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# Stereoselective Synthesis of (−)-Amphidinolide E

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*Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday*

**Abstract:** The total synthesis of (−)-amphidinolide E was accomplished by following a synthetic scheme that incorporates the labile C2 stereocenter at a very late stage. The oxolane unit was prepared by β-alkoxyacrylate radical cyclization. The enyne metathesis reaction was employed for the synthesis of the side chain. The Kocienski–Julia reaction was used for the union of the two major fragments, and the Kita macrolactonization protocol was used for macrolide synthesis.

**Keywords:** amphidinolides · anticancer agents · macrolides · natural products · total synthesis

## Introduction

Symbiotic dinoflagellates of the genus *Amphidinium*, isolated from the internal cells of Okinawan marine flatworms *Amphiscolops* spp., which live on algae or seaweeds in Okinawan coral reefs, are rich sources of bioactive substances. The most prominent secondary metabolites from these sources are amphidinolides, the cytotoxic macrolides of mixed polyketide origin. Until 2003, 34 cytotoxic macrolides have been isolated from *Amphidinium* spp. by Kobayashi and coworkers.[1] Amphidinolide E (**1**) is a unique 18-membered macrolide isolated from the Y-5′ strain of a dinoflagellate *Amphidinium* sp.[2] The structure of **1** features a *cis*-2,5-disubstituted oxolane unit incorporated in the macrolide ring, as well as a prominent triene side chain. Compound **1** exhibited cytotoxic activity against L1210 ($IC_{50}=2.0\ \mu g\,mL^{-1}$) and L5178Y ($IC_{50}=4.8\ \mu g\,mL^{-1}$) murine leukemia cells in vitro. Due to its unique structural features and limited availability, intense synthetic activities have been directed toward **1**;[3] successful total syntheses were reported by us[4] and by Va and Roush.[5] In this paper, we report a full account of our recent efforts on the total synthesis of **1**.

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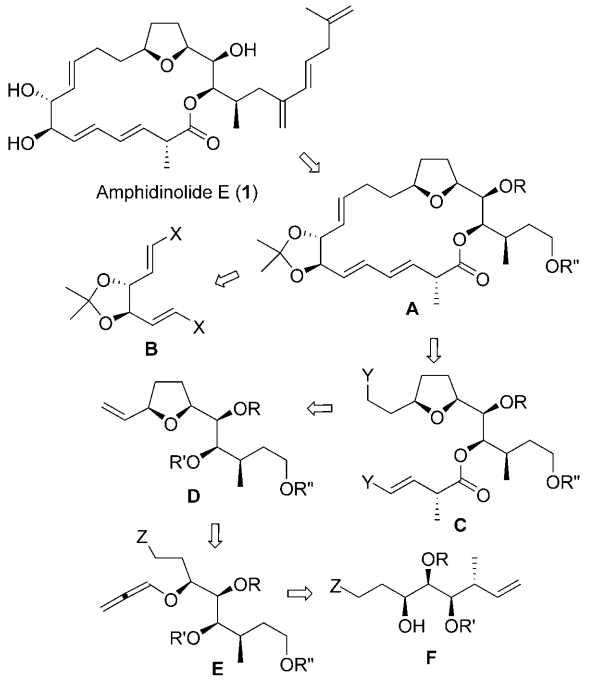
## Results and Discussion

At the outset, macrolide **A** was envisioned as the penultimate target in the synthesis of **1** (Scheme 1). Introduction of the triene side chain was postponed to the last phase of the synthesis. For preparation of macrolide **A**, a double-Suzuki stitching process was envisaged. If successful, coupling of

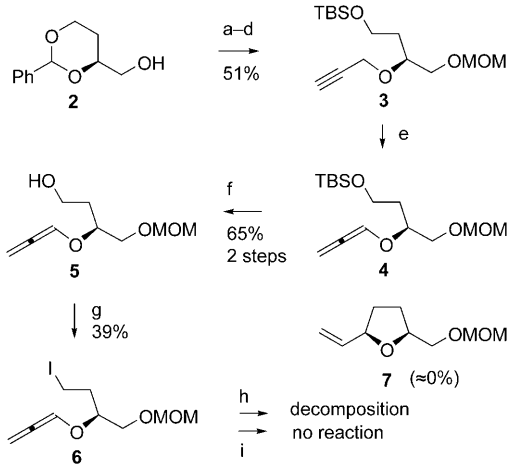



Scheme 1. Retrosynthetic analysis I.

ester **C** ($Y=BR_2$) with the $C_2$-symmetric diene **B** ($X=I$) should furnish a quick access to the macrolide structure. Fragment **B** may be obtained from the known tartrate acetonide precursors. Fragment **C** may be prepared from fragment **D**. Fragment **D** may in turn be obtained by radical cyclization of the allenyl ether derivative **E**, which should be accessible from fragment **F**.

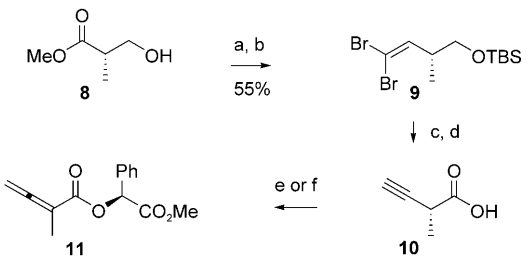
Studies on the radical cyclization of allenyl ethers were first initiated. The known triol derivative **2**[6] was converted into propargyl ether **3** through MOM protection, hydrogenolysis, TBS protection of the primary hydroxy group, and propargylation (Scheme 2). Allenyl ether **4** was prepared




Scheme 2. Attempted radical cyclization of allenyl ether **6**. Reaction conditions: a) MOMCl, DIPEA, $CH_2Cl_2$; b) $H_2$, Pd/C, MeOH; c) TBSCl, imidazole, $CH_2Cl_2$; d) NaH, THF, then $CHCCH_2Br$, reflux; e) *t*BuOK, THF; f) TBAF, THF; g) $CH_3I$, $PPh_3$, DEAD, toluene; h) $Bu_3SnH$ (1.5 equiv), AIBN (0.3 equiv), benzene, reflux; i) $(TMS)_3SiH$ (1.3 equiv), $Et_3B$ (1.5 equiv), toluene, −20 °C. AIBN = 2,2′-azobisisobutyronitrile, DEAD = diethyl azodicarboxylate, DIPEA = diisopropylethylamine, MOM = methoxymethyl, TBAF = tetra-*n*-butylammonium fluoride, TBS = *tert*-butyldimethylsilyl, TMS = trimethylsilyl.

from **3** upon exposure to potassium *tert*-butoxide,[7] and iodide **6** was obtained via the primary alcohol **5**. When **6** was allowed to react under the usual conditions of tributylstannane/AIBN/benzene, a complex product mixture was obtained. No reaction occurred when **6** was allowed to react with tris(trimethylsilyl)silane and triethylborane at −20 °C. The oxolane product **7** was not prepared under these conditions, and it was concluded that allenyl ethers are not productive precursors for radical cyclization.

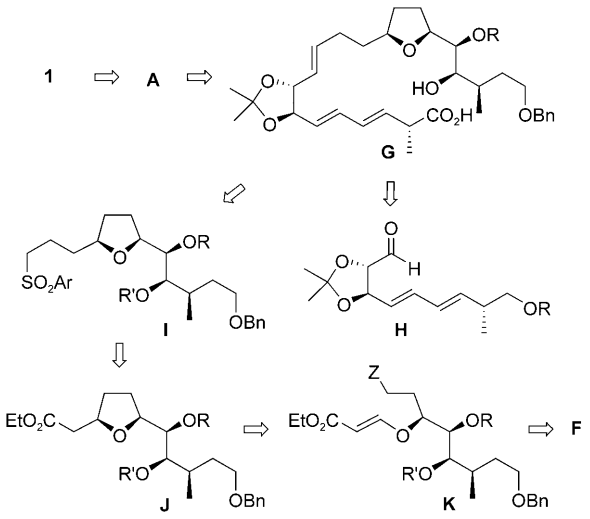
For the preparation of intermediates like **C** for the double-Suzuki stitching scheme, hydroboration of 2-methyl-3-butynoate esters are required, and it was essential to diagnose the fidelity of the C2 stereocenter throughout the manipulation. For this purpose, (*R*)-2-methyl-3-butynoic acid (**10**) was prepared from methyl (*S*)-3-hydroxy-2-methylpropanoate (**8**) via dibromo olefin **9** (Scheme 3).[8] It was soon realized that it was not possible to prepare esters of the acid **10**. When methyl (*S*)-mandelate was allowed to react with **10** in the presence of 2-chloro-1-methylpyridinium iodide




Scheme 3. Attempted esterification of 2-methyl-3-butynoic acid (**10**). Reaction conditions: a) TBSCl, imidazole, $CH_2Cl_2$; b) DIBAL, toluene, −78 °C, then $CBr_4$, $PPh_3$, $CH_2Cl_2$, −78 °C→room temperature; c) *n*BuLi, diethyl ether, −78 °C; d) Jones oxidation, acetone, 0 °C; e) methyl (*S*)-mandelate (1.2 equiv), 2-chloro-1-methylpyridinium iodide (1.3 equiv), TEA (20 equiv), $CH_2Cl_2$, room temperature, 12 h; f) methyl (*S*)-mandelate (2.0 equiv), DCC (2.0 equiv), DMAP (0.05 equiv), $CH_2Cl_2$, −10 °C, 10 h. DCC = dicyclohexylcarbodiimide, DIBAL = diisobutylaluminum hydride, DMAP = 4-dimethylaminopyridine, TEA = triethylamine.

and triethylamine,[9] or in the presence of DCC and DMAP,[10] the only product isolated was 2-methyl-2,3-butadienoate **11**. The message was clear: 2-methyl-3-butynoate esters are too labile for manipulation.

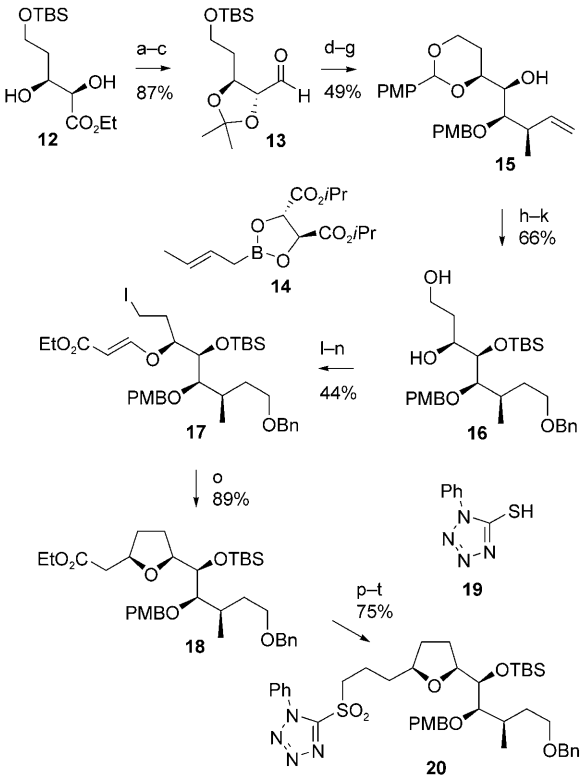
By considering the results described above, it was decided to abandon the double-Suzuki stitching scheme. In particular, it was realized that a successful total synthesis of **1** should avoid intermediates like **C**, which would involve difficult preparation and precarious manipulation. In a second retrosynthetic analysis, lactonization of the seco acid **G** was envisaged for the synthesis of **1**, which may be prepared by Julia coupling of the aldehyde fragment **H** and the sulfone fragment **I** (Scheme 4). Potential problems arising from the intrinsic lability at C2 of **1** would be faced at the end of the macrolide synthesis. Fragment **I** may be prepared from fragment **J**. Fragment **J** may in turn be obtained by radical cyclization of the β-alkoxyacrylate derivative **K**, which should be accessible from fragment **F**.




Scheme 4. Retrosynthetic analysis II. Bn = benzyl.

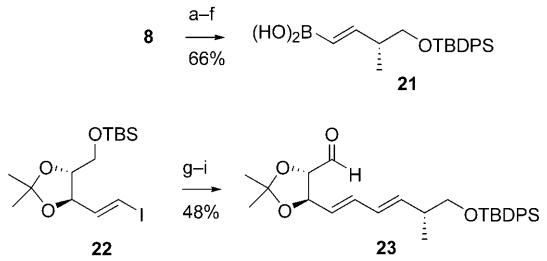
  

In practice, the known diol **12**[11] was first converted into aldehyde **13** by acetonide formation, LAH reduction, and oxidation (Scheme 5). Roush crotylation of **13** with boronate **14**,[12] PMB protection, acetonide deprotection, and cyclic-acetal formation provided alcohol **15**. Diol **16** was prepared from **15** by TBS protection, hydroboration–oxidation, benzyl protection, and acetal deprotection under acidic conditions. Selective tosylation of the primary hydroxy group in **16**, reaction of the secondary hydroxy group with ethyl propiolate in the presence of *N*-methylmorpholine, and iodide substitution led to the formation of iodide **17**. The relative inefficiency of the conversion of **16** into **17** reflects the 1,2-migration tendency of the TBS group under basic conditions. Radical cyclization[13] of **17** proceeded smoothly in the presence of tris(trimethylsilyl)silane and triethylborane at −20 °C, and the oxolane product **18** was isolated in good yield. Conversion of **18** into the homologous sulfone **20** required a five-step sequence that involved DIBAL reduction, Wittig methylenation, hydroboration–oxidation, Mitsunobu-type substitution with thiol **19**, and oxidation with ammonium molybdate/hydrogen peroxide.[14]




Scheme 5. Synthesis of sulfone **20**. Reaction conditions: a) $Me_2C(OMe)_2$, PPTS, $CH_2Cl_2$, reflux; b) LAH, ether; c) $SO_3$·pyr, TEA, DMSO/$CH_2Cl_2$ (1:1); d) **14**, toluene, −78 °C; e) PMBCl, NaH, TBAI, DMF; f) CSA, $CH_2Cl_2$/MeOH (2:1); g) *p*-$MeOC_6H_4CH(OMe)_2$, CSA, $CH_2Cl_2$; h) TBSOTf, 2,6-lutidine, $CH_2Cl_2$; i) $(sia)_2BH$, THF; $H_2O_2$, NaOH (2 N); j) BnBr, NaHMDS, THF/DMF (4:1); k) CSA, $CH_2Cl_2$/MeOH (2:1); l) *p*-TsCl, TEA, $CH_2Cl_2$, 0 °C; m) $CHCCO_2Et$, NMM, $CH_2Cl_2$; n) NaI, acetone, reflux; o) $(TMS)_3SiH$ (1.3 equiv), $Et_3B$ (1.5 equiv), toluene, −20 °C, 2 h; p) DIBAL, THF, −78 °C; q) $Ph_3P^+CH_3I^-$, *n*BuLi, THF, −78 °C; r) $(sia)_2BH$, THF; $H_2O_2$, NaOH (2 N); s) **19**, DIAD, $PPh_3$, THF; t) $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, $H_2O_2$, EtOH. CSA = camphor-10-sulfonic acid, DIAD = diisopropyl azodicarboxylate, DMF = *N*,*N*-dimethylformamide, DMSO = dimethyl sulfoxide, HMDS = 1,1,1,3,3,3-hexamethyldisilazane, LAH = lithium aluminum hydride, NMM = *N*-methylmorpholine, PMB = *p*-methoxybenzyl, PMP = *p*-methoxyphenyl, PPTS = pyridinium *p*-toluenesulfonate, pyr = pyridine, sia = siamyl, TBAI = tetra-*n*-butylammonium iodide, Tf = trifluoromethanesulfonyl, Ts = *p*-toluenesulfonyl.

