H, d, J = 6.7)	0.90 (3H, d, J = 6.8)
30	1.29 (3H, d, J = 6.7)	1.29 (3H, d, J = 6.8)
OMe (3x)	3.43(3H, s), 3.46(3H, s), 3.53(3H, s)	3.43(3H, s), 3.46(3H, s), 3.56(3H, s)
Ph groups	7.31-7.47 (14H, m)	7.31-7.47 (14H, m)
Ph groups	7.61 (1H, d, J = 7.8)	7.60 (1H, d, J = 7.2)

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