For the synthesis of fragment **H**, methyl (*S*)-3-hydroxy-2-methylpropanoate (**8**) was converted into the corresponding TBDPS ether, from which vinyl boronic acid **21** was obtained by reduction, oxidation, Corey–Fuchs homologation,[8] and hydroboration–hydrolysis (Scheme 6).[15] Suzuki coupling[16] of **21** with the known vinyl iodide **22**[17] proceeded smoothly, and the resulting diene was transformed into aldehyde **23** by TBS deprotection and oxidation.

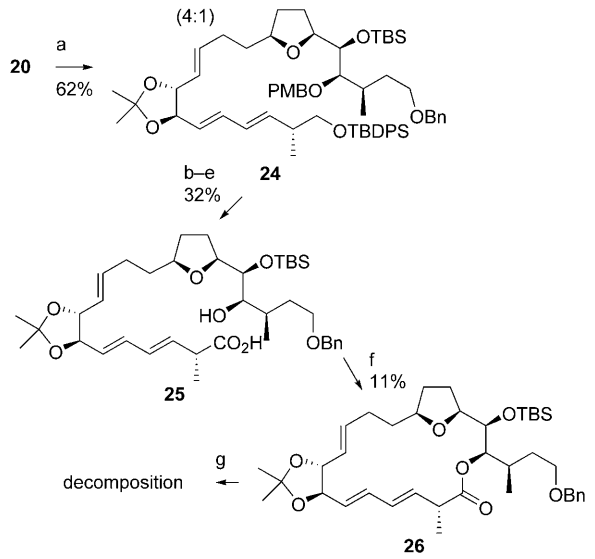



Scheme 6. Synthesis of aldehyde **23**. Reaction conditions: a) TBDPSCl, imidazole, $CH_2Cl_2$, 0 °C→room temperature; b) $LiBH_4$, diethyl ether; c) $SO_3$·pyr, TEA, DMSO/$CH_2Cl_2$ (1:1), 0 °C→room temperature; d) $CBr_4$, $PPh_3$, Zn, $CH_2Cl_2$, 0 °C→room temperature; e) *n*BuLi, THF, −78 °C; f) $BHBr_2$·DMS, $CH_2Cl_2$, 0 °C→room temperature; $H_2O$/diethyl ether (1:3), 0 °C→room temperature; g) **21**, $[Pd(PPh_3)_4]$, TlOEt, THF/$H_2O$ (4:1); h) PPTS, EtOH; i) $SO_3$·pyr, TEA, DMSO/$CH_2Cl_2$ (1:1), 0 °C→room temperature. DMS = dimethylsulfide, TBDPS = *tert*-butyldiphenylsilyl.

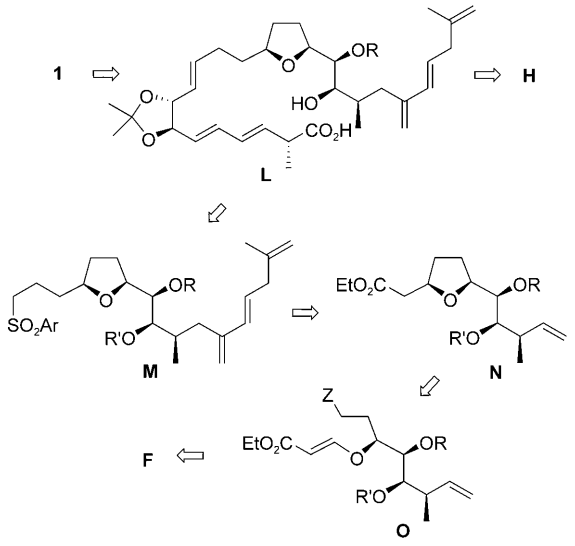
The critical Kocienski–Julia coupling[18] between sulfone **20** and aldehyde **23** proceeded in the presence of potassium hexamethyldisilazide in DME at low temperature (Scheme 7). In this way, a mixture (*E*/*Z* = 4:1) of olefinic products that favored **24** was obtained in 62% yield. Selective TBAF deprotection of the terminal TBDPS group, Dess–Martin oxidation, sodium chlorite oxidation, and ceric ammonium nitrate deprotection of the PMB group led to the isolation of hydroxy carboxylic acid **25** in 32% yield. The relatively low yield reflected problems primarily associated with the PMB-deprotection step: presumably, the ceric salt interfered with the diene group. Under Yamaguchi conditions,[19] hydroxy carboxylic acid **25** cyclized to produce the macrolide derivative **26** in 11% yield. Further manipulation of macrolide **26** was not possible. For example, attempted benzyl deprotection of **26** with lithium di-*tert*-butylbiphenyl failed completely.

The truncated macrolide intermediate **26** was a dead end; it was necessary to revise the synthetic scheme for **1**. In a new retrosynthetic analysis, synthesis of **1** would be accomplished by lactonization of seco acid **L**, which may be prepared by Julia coupling of the aldehyde fragment **H** and the triene sulfone fragment **M** (Scheme 8). Strategically, it was decided to introduce the triene side chain relatively early in



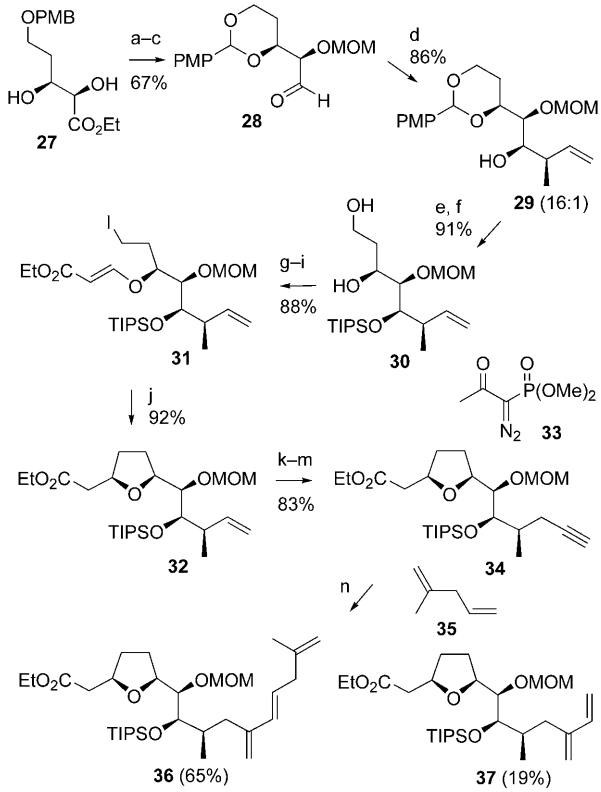

Scheme 7. Synthesis of macrolide **26**. Reaction conditions: a) KHMDS, then DME, −78→−60 °C, then **23**, −78 °C→room temperature; b) TBAF, THF; c) DMP, $CH_2Cl_2$; d) $NaClO_2$, $NaH_2PO_4$, *t*BuOH/2-methyl-2-butene/$H_2O$ (1:1:1); e) CAN, MeCN/$H_2O$ (10:1), 0 °C; f) 2,4,6-$Cl_3PhCOCl$ (9.0 equiv), TEA (15 equiv), THF, room temperature, 3 h, then DMAP (20 equiv), toluene, room temperature, 12 h; g) LiDBB, THF, −78 °C. CAN = cerium(IV) ammonium nitrate, DBB = di-*tert*-butylbiphenyl, DME = 1,2-dimethoxyethane, DMP = Dess–Martin periodinane.




Scheme 8. Retrosynthetic analysis III.

the scheme, thus forestalling difficulties that may arise from manipulations of the unstable macrolide intermediates. In this way, potential problems arising from the intrinsic lability at C2 of **1** would be faced only at the end of the synthetic scheme. Fragment **M** may be prepared from fragment **N**. Fragment **N** may in turn be obtained by radical cyclization of the β-alkoxyacrylate derivative **O**, which should be accessible from fragment **F**. It was also clear from the experiences above that the original set of protecting groups (R = TBS, R′ = PMB) should be changed for successful completion of the synthesis.

The known diol **27**[20] served as the starting material in the synthesis of fragment **M** (Scheme 9). DDQ oxidation of **27** provided the corresponding PMP cyclic acetal, which was




Scheme 9. Synthesis of triene **36**. Reaction conditions: a) DDQ, 3-Å molecular sieves, $CH_2Cl_2$, 0 °C; b) MOMCl, DIPEA, DMAP, $CH_2Cl_2$, reflux; c) DIBAL, $CH_2Cl_2$, −78 °C; d) **14**, 4-Å molecular sieves, toluene, −78 °C; e) TIPSOTf, collidine, $CH_2Cl_2$; f) CAN, MeCN/$H_2O$ (9:1), 0 °C; g) *p*-TsCl, TEA, $CH_2Cl_2$, 0 °C; h) $CHCCO_2Et$, NMM, $CH_2Cl_2$, room temperature; i) NaI, acetone, reflux; j) $(TMS)_3SiH$ (1.3 equiv), $Et_3B$ (1.5 equiv), toluene, −20 °C, 1 h; k) $(sia)_2BH$, THF, 0 °C; $NaBO_3{\cdot}4H_2O$, $H_2O$; l) DMP, $CH_2Cl_2$, 0 °C→room temperature; m) **33**, $Cs_2CO_3$, EtOH, 0 °C→room temperature; n) $CH_2CH_2$, $[(H_2IMes)(PCy_3)Cl_2RuCHPh]$, $CH_2Cl_2$, then **35**, 40 °C, sealed tube, 24 h. Cy = cyclohexyl, DDQ = 2,3-dichloro-5,6-dicyano-*p*-benzoquinone, Mes = mesityl, TIPS = triisopropylsilyl.

converted into aldehyde **28** by MOM protection and DIBAL reduction. Roush crotylation of **28** with boronate **14** provided a product mixture containing mainly the desired homoallylic alcohol **29** (d.r. = 16:1). TIPS protection of **29** and oxidative acetal deprotection with CAN produced diol **30**. Selective tosylation of the primary hydroxy group in **30**, reaction with ethyl propiolate, and iodide substitution led to β-alkoxyacrylate **31**. Radical cyclization of **31** proceeded smoothly in the presence of tris(trimethylsilyl)silane and triethylborane, and the oxolane product **32** was obtained in high yield.

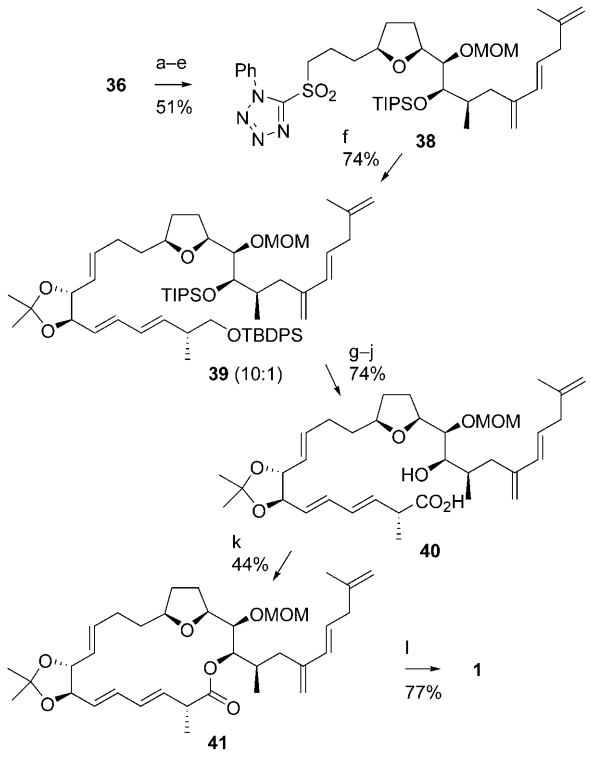
Hydroboration–oxidation of olefin **32** produced the corresponding primary alcohol, which was converted into the corresponding aldehyde. At this point, a variety of ways were

tested for effective buildup of the side-chain unit. For example, Nozaki–Hiyama–Kishi reaction[21] of the aldehyde with 1-iodo-4-methyl-1,4-pentadiene[22] proceeded efficiently to yield a mixture of allylic alcohols, which was eventually converted into the desired triene **36** by oxidation and Wittig olefination. Alternatively, the homologous alkyne **34** was obtained from the aldehyde by reaction with diazophosphonate **33**.[23] Alkyne **34** was first treated with ethylene in the presence of the second-generation Grubbs catalyst,[24] and the crude product was then treated with 2-methyl-1,4-pentadiene (**35**; commercially available). In this way, the desired triene **36** was obtained in 65% yield accompanied by diene **37** in 19% yield (Scheme 9). Subjection of an isolated sample of diene **37** under the same reaction conditions provided additional amounts of triene **36**.

DIBAL reduction of **36** produced the corresponding aldehyde, which was transformed into the homologous aldehyde by Wittig methoxymethylidenation and hydrolysis (Scheme 10). Further reduction by $NaBH_4$, Mitsunobu-type substitution of the primary hydroxy group with thiol **19**, and selective oxidation led to sulfone **38**. Conditions for Kocienski–Julia reaction between sulfone **38** and aldehyde **23** were then investigated; the best result was obtained when the lithio derivative of sulfone **38** prepared in THF was treated with aldehyde **23** in DMF/DMPU (3:1) at −78 °C. In this way, a reaction mixture that favored the desired *E* olefin **39** ($E/Z = 10:1$) was obtained in 74% yield. Selective TBDPS deprotection of **39** proceeded under alkaline conditions, but oxidative conversion of the primary hydroxy group into a carboxylic acid unit proved to be painfully difficult; for example, Dess–Martin oxidation resulted in the scrambling of the NMR signals from the side-chain region. Eventually, it was found that reaction of the primary alcohol with IBX[25] provided the corresponding aldehyde cleanly, which was converted into hydroxy carboxylic acid **40** by oxidation with sodium chlorite and TIPS deprotection.

For the lactonization of **40**, the Kita protocol[26] worked best; macrolide **41** was produced in 44% yield. It was not possible to obtain a reasonable yield of **41** under Yamaguchi-lactonization conditions. MOM and acetonide deprotection of **41** under acidic conditions produced amphidinolide E (**1**) in 77% yield[27] (Scheme 10).




Scheme 10. Synthesis of amphidinolide E (**1**). Reaction conditions: a) DIBAL, THF, −78 °C; b) $Ph_3P^+CH_2OMeCl^-$, *t*BuOK, THF, 0 °C→room temperature, then $Hg(OAc)_2$, THF/$H_2O$ (10:1), 0 °C; c) $NaBH_4$, MeOH; d) **19**, $PPh_3$, DIAD, THF; e) $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, $H_2O_2$, EtOH; f) LiHMDS, THF, −78→−40 °C, then **23**, DMF/DMPU (3:1), −78 °C→room temperature; g) NaOH (15%)/DMPU (1:10); h) IBX, DMSO/THF (1:1); i) $NaClO_2$, $NaH_2PO_4$, *t*BuOH/2-methyl-2-butene/$H_2O$ (1:1:1); j) TBAF, THF; k) EtOCCH (1.5 equiv), $[RuCl_2(p\text{-cymene})]_2$ (0.02 equiv), toluene, 0 °C→room temperature, 30 min, then CSA, room temperature→50 °C, 2 h; l) HCl (4 N), MeOH. DMPU = 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone(*N*,*N*-dimethylpropylene urea), IBX = *o*-iodoxybenzoic acid.

## Conclusions

In this synthesis, a β-alkoxyacrylate radical-cyclization reaction was employed for the stereoselective construction of the oxolane unit in the structure. The general fragility of amphidinolide E (**1**), particularly at C2 and C24, necessitated careful analysis and judicious choice of reaction conditions for a successful culmination of the total synthesis.

## Experimental Section

*General Information*

$^1H$ and $^{13}C$ NMR spectra were obtained on a Bruker DPX-300 (300 MHz), a Bruker Avance-600 (600 MHz), and a Varian/Oxford As-500 (500 MHz) spectrophotometer. Chemical shifts are reported in parts per million relative to tetramethylsilane as an internal standard unless otherwise indicated, and coupling constants are given in Hertz. IR spectra were obtained on a JASCO FTIR-660 plus spectrophotometer. Mass spectra were recorded on a JEOL JMS 600W spectrometer with electron impact (EI) or chemical ionization (CI), as well as a JEOL JMS AX505WA spectrometer with fast atom bombardment (FAB). Significant fragments are reported in the following manner: *m*/*z* (relative intensity). MALDI-TOF spectrometric measurements were performed on a Bruker Autoflex II LIFT-TOF/TOF mass spectrometer (dithranol matrix). Optical rotation data were obtained on a JASCO P-1030 automatic polarimeter.

Reaction progress was checked on TLC plates (Merck 5554 Kiesel gel 60 F254), and the spots were visualized under 254-nm UV light and/or by charring after the TLC plates were dipped in a solution of vanillin (vanillin (9.0 g) and conc. sulfuric acid (1.5 mL) in methanol (300 mL)), $KMnO_4$ ($KMnO_4$ (3 g), ($K_2CO_3$) 20 g, and aq. NaOH (5%, 5 mL) in water (300 mL)), or phosphomolybdic acid (phosphomolybdic acid (250 mg) in ethanol (50 mL)). Column chromatography was performed on silica gel (Merck 9385 Kiesel gel 60) with hexanes/EtOAc. The solvents were simply distilled unless otherwise noted.

Unless otherwise specified, all reactions were conducted under a slight positive pressure of dry nitrogen. The usual workup refers to washing of

the quenched reaction mixture with brine, drying of the organic extracts over anhydrous $MgSO_4$, and evaporation under reduced pressure with a rotary evaporator.

All solvents used in reactions were dried under nitrogen atmosphere. THF was distilled from Na/benzophenone, and $CH_2Cl_2$ was distilled from $P_2O_5$. Benzene was washed with concentrated $H_2SO_4$, distilled from Na/benzophenone, and stored over 4-Å molecular sieves. $Et_2O$ was distilled from LAH. $CH_3CN$ was distilled from $CaH_2$ and stored over 4-Å molecular sieves. Pyridine and TEA were distilled over KOH and stored over 4-Å molecular sieves.

*Boronic Acid* ***21***

Imidazole (2.76 g, 40.6 mmol) and TBDPSCl (8.4 mL, 33 mmol) were added to a solution of methyl (*S*)-(+)-3-hydroxy-2-methylpropanoate (**8**; 3 mL, 27 mmol) in $CH_2Cl_2$ (45 mL) at 0 °C. This mixture was stirred at room temperature for 1 h, and the reaction was quenched by saturated aqueous $NH_4Cl$ (20 mL). The reaction mixture was extracted with $CH_2Cl_2$ (20 mL), and the organic phase was washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (hexanes/EtOAc = 15:1) provided the corresponding ester (9.65 g, 100 %). $R_f = 0.55$ (hexanes/EtOAc = 8:1); $[\alpha]_D^{27} = +15.7$ ($c = 1.00$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 2943$, 1739, 1589, 1466, 1389, 1254, 1199, 1107, 1026, 818, 702, 613, 505 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta = 7.70$–$7.75$ (m, 4H), 7.41–7.50 (m, 6H), 3.89, 3.80 (ABX, $J_{AB} = 9.8$ Hz, $J_{AX} = 6.9$ Hz, $J_{BX} = 5.9$ Hz, 2H), 3.73 (s, 3H), 2.74–2.82 (m, 1H), 1.22 (d, $J = 7.1$ Hz, 3H), 1.10 ppm (s, 9H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta = 175.6$, 135.8, 133.8, 133.7, 129.9, 127.9, 66.2, 51.8, 51.8, 42.6, 27.0, 19.5, 13.7 ppm; MS (CI): $m/z$ (%) = 355 $[M-1]^+$ (1), 341 (2), 325 (6), 299 (28), 279 (100), 213 (2); HRMS (CI): $m/z$ calcd for $C_{21}H_{27}O_3Si$: 355.1729 $[M-1]^+$; found: 355.1729.

$LiBH_4$ (2.0 M in THF, 27 mL, 54 mmol) was added to a solution of the ester (9.65 g, 27.1 mmol) in $Et_2O$ (270 mL) at 0 °C, and the reaction mixture was allowed to warm to room temperature. After 24 h, the reaction was quenched by saturated aqueous $NH_4Cl$ (100 mL). The reaction mixture was extracted with $Et_2O$ (2 × 100 mL), and the organic phase was dried over $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (hexanes/EtOAc = 4:1) gave the corresponding alcohol (8.59 g, 97 %). $R_f = 0.42$ (hexanes/EtOAc = 4:1); $[\alpha]_D^{25} = +3.9$ ($c = 1.00$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3375$, 3138, 3070, 3049, 2958, 1589, 1471, 1427, 1390, 1188, 1113, 939, 741 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta = 7.65$–$7.71$ (m, 4H), 7.35–7.44 (m, 6H), 3.71, 3.60 (ABX, $J_{AB} = 10.0$ Hz, $J_{AX} = 4.7$ Hz, $J_{BX} = 7.6$ Hz, 2H), 3.63–3.68 (m, 2H), 2.71 (dd, $J = 6.1$, 4.9 Hz, 1H), 1.94–2.02 (m, 1H), 1.06 (s, 9H), 0.83 ppm (d, $J = 6.8$ Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta = 135.9$, 135.9, 133.5, 133.5, 130.1, 128.1, 68.8, 67.7, 37.7, 27.2, 19.5, 13.5 ppm; MS (CI): $m/z$ (%) = 329 $[M+1]^+$ (100), 311 (9), 291 (3), 271 (18), 251 (49), 239 (5), 209 (7), 199 (16), 179 (11); HRMS (CI): $m/z$ calcd for $C_{20}H_{29}O_2Si$: 329.1937 $[M+1]^+$; found: 329.1938.

TEA (4.77 mL, 34.2 mmol) was added to a solution of the alcohol (2.25 g, 6.84 mmol) in DMSO (14 mL) and $CH_2Cl_2$ (14 mL) at 0 °C. After the addition of $SO_3$·pyr complex (3.28 g, 20.5 mmol), the mixture was warmed to room temperature and stirred for 1 h. The reaction was quenched by saturated aqueous $NH_4Cl$ (30 mL), and the mixture was extracted with $Et_2O$ (2 × 50 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography provided the corresponding aldehyde (1.99 g, 90 %). $R_f = 0.51$ (hexanes/EtOAc = 8:1); $[\alpha]_D^{25} = +11.4$ ($c = 1.00$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3136$, 3072, 2931, 2858, 2717, 1738, 1589, 1471, 1390, 1113, 823, 741 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta = 9.76$ (d, $J = 1.7$ Hz, 1H), 7.65 (d, $J = 6.6$ Hz, 4H), 7.36–7.46 (m, 6H), 3.90, 3.85 (ABX, $J_{AB} = 10.3$ Hz, $J_{AX} = 4.9$ Hz, $J_{BX} = 6.4$ Hz, 2H), 2.52–2.60 (m, 1H), 1.10 (d, $J = 7.1$ Hz, 3H), 1.04 ppm (s, 9H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta = 204.7$, 135.8, 133.4, 130.1, 130.1, 128.0, 128.0, 64.4, 49.1, 27.0, 19.5, 10.6 ppm; MS (CI): $m/z$ (%) = 327 $[M+1]^+$ (4), 309 (6), 297 (2), 269 (75), 249 (100), 239 (7), 207 (23), 193 (13), 171 (19), 131 (14); HRMS (CI): $m/z$ calcd for $C_{20}H_{27}O_2Si$: 327.1780 $[M+1]^+$; found: 327.1782.

Corey–Fuchs reagent was prepared by adding a solution of $CBr_4$ (19.2 g, 57.9 mmol) in $CH_2Cl_2$ (13 mL) to a cold (0 °C) suspension of Zn powder (3.78 g, 57.9 mmol) and $Ph_3P$ (15.2 g, 57.9 mmol) in $CH_2Cl_2$ (65 mL) followed by stirring for 20 min. A solution of the aldehyde (6.30 g, 19.3 mmol) in $CH_2Cl_2$ (13 mL) was added to the mixture, which was then stirred at room temperature for 4 h and then poured into pentanes (300 mL), filtered to remove the precipitate, and concentrated to give the dibromo olefin. This crude dibromo olefin was dissolved in THF (35 mL) and cooled to −78 °C. *n*BuLi (2.5 M in hexanes, 20 mL, 50 mmol) was added to the solution, and after 1 h, the mixture was treated with saturated aqueous $NaHCO_3$ (50 mL) and extracted with $Et_2O$ (2 × 50 mL). The ether extract was concentrated, and the residue was purified by flash column chromatography (100 % hexanes) to give the corresponding alkyne (5.61 g, 94 % from the aldehyde). $R_f = 0.32$ (hexanes); $[\alpha]_D^{25} = +5.6$ ($c = 1.00$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3309$, 3070, 2935, 2858, 1635, 1469, 1427, 1388, 1257, 1110, 1014, 822, 741 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta = 7.69$–$7.73$ (m, 4H), 7.39–7.47 (m, 6H), 3.76, 3.57 (ABX, $J_{AB} = 9.7$ Hz, $J_{AX} = 5.8$ Hz, $J_{BX} = 7.7$ Hz, 2H), 2.65–2.73 (m, 1H), 2.05 (d, $J = 2.4$ Hz, 1H), 1.26 (d, $J = 7.1$ Hz, 3H), 1.09 ppm (s, 9H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta = 135.9$, 135.9, 133.8, 133.8, 129.9, 127.9, 86.8, 69.3, 67.7, 29.1, 27.1, 19.6, 17.6 ppm; MS (CI): $m/z$ (%) = 323 $[M+1]^+$ (46), 305 (4), 283 (6), 269 (62), 265 (68), 245 (100), 227 (21), 203 (16), 171 (25), 137 (17); HRMS (CI): $m/z$ calcd for $C_{21}H_{27}OSi$: 323.1831 $[M+1]^+$; found: 323.1833.

$BHBr_2{\cdot}SMe_2$ (1 M in $CH_2Cl_2$, 10.4 mL, 10.4 mmol) was added to a solution of the alkyne (2.80 g, 8.69 mmol) in $CH_2Cl_2$ (9 mL) at 0 °C. The mixture was stirred at room temperature for 2 h and cooled to 0 °C before being poured into water (15 mL) and $Et_2O$ (45 mL) at 0 °C. The mixture was stirred at room temperature for 30 min, and the organic phase was washed with water (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc = 1:1) provided boronic acid **21** (2.49 g, 80 %). $R_f = 0.45$ (hexanes/EtOAc = 1:1); $[\alpha]_D^{25} = +5.8$ ($c = 1.00$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3356$, 3070, 2962, 1727, 1631, 1589, 1469, 1389, 1122, 999, 822, 741 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta = 7.62$–$7.70$ (m, 4H), 7.31–7.43 (m, 6H), 6.95 (dd, $J = 17.9$, 6.6 Hz, 1H), 5.57 (d, $J = 17.6$ Hz, 1H), 3.64, 3.55 (ABX, $J_{AB} = 9.8$ Hz, $J_{AX} = 6.1$ Hz, $J_{BX} = 7.1$ Hz, 2H), 2.51–2.61 (m, 1H), 1.08 (d, $J = 6.8$ Hz, 3H), 1.05 ppm (s, 9H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta = 159.9$, 135.9, 134.1, 134.1, 129.9, 127.9 68.2, 42.1, 27.2, 19.6, 16.1 ppm.

*Aldehyde* ***23***

TlOEt (0.22 mL, 3.1 mmol) was added to a solution of boronic acid **21** (755 mg, 2.05 mmol), vinyl iodide **22** (744 mg, 1.86 mmol), and [Pd($PPh_3$)$_4$] (214 mg, 0.185 mmol) in degassed THF (36 mL) and water (9 mL). After being stirred for 2 h at room temperature, the mixture was diluted with hexanes/$Et_2O$ (1:1, 200 mL) and filtered through a pad of silica. The organic phase was concentrated and purified by flash column chromatography (hexanes/EtOAc = 15:1) to afford the corresponding diene (1.09 g, 99 %). $R_f = 0.65$ (hexanes/EtOAc = 8:1); $[\alpha]_D^{26} = +6.1$ ($c = 0.70$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3070$, 2954, 2931, 2858, 1658, 1589, 1469, 1427, 1377, 1254, 1111, 941, 837 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta = 7.65$ (d, $J = 7.8$ Hz, 4H), 7.33–7.44 (m, 6H), 6.25 (dd, $J = 15.2$, 10.3 Hz, 1H), 6.05 (dd, $J = 15.4$, 10.5 Hz, 1H), 5.65 (dd, $J = 15.4$, 7.3 Hz, 1H), 5.56 (dd, $J = 15.3$, 7.5 Hz, 1H), 4.36 (t, $J = 7.5$ Hz, 1H), 3.68–3.78 (m, 3H), 3.54, 3.49 (ABX, $J_{AB} = 9.8$ Hz, $J_{AX} = 6.1$ Hz, $J_{BX} = 6.6$ Hz, 2H), 2.39–2.48 (m, 1H), 1.43 (s, 3H), 1.41 (s, 3H), 1.04 (s, 9H), 1.03 (d, $J = 7.1$ Hz, 3H), 0.89 (s, 9H), 0.06 (s, 3H), 0.06 ppm (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta = 138.6$, 135.9, 135.9, 134.4, 134.1, 134.1, 129.8, 129.2, 128.2, 127.8, 109.1, 81.7, 78.9, 68.6, 62.5, 39.6, 27.4, 27.2, 27.1, 26.1, 19.5, 18.6, 16.7 ppm; MS (CI): $m/z$ (%) = 595 $[M+1]^+$ (29), 579 (9), 565 (4), 537 (100), 521 (42), 479 (28), 459 (30), 405 (35), 327 (47), 281 (64), 251 (33), 209 (45); HRMS (CI): $m/z$ calcd for $C_{35}H_{55}O_4Si_2$: 595.3639 $[M+1]^+$; found: 595.3641.

PPTS (138 mg, 0.549 mmol) was added to a solution of the diene (1.09 g, 1.83 mmol) in EtOH (7 mL). The mixture was stirred for 12 h at room temperature, and the reaction was quenched by TEA (0.2 mL). Volatiles were removed under reduced pressure, and the residue was purified by flash column chromatography (hexanes/EtOAc = 4:1) to give the corresponding alcohol (0.701 g, 80 %). $R_f = 0.65$ (hexanes/EtOAc = 2:1); $[\alpha]_D^{26} = +4.4$ ($c = 0.55$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3471$, 3070, 2958, 2931, 2858, 1658, 1589, 1469, 1427, 1377, 1242, 1111, 991 $cm^{-1}$; $^1H$ NMR (500 MHz,

$CDCl_3$): $\delta = 7.64$ (d, $J = 8.1$ Hz, 4H), 7.31–7.45 (m, 6H), 6.28 (dd, $J = 15.2$, 10.5 Hz, 1H), 6.05 (dd, $J = 15.4$, 10.5 Hz, 1H), 5.68 (dd, $J = 15.2$, 7.3 Hz, 1H), 5.53 (dd, $J = 15.2$, 7.8 Hz, 1H), 4.35 (t, $J = 8.3$ Hz, 1H), 3.80–3.85 (m, 1H), 3.78 (dt, $J = 8.4$, 3.2 Hz, 1H), 3.55–3.61 (m, 1H), 3.46–3.55 (m, 2H), 2.40–2.48 (m, 1H), 1.88 (dd, $J = 8.3$, 4.4 Hz, 1H), 1.45 (s, 3H), 1.44 (s, 3H), 1.04 (s, 9H), 1.03 ppm (d, $J = 6.8$ Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 139.1$, 135.6, 135.2, 133.8, 129.6, 128.7, 127.6, 127.0, 109.1, 81.2, 77.9, 68.3, 60.7, 39.4, 27.1, 27.0, 26.9, 19.3, 16.4 ppm; MS (CI): $m/z$ (%) = 479 $[M-1]^+$ (20), 463 (93), 423 (39), 405 (100), 365 (31), 345 (51), 335 (21), 315 (31), 287 (24), 267 (33), 209 (95), 167 (37); HRMS (CI): $m/z$ calcd for $C_{29}H_{39}O_4Si$: 479.2617 $[M-1]^+$; found: 479.2615.

TEA (0.29 mL, 2.1 mmol) was added to a solution of the alcohol (200 mg, 0.416 mmol) in DMSO (1 mL) and $CH_2Cl_2$ (1 mL) at 0 °C. After the addition of $SO_3$·pyr complex (196 mg, 1.23 mmol), the mixture was warmed to room temperature and stirred for 1 h. The reaction was quenched by saturated aqueous $NH_4Cl$ (5 mL), and the reaction mixture was extracted with $Et_2O$ (2×10 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography provided aldehyde **23** (119 mg, 60%). $R_f = 0.51$ (hexanes/EtOAc = 8:1); $[\alpha]_D^{27} = +11.7$ ($c$ 0.60, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3136$, 3070, 2958, 2931, 2715, 1889, 1824, 1736, 1658, 1589, 1469, 1381, 1219, 1111, 991 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 9.72$ (d, $J = 2.0$ Hz, 1H), 7.58–7.68 (m, 4H), 7.34–7.45 (m, 6H), 6.29 (dd, $J = 15.2$, 10.5 Hz, 1H), 6.05 (dd, $J = 15.3$, 10.4 Hz, 1H), 5.71 (dd, $J = 15.4$, 7.3 Hz, 1H), 5.58 (dd, $J = 15.2$, 7.3 Hz, 1H), 4.51 (t, $J = 7.7$ Hz, 1H), 4.06 (dd, $J = 7.8$, 2.0 Hz, 1H), 3.47–3.56 (m, 2H), 2.39–2.48 (m, 1H), 1.50 (s, 3H), 1.46 (s, 3H), 1.05 (s, 9H), 1.03 ppm (d, $J = 6.9$ Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 199.7$, 139.8, 135.6, 135.1, 133.8, 129.6, 128.3, 127.6, 125.8, 111.3, 84.7, 77.8, 68.3, 39.3, 26.9, 26.8, 26.2, 19.3, 16.3 ppm; MS (CI): $m/z$ (%) = 479 $[M+1]^+$ (5), 463 (2), 421 (59), 401 (22), 379 (17), 363 (24), 343 (29), 301 (10), 269 (40), 223 (34), 165 (58), 135 (39), 101 (100); HRMS (CI): $m/z$ calcd for $C_{29}H_{39}O_4Si$: 479.2617 $[M+1]^+$; found: 479.2619.

*Aldehyde **28***

Molecular sieves (3 Å, 4 g) were added to a solution of diol **27** (9.49 g, 31.8 mmol) in $CH_2Cl_2$ (636 mL) at 0 °C. The mixture was stirred at the same temperature for 30 min, followed by addition of DDQ (10.8 g, 47.7 mmol). After being stirred for 3 h at 0 °C, the reaction mixture was filtered through a short pad of silica. The filtrate was washed with saturated aqueous $NaHCO_3$ (2×100 mL) and brine (50 mL), dried over $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (hexanes/EtOAc = 4:1) yielded the corresponding acetal ester (8.69 g, 94%). $R_f = 0.25$ (hexanes/EtOAc = 2:1); $[\alpha]_D^{18} = +32.9$ ($c = 0.85$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3502$, 2972, 2933, 2854, 2708, 1745, 1614, 1518, 1302, 1246, 1030, 831 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 7.35$ (d, $J = 8.8$ Hz, 2H), 6.87 (d, $J = 8.8$ Hz, 2H), 5.49 (s, 1H), 4.22–4.35 (m, 4H), 4.16 (dd, $J = 8.8$, 2.4 Hz, 1H), 3.99 (td, $J = 12.0$, 2.2 Hz, 1H), 3.80 (s, 3H), 3.01 (d, $J = 8.8$ Hz, 1H), 2.30 (qd, $J = 12.6$, 5.1 Hz, 1H), 1.49 (d, $J = 13.4$ Hz, 1H), 1.30 ppm (t, $J = 7.34$ Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 172.4$, 160.1, 130.9, 127.4, 113.7, 101.1, 77.1, 73.4, 66.8, 62.0, 55.5, 26.5, 14.5 ppm; MS (CI): $m/z$ (%) = 297 $[M+1]^+$ (100), 267 (2), 223 (3), 193 (30), 161 (61), 137 (38), 87 (7); HRMS (CI): $m/z$ calcd for $C_{15}H_{21}O_6$: 297.1338 $[M+1]^+$; found: 297.1337.

DMAP (4.28 g, 35.0 mmol) and DIPEA (19.9 mL, 115 mmol) were added to a solution of the acetal (11.3 g, 38.1 mmol) in $CH_2Cl_2$ (760 mL) at 0 °C. MOMCl (7.2 mL, 95 mmol) was slowly added to the mixture, which was heated under reflux for 10 h before the reaction was quenched by saturated aqueous $NH_4Cl$ (500 mL). The aqueous phase was extracted with $Et_2O$ (400 mL), and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc = 4:1) provided the corresponding MOM ether (12.4 g, 95%). $R_f = 0.25$ (hexanes/EtOAc = 2:1); $[\alpha]_D^{16} = +40.8$ ($c = 1.93$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 2964$, 2935, 2898, 2840, 1747, 1616, 1587, 1518, 1466, 1250, 1109, 1032, 829 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 7.38$ (d, $J = 8.8$ Hz, 2H), 6.86 (d, $J = 8.8$ Hz, 2H), 5.48 (s, 1H), 4.75 (s, 2H), 4.21–4.32 (m, 5H), 3.97 (td, $J = 12.0$, 2.5 Hz, 1H), 3.78 (s, 3H), 3.39 (s, 3H), 2.13 (qd, $J = 12.7$, 5.1 Hz, 1H), 1.45 (br d, $J = 11.7$ Hz, 1H), 1.29 ppm (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 170.2$, 160.1, 131.1, 127.6, 113.7, 101.5, 96.8, 77.9, 77.5, 66.7, 61.4, 56.3, 55.5, 26.7, 14.5 ppm; MS (EI): $m/z$ (%) = 340 $[M]^+$ (23), 309 (4), 295 (11), 278 (3), 262 (1), 221 (2), 193 (100), 152 (19), 135 (54), 121 (21), 109 (5); HRMS (EI): $m/z$ calcd for $C_{17}H_{24}O_7$: 340.1522 $[M]^+$; found: 340.1524.

DIBAL (1 M in hexanes, 110 mL, 110 mmol) was added dropwise to a solution of the MOM ether ester (7.49 g, 22.0 mmol) in $CH_2Cl_2$ (110 mL) at −78 °C. After 2 h, MeOH was carefully added at −78 °C until the reaction mixture stopped foaming. The mixture was warmed to room temperature, diluted with $Et_2O$ (100 mL), and washed with saturated aqueous $NH_4Cl$ (50 mL) and $NaHCO_3$ (50 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc = 2:1) provided aldehyde **28** (4.91 g, 75%) as a white solid. $R_f = 0.23$ (hexanes/EtOAc = 1:1); $[\alpha]_D^{23} = +15.4$ ($c = 1.25$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 2958$, 2868, 1736, 1614, 1587, 1516, 1464, 1362, 1302, 1250, 1153, 1105, 1034 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 9.80$ (d, $J = 1.2$ Hz, 1H), 7.37 (d, $J = 8.8$ Hz, 2H), 6.87 (d, $J = 8.8$ Hz, 2H), 5.47 (s, 1H), 4.80, 4.77 (ABq, $J_{AB} = 6.9$ Hz, 2H), 4.28–4.37 (m, 2H), 4.08 (d, $J = 4.4$ Hz, 1H), 3.98 (td, $J = 12.0$, 2.4 Hz, 1H), 3.80 (s, 3H), 3.43 (s, 3H), 2.14 (qd, $J = 12.4$, 5.1 Hz, 1H), 1.54 ppm (dd, $J = 13.5$, 1.5 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 202.3$, 160.2, 130.8, 127.6, 113.8, 101.7, 97.4, 83.1, 77.2, 66.8, 56.4, 55.5, 26.8 ppm; MS (EI): $m/z$ (%) = 296 $[M]^+$ (32), 265 (6), 251 (5), 223 (3), 193 (100), 181 (5), 152 (6), 135 (79), 109 (15), 77 (12), 57 (9); HRMS (EI): $m/z$ calcd for $C_{15}H_{20}O_6$: 296.1260 $[M]^+$; found: 296.1265.

*Homoallylic Alcohol **29***

Powdered 4-Å molecular sieves (2 g) were poured into dry toluene (80 mL), and the mixture was cooled to −78 °C followed by the addition of boronate **14** (11 g, 35 mmol). A solution of aldehyde **28** (6.99 g, 23.6 mmol) in dry toluene (100 mL) was added dropwise to the mixture, which was then stirred for 36 h at −78 °C. NaOH (2 N, 40 mL) was added to hydrolyze DIPT, and the two-phase mixture was warmed to 0 °C and stirred for 1 h before being filtered through a pad of celite. The aqueous phase was extracted with $Et_2O$ (4×30 mL). The combined organic extracts were dried over $K_2CO_3$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc = 3:1) provided the homoallylic alcohol **29** (7.16 g, 86%, d.r. = 16:1) as a white solid. $R_f = 0.45$ (hexanes/EtOAc = 1:1); $[\alpha]_D^{18} = -5.6$ ($c = 0.60$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3435$, 3080, 2925, 1614, 1589, 1518, 1464, 1373, 1304, 1250, 1173, 1144, 1101 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 7.40$ (d, $J = 8.8$ Hz, 2H), 6.89 (d, $J = 8.6$ Hz, 2H), 5.86 (ddd, $J = 12.7$, 10.2, 8.6 Hz, 1H), 5.49 (s, 1H), 5.16 (d, $J = 9.5$ Hz, 1H), 5.13 (d, $J = 2.4$ Hz, 1H), 4.93, 4.78 (ABq, $J_{AB} = 6.7$ Hz, 1H), 4.30 (dd, $J = 11.5$, 4.4 Hz, 1H), 4.18–4.24 (m, 1H), 3.96 (td, $J = 12.0$, 2.5 Hz, 1H), 3.81 (s, 3H), 3.66 (dd, $J = 6.2$, 3.1 Hz, 1H), 3.47–3.53 (m, 1H), 3.43 (s, 3H), 2.48–2.57 (m, 1H), 2.35 (d, $J = 5.6$ Hz, 1H), 1.96 (qd, $J = 12.3$, 5.0 Hz, 1H), 1.59 (dd, $J = 13.0$, 1.2 Hz, 1H), 1.10 ppm (d, $J = 6.8$ Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 160.1$, 140.9, 131.4, 127.5, 116.3, 113.8, 101.4, 98.6, 80.3, 79.0, 73.4, 66.9, 56.5, 55.5, 41.4, 27.4, 16.9 ppm; MS (CI): $m/z$ (%) = 353 $[M+1]^+$ (100), 321 (69), 297 (28), 265 (3), 245 (4), 193 (75), 181 (43), 155 (11), 137 (32), 99 (5), 87(5); HRMS (CI): $m/z$ calcd for $C_{19}H_{29}O_6$: 353.1964 $[M+1]^+$; found: 353.1966.

*Diol **30***

Collidine (3.40 mL, 25.6 mmol) was added to a solution of homoallylic alcohol **29** (4.50 g, 12.8 mmol) in $CH_2Cl_2$ (25 mL). After the mixture was cooled to 0 °C, TIPSOTf (4.20 mL, 15.6 mmol) was added dropwise, and the resulting mixture was warmed to room temperature. The reaction was completed within 2 h and quenched by saturated aqueous $NH_4Cl$ (10 mL). The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc = 6:1) provided the TIPS ether (6.43 g, 99%). $R_f = 0.55$ (hexanes/EtOAc = 4:1); $[\alpha]_D^{16} = +11.2$ ($c = 0.89$, $CHCl_3$); IR (neat): $\tilde{\nu}_{max} = 3074$, 2943, 2893, 2866, 1616, 1518, 1464, 1250, 1171, 1103, 1038, 916, 827 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 7.41$ (d, $J = 8.8$ Hz, 2H), 6.88 (d, $J = 8.8$ Hz, 2H), 6.02 (ddd, $J = 17.5$, 10.3, 7.6 Hz, 1H), 5.45 (s, 1H), 5.06 (d, $J = 17.4$ Hz, 1H), 5.00 (d, $J = 10.3$ Hz, 1H), 4.77, 4.75 (ABq, $J_{AB} = 7.0$ Hz, 2H), 4.24 (dd, $J = 11.4$, 3.8 Hz, 1H), 4.10–4.15 (m, 2H), 3.90 (td, $J = 12.5$, 2.2 Hz, 1H), 3.81 (s, 3H), 3.61 (t, $J = 5.5$ Hz, 1H), 3.39 (s, 3H), 2.65–2.73

(m, 1H), 2.08 (qd, $J$=12.5, 4.9 Hz, 1H), 1.61 (dd, $J$=13.3, 1.3 Hz, 1H), 1.17 (d, $J$=7.1 Hz, 3H), 1.12 ppm (s, 21H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=160.0, 141.7, 131.7, 127.5, 114.3, 113.6, 101.3, 98.6, 82.1, 77.4, 76.8, 67.1, 56.1, 55.5, 41.2, 28.5, 18.6, 18.5, 17.9, 13.4 ppm; MS (CI): $m/z$ (%)= 509 $[M+1]^+$ (35), 477 (83), 465 (20), 431 (3), 373 (11), 329 (100), 311 (19), 297 (8), 267 (7), 241 (45), 181 (46); HRMS (CI): $m/z$ calcd for $C_{28}H_{49}O_6Si$: 509.3298 $[M+1]^+$; found: 509.3296.

CAN (17.0 g, 31.0 mmol) was added to a solution of the TIPS ether (5.18 g, 10.2 mmol) in $CH_3CN$ (500 mL) and water (55 mL) at 0 °C. The reaction mixture was stirred for 2 h at the same temperature and treated with saturated aqueous $NaHCO_3$ (100 mL). TEA (5 mL) was added to prevent acetal formation, and the mixture was diluted with $Et_2O$ (500 mL). The organic phase was washed with brine (100 mL), dried over $Na_2SO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc=4:1) provided diol **30** (3.68 g, 92%). $R_f$=0.21 (hexanes/EtOAc=2:1); $[\alpha]_D^{16}$=+29.2 ($c$=1.11, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3419, 3076, 2945, 2893, 2868, 1639, 1464, 1385, 1254, 1213, 1151, 1099, 1038 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=6.02 (ddd, $J$=17.5, 10.3, 7.6 Hz, 1H), 5.04–5.10 (m, 2H), 4.78, 4.72 (ABq, $J_{AB}$=6.9 Hz, 2H), 4.05 (dd, $J$=5.5, 3.5 Hz, 1H), 3.98–4.03 (m, 1H), 3.78–3.86 (m, 2H), 3.42 (s, 3H), 2.84 (d, $J$=5.9 Hz, 1H), 2.67 (dd, $J$=6.8, 4.2 Hz, 1H), 2.58–2.63 (m, 1H), 1.75–1.88 (m, 2H), 1.14 (d, $J$=7.1 Hz, 3H), 1.10 ppm (s, 21H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=141.3, 115.1, 98.4, 83.8, 76.5, 70.5, 61.9, 56.2, 41.1, 36.6, 18.5, 17.9, 13.4 ppm; MS (CI): $m/z$ (%)=391 $[M+1]^+$ (12), 371 (4), 359 (100), 341 (2), 315 (9), 285 (19), 273 (7), 241 (16), 229 (12), 185 (38), 155 (37); HRMS (CI): $m/z$ calcd for $C_{20}H_{43}O_5Si$: 391.2880 $[M+1]^+$; found: 391.2881.

*Iodide **31***

A solution of diol **30** (8.65 g, 22.1 mmol) and TEA (6.20 mL, 44.4 mmol) in $CH_2Cl_2$ (200 mL) was treated with *p*-toluenesulfonyl chloride (5.06 g, 26.6 mmol). The mixture was stirred at 0 °C for 6 h, and the reaction was quenched by saturated aqueous $NH_4Cl$ (100 mL). The reaction mixture was extracted with $Et_2O$ (2×50 mL), dried over $MgSO_4$, filtered, and concentrated, and the crude products were separated by flash column chromatography (hexanes/EtOAc=6:1) to give the corresponding tosylate (12.0 g, 99%). $R_f$=0.22 (hexanes/EtOAc=8:1); $[\alpha]_D^{19}$=+9.4 ($c$=3.60, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3543, 3070, 2945, 2893, 2868, 2725, 1638, 1599, 1464, 1362, 1176, 1038, 918, 814, 663 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=7.79 (d, $J$=8.3 Hz, 2H), 7.33 (d, $J$=8.3 Hz, 2H), 5.96 (ddd, $J$=17.5, 10.3, 7.5 Hz, 1H), 5.04 (d, $J$=12.5 Hz, 1H), 5.02 (d, $J$=5.4 Hz, 1H), 4.74, 4.65 (ABq, $J_{AB}$=6.9 Hz, 2H), 4.15–4.25 (m, 2H), 4.02 (dd, $J$=5.9, 3.4 Hz, 1H), 3.77–3.85 (m, 1H), 3.36 (s, 3H), 3.31 (dd, $J$=5.9, 3.4 Hz, 1H), 2.52–2.59 (m, 1H), 2.44 (s, 3H), 2.34 (d, $J$=7.1 Hz, 1H), 1.90–1.97 (m, 1H), 1.79–1.86 (m, 1H), 1.11 (d, $J$=6.8 Hz, 3H), 1.08 ppm (s, 21H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=144.8, 141.0, 133.6, 130.0, 128.1, 115.2, 98.4, 83.2, 76.4, 68.1, 66.1, 56.2, 41.1, 34.4, 21.8, 18.5, 18.4, 17.5, 13.3 ppm; MS (FAB): $m/z$ (%)=545 $[M+1]^+$ (14), 513 (53), 469 (16), 439 (6), 285 (80), 241 (50), 229 (29), 157 (69), 137 (100), 99 (62), 45 (82); HRMS (FAB): $m/z$ calcd for $C_{27}H_{49}O_7SSi$: 545.2968 $[M+1]^+$; found: 545.2953.

Ethyl propiolate (2.60 mL, 25.6 mmol) and *N*-methylmorpholine (0.56 mL, 5.1 mmol) were added to a solution of the tosylate (9.30 g, 17.1 mmol) in $CH_2Cl_2$ (17 mL). The reaction mixture was stirred for 12 h and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc=8:1) to give the corresponding β-alkoxyacrylate (10.57 g, 96%). $R_f$=0.44 (hexanes/EtOAc=8:1); $[\alpha]_D^{19}$=−3.4 ($c$=3.95, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3080, 2945, 2868, 1711, 1639, 1599, 1464, 1367, 1284, 1178, 1132, 1099, 1039, 964 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=7.77 (d, $J$=8.3 Hz, 2H), 7.32–7.36 (m, 3H), 5.89 (ddd, $J$=17.6, 10.0, 8.1 Hz, 1H), 5.17 (d, $J$=12.2 Hz, 1H), 5.04 (d, $J$=17.4 Hz, 1H), 5.00 (d, $J$=10.3 Hz, 1H), 4.63, 4.56 (ABq, $J_{AB}$=6.9 Hz, 2H), 4.20–4.25 (m, 1H), 4.17 (q, $J$=7.1 Hz, 2H), 4.10–4.15 (m, 1H), 3.94–4.01 (m, 2H), 3.50 (t, $J$=6.0 Hz, 1H), 3.31 (s, 3H), 2.50–2.57 (m, 1H), 2.44 (s, 3H), 2.33–2.41 (m, 1H), 1.79–1.88 (m, 1H), 1.29 (t, $J$=7.2 Hz, 3H), 1.11 (d, $J$=6.8 Hz, 3H), 1.07 ppm (s, 21H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=168.0, 163.3, 145.1, 140.5, 133.0, 130.1, 128.1, 115.7, 98.7, 97.6, 82.1, 80.7, 76.6, 66.5, 60.0, 56.1, 40.8, 30.9, 21.9, 18.5, 18.5, 14.6, 13.3 ppm; MS (FAB): $m/z$ (%)=643 $[M+1]^+$ (7), 611 (7), 599 (3), 511 (2), 465 (11), 439 (13), 383 (15), 311 (13), 285 (79), 241 (74), 157 (100); HRMS (FAB): $m/z$ calcd for $C_{32}H_{55}O_9SSi$: 643.3336 $[M+1]^+$; found: 643.3328.

NaI (3.92 g, 26.2 mmol) was added to a solution of the β-alkoxyacrylate (8.41 g, 13.1 mmol) in acetone (260 mL), and the mixture was heated under reflux for 3 h. The reaction was quenched by water (50 mL), and the reaction mixture was extracted with $Et_2O$ (2×100 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated, and the crude products were purified by flash column chromatography (hexanes/EtOAc=11:1) to give iodide **31** (7.31 g, 93%). $R_f$=0.44 (hexanes/EtOAc=8:1); $[\alpha]_D^{24}$=−4.5 ($c$=9.40, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3076, 2945, 2897, 2868, 1712, 1643, 1463, 1369, 1282, 1132, 1039, 918, 831 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=7.51 (d, $J$=12.2 Hz, 1H), 5.94 (ddd, $J$=17.5, 10.1, 7.6 Hz, 1H), 5.29 (d, $J$=12.2 Hz, 1H), 5.11 (d, $J$=17.4 Hz, 1H), 5.08 (d, $J$=10.5 Hz, 1H), 4.69, 4.60 (ABq, $J_{AB}$=7.1 Hz, 2H), 4.20–4.25 (m, 1H), 4.16 (q, $J$=7.0 Hz, 2H), 4.02 (dd, $J$=5.9, 3.7 Hz, 1H), 3.56 (t, $J$=5.9 Hz, 1H), 3.37 (s, 3H), 3.21–3.25 (m, 1H), 3.08–3.14 (m, 1H), 2.56–2.63 (m, 1H), 2.40–2.48 (m, 1H), 2.05–2.13 (m, 1H), 1.28 (t, $J$=7.1 Hz, 3H), 1.15 (d, $J$=7.1 Hz, 3H), 1.11 ppm (s, 21H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=167.2, 162.6, 139.8, 114.6, 97.7, 96.8, 83.7, 80.4, 75.6, 59.0, 55.3, 40.1, 34.2, 17.6, 17.5, 17.0, 13.7, 12.4 ppm; MS (FAB): $m/z$ (%)=599 $[M+1]^+$ (8), 567 (15), 555 (5), 537 (2), 499 (1), 395 (32), 311 (21), 241 (92), 229 (22), 197 (17), 157 (100), 115 (71); HRMS (FAB): $m/z$ calcd for $C_{25}H_{48}O_6SiI$: 599.2265 $[M+1]^+$; found: 599.2265.

*Ester **32***

TTMSS (3.30 mL, 10.7 mmol) was added to a solution of iodide **31** (4.92 g, 8.23 mmol) in toluene at −20 °C, followed by the addition of $Et_3B$ (1 M in toluene, 12.3 mL, 12.3 mmol). After 1 h, the reaction mixture was quickly filtered through a pad of silica gel. The silica-gel pad was rinsed with $Et_2O$ (150 mL). The combined organic extracts were concentrated, and the residue was purified by flash column chromatography (hexanes/EtOAc=25:1) to give ester **32** (3.58 g, 92%). $R_f$=0.42 (hexanes/EtOAc=8:1); $[\alpha]_D^{17}$=+10.0 ($c$=0.57, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3074, 2945, 2868, 1738, 1639, 1464, 1383, 1192, 1151, 1099, 1038, 916, 679 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=5.98 (ddd, $J$=17.5, 10.1, 7.8 Hz, 1H), 5.01 (d, $J$=17.4 Hz, 1H), 4.97 (d, $J$=10.3 Hz, 1H), 4.73, 4.72 (ABq, $J_{AB}$=6.9 Hz, 2H), 4.23 (quint, $J$=6.7 Hz, 1H), 4.09–4.15 (m, 3H), 3.98 (t, $J$=4.8 Hz, 1H), 3.47 (t, $J$=5.5 Hz, 1H), 3.38 (s, 3H), 2.63, 2.43 (ABX, $J_{AB}$=15.0 Hz, $J_{AX}$=6.7 Hz, $J_{BX}$=6.7 Hz, 2H), 2.55–2.60 (m, 1H), 1.99–2.07 (m, 1H), 1.90–1.99 (m, 2H), 1.57–1.65 (m, 1H), 1.25 (t, $J$=7.2 Hz, 3H), 1.08–1.13 ppm (m, 24H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=171.7, 141.8, 114.3, 98.1, 82.9, 79.2, 77.0, 75.4, 60.6, 56.1, 41.3, 41.3, 31.7, 28.0, 18.6, 18.5, 18.5, 18.2, 14.4, 13.4 ppm; MS (CI): $m/z$ (%)=473 $[M+1]^+$ (5), 455 (1), 441 (100), 411 (20), 397 (20), 367 (12), 299 (8), 267 (42), 237 (57), 219 (10), 157 (79), 131 (5); HRMS (CI): $m/z$ calcd for $C_{25}H_{49}O_6Si$: 473.3298 $[M+1]^+$; found: 473.3294.

*Alkyne **34***

A solution of 2-methyl-2-butene (1.90 mL, 18.0 mmol) in THF (5 mL) was cooled to 0 °C, and borane/THF complex (1 M in hexanes, 8.80 mL, 8.80 mmol) was added. After 1 h at 0 °C, the solution of disiamylborane was added by cannula to a solution of ester **32** (2.10 g, 4.44 mmol) in THF (2 mL) at 0 °C over 15 min. The resulting solution was stirred at 0 °C for 3 h and poured into water (37 mL). Sodium perborate tetrahydrate (1.35 g, 8.77 mmol) was then added, and the white suspension was stirred vigorously for 1 h at room temperature. The mixture was extracted with $Et_2O$ (3×20 mL), dried over $Na_2SO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc=2:1) provided the corresponding alcohol (2.00 g, 92%). $R_f$=0.18 (hexanes/EtOAc=4:1); $[\alpha]_D^{19}$=+8.1 ($c$=3.05, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3454, 2945, 2891, 2868, 1738, 1464, 1383, 1300, 1196, 1151, 1039, 883, 679 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=4.74, 4.68 (ABq, $J_{AB}$=6.9 Hz, 2H), 4.29 (quint, $J$=6.6 Hz, 1H), 4.25 (td, $J$=7.5, 3.2 Hz, 1H), 4.10–4.17 (m, 2H), 3.96 (dd, $J$=5.1, 3.2 Hz, 1H), 3.68–3.75 (m, 1H), 3.54–3.61 (m, 1H), 3.45 (dd, $J$=5.1, 2.9 Hz, 1H), 3.39 (s, 3H), 2.67, 2.46 (ABX, $J_{AB}$=15.4 Hz, $J_{AX}$=6.9 Hz, $J_{BX}$=6.6 Hz, 2H), 2.31 (t, $J$=5.3 Hz, 1H), 2.01–2.11 (m, 2H), 1.90–1.98 (m, 3H), 1.59–1.68 (m, 1H), 1.31–1.40 (m, 1H), 1.25 (t, $J$=

7.1 Hz, 3H), 1.09 (s, 21H), 1.03 ppm (d, $J$=6.8 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=171.7, 98.0, 82.1, 77.3, 77.0, 75.9, 61.4, 60.6, 56.1, 40.8, 35.2, 31.5, 31.2, 28.6, 19.1, 18.5, 14.4, 13.2 ppm; MS (FAB): $m/z$ (%)=491 $[M+1]^+$ (1), 460 (2), 447 (1), 415 (3), 385 (3), 307 (24), 289 (14), 255 (9), 154 (100), 136 (69), 107 (22), 85 (18); HRMS (FAB): $m/z$ calcd for $C_{25}H_{51}O_7Si$: 491.3404 $[M+1]^+$; found: 491.3398.

Dess–Martin periodinane (2.12 g, 5.00 mmol) was added to a solution of the alcohol (1.23 g, 2.51 mmol) and pyridine (0.81 mL, 10 mmol) in $CH_2Cl_2$ (25 mL) at 0°C. The reaction mixture was warmed to room temperature, stirred for 3 h, and then treated with saturated aqueous $Na_2S_2O_3$ (10 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc=8:1) provided the corresponding aldehyde (1.16 g, 95%). $R_f$=0.45 (hexanes/EtOAc=4:1); $[\alpha]_D^{19}=-8.0$ ($c$=1.23, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=2945, 2893, 2868, 2715, 1732, 1464, 1383, 1300, 1194, 1151, 1039, 883, 679 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=9.71 (d, $J$=2.4 Hz, 1H), 4.72, 4.69 (ABq, $J_{AB}$=6.9 Hz, 2H), 4.20–4.29 (m, 2H), 4.08–4.16 (m, 2H), 3.94 (t, $J$=4.4 Hz, 1H), 3.47 (t, $J$=3.7 Hz, 1H), 3.39 (s, 3H), 2.87 (dd, $J$=16.6, 3.4 Hz, 1H), 2.64, 2.45 (ABX, $J_{AB}$=15.4 Hz, $J_{AX}$=6.9 Hz, $J_{AB}$=6.5 Hz, 2H), 2.54–2.61 (m, 1H), 2.14 (ddd, $J$=16.7, 9.5, 3.2 Hz, 1H), 2.00–2.08 (m, 1H), 1.88–2.00 (m, 2H), 1.59–1.68 (m, 1H), 1.25 (t, $J$=7.2 Hz, 3H), 1.09 (s, 21H), 1.05 ppm (d, $J$=7.1 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=204.0, 171.6, 97.9, 82.3, 77.0, 76.7, 75.9, 60.6, 56.1, 47.5, 40.9, 31.3, 30.1, 28.5, 19.4, 18.4, 18.4, 14.4, 13.1 ppm; MS (CI): $m/z$ (%)=489 $[M+1]^+$ (2), 457 (30), 427 (67), 413 (42), 383 (21), 283 (39), 265 (23), 253 (100), 235 (16), 157 (38), 111 (8), 59 (2); HRMS (CI): $m/z$ calcd for $C_{25}H_{49}O_7Si$: 489.3248 $[M+1]^+$; found: 489.3241.

A solution of dimethyl 1-diazo-2-oxopropylphosphonate (**33**; 263 mg, 1.37 mmol) in EtOH (2.4 mL) was added slowly to a solution of the aldehyde (268 mg, 0.548 mmol) and $Cs_2CO_3$ (536 mg, 1.64 mmol) in EtOH (7.2 mL) at 0°C. The reaction mixture was stirred for 1 h at room temperature, diluted with $Et_2O$ (15 mL), and treated with saturated aqueous $NH_4Cl$ (5 mL). The mixture was extracted with $Et_2O$ (2×10 mL), and the organic extracts were washed with brine (10 mL) and dried over $Na_2SO_4$. After filtration and evaporation, flash column chromatography (hexanes/EtOAc=10:1) provided alkyne **34** (252 mg, 95%). $R_f$=0.54 (hexanes/EtOAc=8:1); $[\alpha]_D^{24}=+17.8$ ($c$=0.58, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3311, 2945, 2891, 2868, 1738, 1464, 1385, 1300, 1190, 1151, 1038, 883, 679 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=4.72, 4.70 (ABq, $J$=6.6 Hz, 2H), 4.26 (quint, $J$=6.7 Hz, 1H), 4.09–4.20 (m, 3H), 3.91 (dd, $J$=6.2, 4.3 Hz, 1H), 3.53 (t, $J$=4.5 Hz, 1H), 3.39 (s, 3H), 2.66, 2.45 (ABX, $J_{AB}$=15.2 Hz, $J_{AX}$=6.6 Hz, $J_{BX}$=6.9 Hz, 2H), 2.52 (m, 1H), 2.09–2.16 (m, 1H), 2.01–2.10 (m, 2H), 1.91–1.99 (m, 3H), 1.58–1.67 (m, 1H), 1.25 (t, $J$=7.1 Hz, 3H), 1.15 (d, $J$=6.6 Hz, 3H), 1.06–1.11 ppm (m, 21H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=171.6, 97.7, 84.4, 82.7, 78.5, 76.2, 75.7, 69.3, 60.6, 56.0, 41.2, 36.3, 31.4, 28.3, 22.7, 18.5, 17.1, 14.4, 13.3 ppm; MS (CI): $m/z$ (%)=483 $[M-1]^+$ (2), 453 (61), 441 (31), 423 (8), 409 (15), 391 (4), 343 (4), 279 (40), 249 (100), 157 (31), 145 (6), 111 (2); HRMS (CI): $m/z$ calcd for $C_{26}H_{47}O_6Si$: 483.3142 $[M-1]^+$; found: 483.3145.

*Triene **36***

Grubbs second-generation catalyst (25 mg, 0.030 mmol) was added to a solution of alkyne **34** (143 mg, 0.295 mmol) in $CH_2Cl_2$ (1.5 mL), and the mixture was stirred under ethylene atmosphere. The reaction, monitored by TLC, was completed within 3 h at room temperature. After removal of the ethylene balloon, 2-methyl-1,4-pentadiene (**35**; 0.35 mL, 3.0 mmol) was added to the mixture, and the reaction vial was sealed and heated to 40°C. Another portion of **35** (0.35 mL, 3.0 mmol) was added to the mixture after 4 h, and the reaction mixture was further stirred for 20 h. Volatiles were removed under reduced pressure, and the residue was purified by flash column chromatography (benzene/EtOAc=100:1) to give triene **36** (102 mg, 65%) along with diene **37** (29.0 mg, 19%). $R_f$=0.56 (pentanes/$Et_2O$=4:1); $[\alpha]_D^{20}=+3.6$ ($c$=1.12, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3076, 2945, 2891, 2868, 1738, 1651, 1604, 1464, 1383, 1298, 1186, 1151, 1038, 885, 679 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=6.06 (d, $J$=15.9 Hz, 1H), 5.74 (dt, $J$=15.9, 7.1 Hz, 1H), 4.98 (d, $J$=1.7 Hz, 1H), 4.87 (s, 1H), 4.74 (s, 3H), 4.71 (s, 1H), 4.25 (quint, $J$=6.6 Hz, 1H), 4.08–4.17 (m, 3H), 3.89 (dd, $J$=6.4, 4.4 Hz, 1H), 3.58 (dd, $J$=5.9, 4.2 Hz, 1H), 3.40 (s, 3H), 2.78 (br d, $J$=6.8 Hz, 2H), 2.75 (br s, 1H), 2.65, 2.44 (ABX, $J_{AB}$=15.0 Hz, $J_{AX}$=6.5 Hz, $J_{BX}$=7.0 Hz, 2H), 1.97–2.10 (m, 3H), 1.91–1.97 (m, 1H), 1.86 (dd, $J$=11.3, 11.1 Hz, 1H), 1.72 (s, 3H), 1.60–1.67 (m, 1H), 1.26 (t, $J$=7.1 Hz, 3H), 1.08–1.15 (m, 21H), 0.95 ppm (d, $J$=6.6 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=171.5, 145.1, 144.7, 133.8, 128.0, 115.5, 110.9, 97.8, 83.0, 79.4, 77.7, 75.4, 60.5, 55.9, 41.6, 41.3, 36.5, 35.3, 31.5, 28.1, 22.6, 18.6, 18.5, 16.5, 14.4, 13.3 ppm; MS (CI): $m/z$ (%)=565 $[M-1]^+$ (2), 535 (13), 523 (30), 491 (10), 479 (2), 361 (100), 331 (45), 299 (5), 187 (28), 175 (15), 157 (76), 131 (5); HRMS (CI): $m/z$ calcd for $C_{32}H_{57}O_6Si$: 565.3924 $[M-1]^+$; found: 565.3924

*Sulfone **38***

DIBAL (1 M in toluene, 1.40 mL, 1.40 mmol) was added dropwise to a solution of triene **36** (276 mg, 0.471 mmol) in THF (2.5 mL) at −78°C. After 1 h, MeOH was carefully added to the reaction mixture at −78°C until foaming stopped. The mixture was warmed to room temperature, diluted with $Et_2O$ (100 mL), and washed with saturated aqueous $NH_4Cl$ (50 mL) and $NaHCO_3$ (50 mL), and the organic phase was dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc=4:1) provided the corresponding aldehyde (236 mg, 96%). $R_f$=0.27 (hexanes/EtOAc=2:1); $[\alpha]_D^{20}=+3.2$ ($c$=0.78, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3076, 2945, 2893, 2868, 2725, 2360, 1728, 1651, 1604, 1464, 1385, 1215, 1151, 1039, 883, 679 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=9.80 (t, $J$=2.2 Hz, 1H), 6.06 (d, $J$=15.9 Hz, 1H), 5.72 (dt, $J$=14.7, 7.6 Hz, 1H), 4.97 (d, $J$=1.7 Hz, 1H), 4.86 (s, 1H), 4.75, 4.69 (ABq, $J_{AB}$=6.9 Hz, 2H), 4.73 (s, 1H), 4.70 (s, 1H), 4.29 (quint, $J$=6.4 Hz, 1H), 4.13 (q, $J$=5.9 Hz, 1H), 3.89 (dd, $J$=6.2, 4.5 Hz, 1H), 3.58 (t, $J$=5.4 Hz, 1H), 3.38 (s, 3H), 2.77 (br. d., $J$=4.6 Hz, 2H), 2.74 (br s, 1H), 2.68, 2.56 (ABXY, $J_{AB}$=16.1 Hz, $J_{AX}$=7.1 Hz, $J_{AY}$=2.5 Hz, $J_{BX}$=5.4 Hz, $J_{BY}$=2.0 Hz, 2H), 1.91–2.12 (m, 4H), 1.85 (dd, $J$=13.4, 11.0 Hz, 1H), 1.71 (s, 3H), 1.57–1.64 (m, 1H), 1.11 (s, 21H), 0.94 ppm (d, $J$=6.8 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=201.9, 145.1, 144.8, 133.9, 128.1, 115.7, 111.0, 97.8, 82.9, 79.4, 77.6, 74.2, 56.1, 49.8, 41.6, 36.5, 35.3, 31.8, 28.2, 22.7, 18.6, 18.5, 16.6, 13.3 ppm; MS (CI): $m/z$ (%)=523 $[M+1]^+$ (3), 505 (2), 491 (19), 479 (33), 447 (16), 429 (6), 373 (4), 331 (8), 317 (100), 287 (37), 161 (42); HRMS (CI): $m/z$ calcd for $C_{30}H_{55}O_5Si$: 523.3819 $[M+1]^+$; found: 523.3828.

Potassium *tert*-butoxide (116 mg, 1.04 mmol) was added to a solution of (methoxymethyl)triphenylphosphonium chloride (387 mg, 1.13 mmol) in THF (5 mL) at 0°C. The resulting red solution was stirred for 10 min at the same temperature, followed by dropwise addition of a solution of the aldehyde (236 mg, 0.451 mmol) in THF (3 mL). The reaction mixture was stirred for 30 min at 0°C, warmed to room temperature, and then further stirred for 30 min. Saturated aqueous $NaHCO_3$ (5 mL) was added to quench the reaction, and the reaction mixture was extracted with $Et_2O$ (2×20 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated. The crude enol ether was dissolved in THF (10 mL) and water (1 mL), and the solution was cooled to 0°C. Mercuric acetate (430 mg, 1.35 mmol) was added in one portion, and the mixture was stirred for 30 min at 0°C. The reaction mixture was treated with saturated aqueous KI (10 mL) and extracted with $Et_2O$ (2×20 mL), and the organic phase was washed with saturated aqueous KI (3×10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc=4:1) provided the homologous aldehyde (189 mg, 78%). $R_f$=0.25 (hexanes/EtOAc=4:1); $[\alpha]_D^{20}=-1.0$ ($c$=0.54, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$=3076, 2945, 2893, 2868, 2725, 2360, 1728, 1651, 1604, 1464, 1385, 1215, 1151, 1039, 883, 679 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=9.78 (s, 1H), 6.06 (d, $J$=15.7 Hz, 1H), 5.73 (dt, $J$=15.3, 7.3 Hz, 1H), 4.97 (s, 1H), 4.87 (s, 1H), 4.73 (s, 1H), 4.75, 4.71 (ABq, $J_{AB}$=6.9 Hz, 2H), 4.70 (s, 1H), 4.06 (q, $J$=6.8 Hz, 1H), 3.88 (dd, $J$=6.4, 4.2 Hz, 1H), 3.80–3.86 (m, 1H), 3.57 (dd, $J$=5.9, 4.4 Hz, 1H), 3.39 (s, 3H), 2.77 (br d, $J$=6.8 Hz, 3H), 2.44–2.62 (m, 2H), 1.91–2.03 (m, 3H), 1.83–1.90 (m, 3H), 1.75–1.83 (m, 1H), 1.71 (s, 3H), 1.50–1.57 (m, 1H), 1.11 (s, 21H), 0.95 ppm (d, $J$=6.8 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$=202.7, 145.1, 133.8, 128.1, 115.7, 111.0, 97.9, 83.3, 79.3, 78.0, 77.9, 56.0, 41.6, 41.0, 36.5, 35.2, 31.5, 28.4, 28.2, 22.7, 18.6, 18.6, 16.6, 13.3 ppm.

Sodium borohydride (27.0 mg, 0.714 mmol) was added to a solution of the homologous aldehyde (189 mg, 0.352 mmol) in MeOH (3.5 mL) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 30 min. The reaction mixture was treated with saturated aqueous $NH_4Cl$ (2 mL) and extracted with $Et_2O$ (2×10 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc = 2:1) provided the corresponding alcohol (175 mg, 92 %). $R_f$ = 0.21 (hexanes/EtOAc = 2:1); $[\alpha]_D^{21} = -7.0$ ($c$ = 0.39, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3435, 3076, 2943, 2868, 1651, 1604, 1464, 1385, 1244, 1217, 1149, 1097, 1034, 968, 883, 679 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 6.06 (d, $J$ = 15.8 Hz, 1H), 5.73 (dt, $J$ = 15.8, 7.0 Hz, 1H), 4.97 (d, $J$ = 1.8 Hz, 1H), 4.87 (s, 1H), 4.75 (s, 2H), 4.73 (s, 1H), 4.70 (s, 1H), 4.08 (q, $J$ = 7.0 Hz, 1H), 3.89 (dd, $J$ = 6.6, 4.0 Hz, 1H), 3.80–3.86 (m, 1H), 3.61–3.69 (m, 2H), 3.59 (dd, $J$ = 6.2, 4.0 Hz, 1H), 3.39 (s, 3H), 2.77 (br d, $J$ = 7.0 Hz, 3H), 2.48 (br s, 1H), 1.97–2.05 (m, 2H), 1.88–1.96 (m, 2H), 1.82–1.88 (m, 1H), 1.71 (s, 3H), 1.63–1.69 (m, 3H), 1.56–1.62 (m, 1H), 1.48–1.56 (m, 1H), 1.11 (s, 21H), 0.95 ppm (d, $J$ = 6.6 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 145.1, 144.8, 133.8, 128.1, 115.6, 111.0, 98.1, 83.6, 79.4, 79.3, 78.0, 63.1, 56.0, 41.6, 36.5, 35.2, 32.9, 31.8, 30.2, 28.1, 22.7, 18.6, 18.6, 16.6, 13.3, 13.3 ppm.

$Ph_3P$ (239 mg, 0.913 mmol), 1-phenyl-1*H*-tetrazole-5-thiol (**19**; 163 mg, 0.913 mmol), and DIAD (0.19 mL, 0.96 mmol) were added to a solution of the alcohol (164 mg, 0.304 mmol) in THF at 0 °C. After the mixture was stirred for 10 min at room temperature, the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (hexanes/EtOAc = 10:1) to afford the corresponding sulfide (200 mg, 94 %). $R_f$ = 0.52 (hexanes/EtOAc = 4:1); $[\alpha]_D^{21} = +1.7$ ($c$ = 0.34, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3074, 2943, 2866, 2729, 1649, 1599, 1500, 1462, 1387, 1277, 1244, 1149 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 7.52–7.59 (m, 5H), 6.05 (d, $J$ = 15.8 Hz, 1H), 5.72 (dt, $J$ = 15.8, 7.0 Hz, 1H), 4.96 (d, $J$ = 1.8 Hz, 1H), 4.86 (s, 1H), 4.73 (s, 3H), 4.69 (s, 1H), 4.05 (q, $J$ = 6.8 Hz, 1H), 3.87 (dd, $J$ = 6.6, 4.0 Hz, 1H), 3.79–3.85 (m, 1H), 3.57 (dd, $J$ = 6.2, 4.0 Hz, 1H), 3.43 (t, $J$ = 7.3 Hz, 2H), 3.38 (s, 3H), 2.76 (d, $J$ = 8.4 Hz, 3H), 1.87–2.03 (m, 6H), 1.80–1.87 (m, 1H), 1.70 (s, 3H), 1.64–1.69 (m, 2H), 1.48–1.54 (m, 1H), 1.10 (s, 18H), 1.09 (s, 3H), 0.94 ppm (d, $J$ = 7.0 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 154.7, 145.1, 144.8, 134.0, 133.8, 130.3, 130.0, 128.1, 124.1, 115.6, 111.0, 97.8, 83.2, 79.3, 78.4, 77.8, 56.0, 41.6, 36.6, 35.3, 34.9, 33.6, 31.6, 28.1, 26.2, 22.7, 18.6, 18.5, 16.6, 13.3 ppm; MS (FAB): $m/z$ (%) = 699 $[M+1]^+$ (0.7), 683 (1), 667 (1), 655 (1), 475 (4), 363 (5), 289 (73), 227 (14), 157 (57), 115 (87), 45 (100); HRMS (FAB): $m/z$ calcd for $C_{38}H_{63}N_4O_4SSi$: 699.4339 $[M+1]^+$; found: 699.4319.

A solution of the sulfide (200 mg, 0.286 mmol) in EtOH (3 mL) at 0 °C was treated with a solution of ammonium molybdate tetrahydrate (70.4 mg, 0.0572 mmol) in $H_2O_2$ (30 % in water, 0.25 mL, 2.8 mmol). The resultant suspension was stirred at room temperature for 12 h, diluted with water (5 mL), and extracted with $Et_2O$ (2×20 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc = 8:1) provided sulfone **38** (166 mg, 79 %). $R_f$ = 0.52 (hexanes/EtOAc = 4:1); $[\alpha]_D^{21} = -2.1$ ($c$ = 1.07, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3076, 2945, 2868, 1644, 1597, 1498, 1482, 1342, 1153, 1099, 1039, 966, 885, 687 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 7.67–7.71 (m, 2H), 7.57–7.64 (m, 3H), 6.05 (d, $J$ = 15.9 Hz, 1H), 5.73 (dt, $J$ = 15.9, 7.1 Hz, 1H), 4.96 (d, $J$ = 1.7 Hz, 1H), 4.86 (s, 1H), 4.74, 4.70 (ABq, $J_{AB}$ = 6.6 Hz, 2H) 4.73 (s, 1H), 4.69 (s, 1H), 4.07 (q, $J$ = 6.9 Hz, 1H), 3.88 (dd, $J$ = 6.6, 4.2 Hz, 1H), 3.81–3.85 (m, 1H), 3.82 (t, $J$ = 7.9 Hz, 2H), 3.58 (dd, $J$ = 5.6, 4.4 Hz, 1H), 3.38 (s, 3H), 2.76 (d, $J$ = 8.6 Hz, 3H), 1.89–2.12 (m, 6H), 1.84 (dd, $J$ = 13.3, 11.1 Hz, 1H), 1.71 (s, 3H), 1.67–1.76 (m, 2H), 1.50–1.57 (m, 1H), 1.11 (s, 18H), 1.10 (s, 3H), 0.94 ppm (d, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 153.7, 145.1, 144.8, 133.9, 133.3, 131.6, 129.9, 128.0, 125.3, 115.6, 111.0, 97.9, 83.2, 79.3, 78.2, 77.8, 56.2, 56.0, 41.6, 36.5, 35.2, 34.2, 31.5, 28.1, 22.7, 19.6, 18.6, 18.6, 16.6, 13.3 ppm; MS (CI): $m/z$ (%) = 731 $[M+1]^+$ (1), 715 (2), 699 (3), 586 (1), 525 (9), 497 (7), 467 (3), 396 (3), 321 (9), 223 (8), 195 (38), 147 (59), 119 (98), 94 (100); HRMS (CI): $m/z$ calcd for $C_{38}H_{63}N_4O_6SSi$: 731.4237 $[M+1]^+$; found: 731.4245.

*Olefin **39***

LiHMDS (1 M in THF, 0.50 mL, 0.50 mmol) was added dropwise to a solution of sulfone **38** (245 mg, 0.335 mmol) in THF (1.7 mL) at −78 °C. The resulting yellow solution was stirred at −40 °C for 1 h and then cooled to −78 °C. A solution of aldehyde **23** (240 mg, 5.01 mmol) in DMF (5.1 mL) and DMPU (1.7 mL) was added slowly to the solution of lithiated sulfone, and the reaction mixture was allowed to warm slowly to room temperature and stirred for 12 h. The reaction mixture was partitioned between water (10 mL) and $Et_2O$ (10 mL), and the aqueous phase was extracted with $Et_2O$ (2×20 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography (hexanes/EtOAc = 8:1) to give olefin **39** (244 mg, 74 %, $E/Z$ = 10:1). $R_f$ = 0.55 (hexanes/EtOAc = 4:1); $[\alpha]_D^{25} = +3.0$ ($c$ = 0.35, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3072, 2933, 2866, 1651, 1603, 1464, 1429, 1238, 1111, 1051, 989, 885, 702 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 7.62–7.67 (m, 4H), 7.34–7.43 (m, 6H), 6.24 (dd, $J$ = 15.3, 10.4 Hz, 1H), 6.05 (d, $J$ = 16.6 Hz, 1H), 6.01–6.06 (m, 1H), 5.69–5.83 (m, 2H), 5.64 (dd, $J$ = 15.4, 7.1 Hz, 1H), 5.50 (dd, $J$ = 15.2, 6.8 Hz, 1H), 5.41 (dd, $J$ = 15.4, 7.3 Hz, 1H), 4.97 (d, $J$ = 1.7 Hz, 1H), 4.86 (s, 1H), 4.74 (s, 2H), 4.73 (s, 1H), 4.69 (s, 1H), 4.01–4.11 (m, 3H), 3.87 (dd, $J$ = 6.5, 4.0 Hz, 1H), 3.72–3.81 (m, 1H), 3.57 (dd, $J$ = 6.6, 3.9 Hz, 1H), 3.54, 3.49 (ABX, $J_{AB}$ = 9.8 Hz, $J_{AX}$ = 6.4 Hz, $J_{BX}$ = 6.6 Hz, 2H), 3.38 (s, 3H), 2.76 (d, $J$ = 8.3 Hz, 3H), 2.39–2.48 (m, 1H), 2.11–2.20 (m, 1H), 2.03–2.11 (m, 1H), 1.94–2.02 (m, 2H), 1.81–1.92 (m, 3H), 1.71 (s, 3H), 1.60–1.68 (m, 1H), 1.45–1.54 (m, 2H), 1.43 (s, 3H), 1.43 (s, 3H), 1.11 (s, 18H), 1.10 (s, 3H), 1.04 (s, 9H), 1.03 (d, $J$ = 6.9 Hz, 3H), 0.94 ppm (d, $J$ = 6.6 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 145.1, 144.8, 138.6, 136.5, 135.9, 135.8, 134.5, 134.1, 134.1, 133.8, 129.8, 129.2, 128.1, 127.8, 126.9, 126.0, 115.6, 111.0, 108.8, 97.8, 83.3, 82.6, 82.0, 79.3, 78.6, 77.9, 68.6, 55.9, 41.7, 39.5, 36.6, 35.5, 35.3, 31.6, 29.3, 28.2, 27.3, 27.1, 22.6, 19.5, 18.6, 18.6, 16.6, 16.5, 13.3 ppm; MS (MALDI-TOF): $m/z$ = 1005 $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{60}H_{94}O_7Si_2Na$: 1005.6436 $[M+Na]^+$; found: 1005.6472.

*Seco Acid **40***

Aqueous sodium hydroxide (15 %, 1 mL) was added to a solution of olefin **39** (185 mg, 0.188 mmol) in DMPU (10 mL) at room temperature, and the resulting mixture was stirred vigorously for 2 h. The reaction mixture was diluted with $Et_2O$ (20 mL) and then treated with saturated aqueous $NH_4Cl$ (10 mL). The aqueous phase was extracted with $Et_2O$ (2×10 mL), and the combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (hexanes/EtOAc = 4:1) provided the corresponding alcohol (123 mg, 88 %). $R_f$ = 0.22 (hexanes/EtOAc = 4:1); $[\alpha]_D^{25} = +5.8$ ($c$ = 0.58, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3448, 3093, 3078, 2943, 2868, 1649, 1604, 1462, 1377, 1238, 1153, 1038, 991, 885, 679, 511 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 6.27 (dd, $J$ = 15.2, 10.3 Hz, 1H), 6.13 (dd, $J$ = 15.2, 10.5 Hz, 1H), 6.05 (d, $J$ = 15.9 Hz, 1H), 5.68–5.85 (m, 2H), 5.60 (dd, $J$ = 15.2, 7.8 Hz, 1H), 5.55 (dd, $J$ = 17.5, 7.3 Hz, 1H), 5.41 (dd, $J$ = 15.4, 7.3 Hz, 1H), 4.97 (s, 1H), 4.87 (s, 1H), 4.75 (s, 2H), 4.73 (s, 1H), 4.70 (s, 1H), 4.01–4.11 (m, 3H), 3.85–3.91 (m, 1H), 3.74–3.82 (m, 1H), 3.57 (dd, $J$ = 6.4, 3.9 Hz, 1H), 3.48–3.55 (m, 1H), 3.41–3.47 (m, 1H), 3.39 (s, 3H), 2.77 (d, $J$ = 6.8 Hz, 2H), 2.75 (br s, 1H), 2.36–2.46 (m, 1H), 2.06–2.20 (m, 2H), 1.95–2.04 (m, 2H), 1.83–1.93 (m, 3H), 1.71 (s, 3H), 1.61–1.68 (m, 1H), 1.46–1.56 (m, 2H), 1.43 (s, 6H), 1.11 (s, 18H), 1.10 (br s, 3H), 1.02 (d, $J$ = 6.6 Hz, 3H), 0.95 ppm (d, $J$ = 6.6 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 145.1, 144.8, 137.8, 136.6, 134.0, 133.8, 130.4, 128.1, 127.7, 125.9, 115.6, 111.0, 108.9, 97.8, 83.3, 82.5, 81.9, 79.3, 78.5, 77.9, 67.5, 56.0, 41.6, 39.9, 36.6, 35.4, 35.3, 31.5, 29.4, 28.2, 27.3, 27.2, 22.6, 18.6, 18.6, 16.5, 16.5, 13.3 ppm; MS (MALDI-TOF): $m/z$ = 767 $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{44}H_{76}O_7SiNa$: 767.5258 $[M+Na]^+$; found: 767.5253.

IBX (88.0 mg, 0.314 mmol) was dissolved in DMSO (1 mL). The opaque mixture cleared upon stirring at room temperature for 20 min. A solution of the alcohol (77.7 mg, 0.104 mmol) in THF (1 mL) was added dropwise to this solution. After being stirred for 3 h, the reaction mixture was treated with saturated aqueous $Na_2S_2O_3$ (3 mL) and extracted with $Et_2O$ (2×10 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (2×5 mL) and brine (5 mL), dried over $MgSO_4$, filtered, and

concentrated. The crude aldehyde product was dissolved in *t*BuOH (3.3 mL) and 2-methyl-2-butene (3.3 mL). After the solution was cooled to 0 °C, a solution of $NaClO_2$ (59.0 mg, 0.522 mmol) and $NaH_2PO_4$ (50.0 mg, 0.626 mmol) in water (3.3 mL) was added. The reaction mixture was stirred vigorously for 5 h at room temperature, and treated with EtOAc (30 mL) and water (10 mL). The aqueous phase was extracted with EtOAc (2×10 mL), and the combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography ($CHCl_3$/MeOH = 30:1) provided the corresponding carboxylic acid (70.4 mg, 89 %). $R_f$ = 0.43 ($CHCl_3$/MeOH = 10:1); $[\alpha]_D^{25} = -16.3$ ($c$ = 0.25, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3076, 2941, 2868, 1736, 1711, 1653, 1604, 1462, 1390, 1371, 1151, 1036, 989, 885, 806, 679 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 6.27 (dd, $J$ = 15.2, 10.5 Hz, 1H), 6.15 (dd, $J$ = 15.2, 10.5 Hz, 1H), 6.05 (d, $J$ = 15.7 Hz, 1H), 5.69–5.81 (m, 3H), 5.58 (dd, $J$ = 15.2, 7.1 Hz, 1H), 5.40 (dd, $J$ = 15.4, 7.3 Hz, 1H), 4.97 (d, $J$ = 1.5 Hz, 1H), 4.87 (s, 1H), 4.76, 4.74 (ABq, $J_{AB}$ = 6.9 Hz, 2H), 4.73 (s, 1H), 4.69 (s, 1H), 4.01–4.11 (m, 3H), 3.86 (dd, $J$ = 6.5, 4.0 Hz, 1H), 3.75–3.81 (m, 1H), 3.57 (dd, $J$ = 6.5, 4.0 Hz, 1H), 3.39 (s, 3H), 3.16–3.23 (m, 1H), 2.76 (d, $J$ = 6.8 Hz, 3H), 2.12–2.21 (m, 1H), 2.02–2.11 (m, 1H), 1.94–2.01 (m, 2H), 1.81–1.93 (m, 3H), 1.71 (s, 3H), 1.59–1.68 (m, 1H), 1.46–1.53 (m, 2H), 1.43 (s, 3H), 1.42 (s, 3H), 1.30 (d, $J$ = 6.8 Hz, 3H), 1.10 (s, 18H), 1.10 (s, 3H), 0.94 ppm (d, $J$ = 6.6 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 179.4, 145.1, 144.8, 136.8, 133.8, 133.3, 133.0, 130.9, 128.9, 128.1, 125.8, 115.6, 111.0, 109.0, 97.8, 83.4, 82.6, 81.7, 79.3, 78.6, 77.8, 55.9, 42.7, 41.6, 36.6, 35.5, 35.3, 31.5, 29.3, 28.1, 27.3, 27.2, 22.6, 18.6, 18.6, 17.2, 16.5, 13.3 ppm; MS (MALDI-TOF): $m/z$ = 781 $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{44}H_{74}O_8SiNa$: 781.5051 $[M+Na]^+$; found: 781.5059.

TBAF (1 M in THF, 0.28 mL, 0.28 mmol) was added dropwise to a solution of the carboxylic acid (70.4 mg, 0.0927 mmol) in THF (3 mL). After 1 h, another portion of TBAF (1 M in THF, 0.10 mL, 0.10 mmol) was added to the brown reaction mixture, which was then stirred for 1 h. A final portion of TBAF (1 M in THF, 0.10 mL, 0.10 mmol) was then added, and after further stirring for 1 h, the reaction mixture was filtered through a short column of silica gel. The silica-gel column was washed with hexanes/EtOAc/AcOH (1:1:0.01, 100 mL). The combined filtrates were concentrated, and the residue was purified by flash column chromatography ($CHCl_3$/MeOH = 30:1) to afford seco acid **40** (52.6 mg, 94 %). $R_f$ = 0.35 ($CHCl_3$/MeOH = 10:1); $[\alpha]_D^{25} = -73.8$ ($c$ = 0.97, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3454, 3076, 2981, 2933, 1732, 1651, 1604, 1456, 1379, 1223, 1153, 1097, 1028, 991, 887, 731, 584 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 6.12–6.24 (m, 2H), 6.06 (d, $J$ = 15.7 Hz, 1H), 5.66–5.79 (m, 3H), 5.56 (dd, $J$ = 14.6, 7.5 Hz, 1H), 5.39 (dd, $J$ = 15.3, 7.7 Hz, 1H), 5.01 (d, $J$ = 6.8 Hz, 1H), 4.98 (d, $J$ = 1.5 Hz, 1H), 4.87 (s, 1H), 4.72 (s, 1H), 4.69 (d, $J$ = 6.6 Hz, 1H), 4.69 (s, 1H), 3.94–4.07 (m, 3H), 3.65–3.72 (m, 1H), 3.62 (d, $J$ = 7.6 Hz, 1H), 3.36 (s, 3H), 3.21 (d, $J$ = 9.0 Hz, 1H), 3.11–3.19 (m, 1H), 2.89–2.95 (m, 1H), 2.71–2.80 (m, 2H), 2.14–2.22 (m, 1H), 2.03–2.13 (m, 1H), 1.83–1.95 (m, 3H), 1.73–1.82 (m, 2H), 1.70 (s, 3H), 1.46–1.54 (m, 2H), 1.42 (s, 6H), 1.37–1.45 (m, 1H), 1.27 (d, $J$ = 7.1 Hz, 3H), 0.84 ppm (d, $J$ = 6.6 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 177.7, 145.2, 145.0, 137.3, 134.3, 134.1, 134.0, 131.2, 128.7, 128.3, 126.3, 116.0, 111.2, 109.3, 97.5, 82.6, 82.5, 80.8, 79.3, 79.0, 77.1, 56.6, 43.5, 41.7, 36.3, 35.1, 34.8, 30.4, 29.4, 28.5, 27.5, 27.4, 22.9, 17.5, 16.0 ppm; MS (MALDI-TOF): $m/z$ = 625 $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{35}H_{54}O_8Na$: 625.3716 $[M+Na]^+$; found: 625.3731.

*Macrolide **41***

Ethoxyacetylene (40 % in hexanes, 0.030 mL, 0.13 mmol) was added to a solution of seco acid **40** (52.6 mg, 0.0873 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (1.0 mg, 0.0016 mmol) in toluene (8 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 30 min. The dark-red solution was filtered through a pad of silica gel, which was then washed with dry $Et_2O$ (50 mL) under $N_2$ atmosphere. The filtrate was concentrated under reduced pressure. The crude ethoxyvinyl ester was dissolved in toluene (3 mL) and added to a solution of CSA (2.0 mg, 0.0087 mmol) in toluene (14 mL). The reaction mixture was heated to 50 °C for 2 h, filtered through a pad of silica gel, and concentrated. The residue was purified by flash column chromatography (hexanes/EtOAc = 10:1) to afford macrolide **41** (22.5 mg, 44 %). $R_f$ = 0.45 (hexanes/EtOAc = 4:1); $[\alpha]_D^{25} = -178.7$ ($c$ = 0.46, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3443, 3063, 3078, 2981, 2929, 1732, 1653, 1604, 1454, 1377, 1238, 1171, 1090, 1030, 991, 885, 758, 580 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 6.30 (dd, $J$ = 14.9, 10.8 Hz, 1H), 6.19 (dd, $J$ = 14.9, 10.8 Hz, 1H), 6.04 (d, $J$ = 15.7 Hz, 1H), 5.68–5.76 (m, 2H), 5.55 (dd, $J$ = 14.7, 9.3 Hz, 2H), 5.31 (ddd, $J$ = 15.2, 8.6, 1.5 Hz, 1H), 5.12 (d, $J$ = 7.1 Hz, 1H), 4.98 (s, 1H), 4.87 (s, 1H), 4.73 (s, 1H), 4.70 (s, 1H), 4.67 (d, $J$ = 6.8 Hz, 1H), 4.64 (dd, $J$ = 10.3, 1.2 Hz, 1H), 4.02 (t, $J$ = 8.5 Hz, 1H), 3.98 (t, $J$ = 8.5 Hz, 1H), 3.72 (dd, $J$ = 8.9, 1.3 Hz, 1H), 3.52 (td, $J$ = 9.3, 6.4 Hz, 1H), 3.36 (s, 3H), 3.24–3.32 (m, 2H), 2.77 (d, $J$ = 7.1 Hz, 2H), 2.30–2.39 (m, 3H), 1.86–1.98 (m, 2H), 1.82 (dd, $J$ = 14.3, 11.9 Hz, 1H), 1.71 (s, 3H), 1.62–1.70 (m, 1H), 1.46–1.54 (m, 2H), 1.43 (s, 3H), 1.43 (s, 3H), 1.26–1.32 (m, 1H), 1.24 (d, $J$ = 6.6 Hz, 3H), 1.11–1.19 (m, 1H), 0.91 ppm (d, $J$ = 6.6 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 174.5, 144.5, 144.1, 138.5, 135.8, 135.4, 133.3, 131.3, 127.9, 127.7, 125.4, 115.7, 110.8, 109.0, 97.2, 83.0, 82.3, 80.7, 79.2, 78.0, 77.7, 77.2, 56.3, 44.0, 41.3, 35.8, 32.1, 31.6, 28.8, 27.7, 27.1, 27.1, 22.5, 17.1, 14.7 ppm; MS (MALDI-TOF): $m/z$ = 607 $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{35}H_{52}O_7Na$: 607.3611 $[M+Na]^+$; found: 607.3627.

*Amphidinolide E (**1**)*

Aqueous hydrochloric acid (4 N, 0.3 mL) was added dropwise to a solution of macrolide **41** (22.5 mg, 0.0385 mmol) in MeOH (3.6 mL). After 1 h, MeOH (0.5 mL) and aqueous HCl (4 N, 0.2 mL) were added to the mixture. After 2 h, MeOH (0.5 mL) and aqueous HCl (4 N, 0.1 mL) were again added to the mixture. After 1 h, the mixture was diluted with $Et_2O$ (10 mL), and the reaction was carefully quenched by saturated aqueous $NaHCO_3$ (5 mL). The aqueous phase was extracted with EtOAc (3× 10 mL), and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography ($CHCl_3$/MeOH = 100:1) to afford amphidinolide E (**1**; 14.8 mg, 77 %). $R_f$ = 0.25 ($CHCl_3$/MeOH = 20:1); $[\alpha]_D^{30} = -131.1$ ($c$ = 0.21, $CHCl_3$); IR (neat): $\tilde{\nu}_{max}$ = 3417, 3076, 2925, 2854, 2731, 1865, 1732, 1668, 1606, 1456, 1377, 1319, 1248, 1169, 1088, 1047, 991, 889 $cm^{-1}$; $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 6.23 (dd, $J$ = 14.7, 10.7 Hz,1H), 6.15 (dd, $J$ = 14.8, 10.8 Hz, 1H), 6.05 (d, $J$ = 15.7 Hz, 1H), 5.69 (dt, $J$ = 15.7, 6.9 Hz, 1H), 5.62–5.66 (m, 1H), 5.62 (dd, $J$ = 14.5, 9.7 Hz, 1H), 5.53 (dd, $J$ = 14.9, 9.1 Hz, 1H), 5.27 (dd, $J$ = 15.3, 8.4 Hz, 1H), 4.98 (s, 1H), 4.87 (s, 1H), 4.75 (s, 1H), 4.71 (s, 1H), 4.66 (d, $J$ = 9.6 Hz, 1H), 3.94 (t, $J$ = 8.5 Hz, 1H), 3.88 (t, $J$ = 8.9 Hz, 1H), 3.71 (d, $J$ = 7.5 Hz, 1H), 3.56 (dt, $J$ = 7.2 Hz, 1H), 3.38–3.44 (m, 1H), 3.23–3.29 (m, 1H), 2.73–2.83 (m, 2H), 2.40 (dd, $J$ = 13.6, 2.1 Hz, 1H), 2.23–2.33 (m, 2H), 1.84–1.92 (m, 1H), 1.75–1.82 (m, 2H), 1.72 (s, 3H), 1.57–1.64 (m, 1H), 1.43–1.50 (m, 1H), 1.36–1.43 (m, 1H), 1.28–1.35 (m, 2H), 1.25 (d, $J$ = 6.7 Hz, 3H), 0.92 ppm (d, $J$ = 6.7 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 174.4, 144.7, 144.0, 135.1, 134.9, 134.1, 133.3, 131.4, 131.4, 129.4, 127.9, 115.7, 110.7, 79.9, 78.3, 78.1, 77.6, 76.6, 73.2, 44.1, 41.3, 36.1, 32.6, 32.3, 29.9, 29.0, 27.1, 22.5, 17.5, 15.4 ppm; MS (CI): $m/z$ (%) = 501 $[M+1]^+$ (18), 483 (100), 465 (93), 449 (21), 401 (18), 345 (18), 291 (22), 257 (12), 179 (22), 121 (12), 109 (13), 71 (10), 57 (12); HRMS (CI): $m/z$ calcd for $C_{30}H_{45}O_6$: 501.3216 $[M+1]^+$; found: 501.3213.

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