# Total Synthesis and Absolute Configuration of (−)-Anthoplalone

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*Received February 17, 1999*

We report the total synthesis of the cytotoxic agent (−)-anthoplalone and the determination of its absolute stereochemistry. The cyclopropane moiety was prepared using a nonracemic bicyclic chloroallyl phosphonamide anion addition to *tert*-butyl 3,3-dimethyl acrylate. Several pathways were studied to secure the *E*-trisubstituted olefin of the left part of the molecule.

## Introduction

The secosesquiterpene anthoplalone **1**, isolated from the Okinawan actinian *Anthopleura pacifica*,[1] exhibits antitumor activity against murine melanoma cells at a concentration of 22 $\mu$g/mL, and it is thought to be biosynthetically related to lepidozenal **2**, which inhibits the growth of rice seedlings.[2] The absolute stereochemistry of anthoplalone has only been inferred from the stereochemistry of lepidozenes such as **3**,[1] while its relative stereochemistry has been implied from the coupling constant ($J$ = 6.0 Hz) of the cyclopropane ring protons.[3] This determination was confirmed by McMurry and Bosch[4] and by Fukumoto,[5] who independently reported the synthesis of racemic anthoplalone. The first synthesis[4] started with geranyl acetone which was converted in some steps to a mixture of cis and trans substituted cyclopropane precursors to **1**, even though the natural product had not been reported yet at the time. Preparative HPLC allowed the separation of **1** and its cis isomer, which was transformed into isomeric bicyclogermacranes related to lepidozene. The Fukumoto synthesis[5] of racemic **1** started with a bicyclic cyclobutane intermediate obtained by a multistep procedure. A rearrangement reaction led to a cyclopropane analogue, which was in turn subjected to a sequence of functional adjustments to provide a ketone precursor. A Julia type coupling led to a predominantly *Z*-trisubstituted olefin, which was partially isomerized to the desired *E*-configuration as in **1**. In this article, we report the first enantioselective synthesis of (−)-anthoplalone **1** and the assignment of its absolute configuration.

## Results and Discussion

Despite its relatively simple structure, the synthesis of anthoplalone presents two potential difficulties that

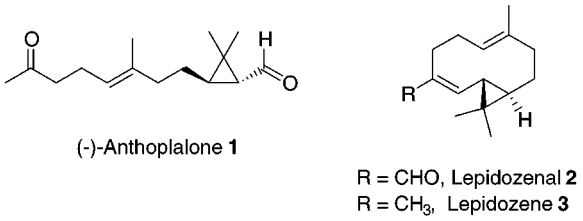


**Figure 1.**

are concerned with the stereochemistry of the cyclopropane and with the control of the geometry of the isolated double bond.[6] Interestingly, these issues were the stumbling blocks in the McMurry and Fukumoto syntheses, respectively. Among several approaches, we chose first to disconnect at the allylic position, in order to couple an allylic anion with a cyclopropyl methyl electrophile as shown in Figure 2. The strong preference for the regioselective α-addition of allyl sulfone anions to various electrophiles encouraged us to explore this approach first.[7]

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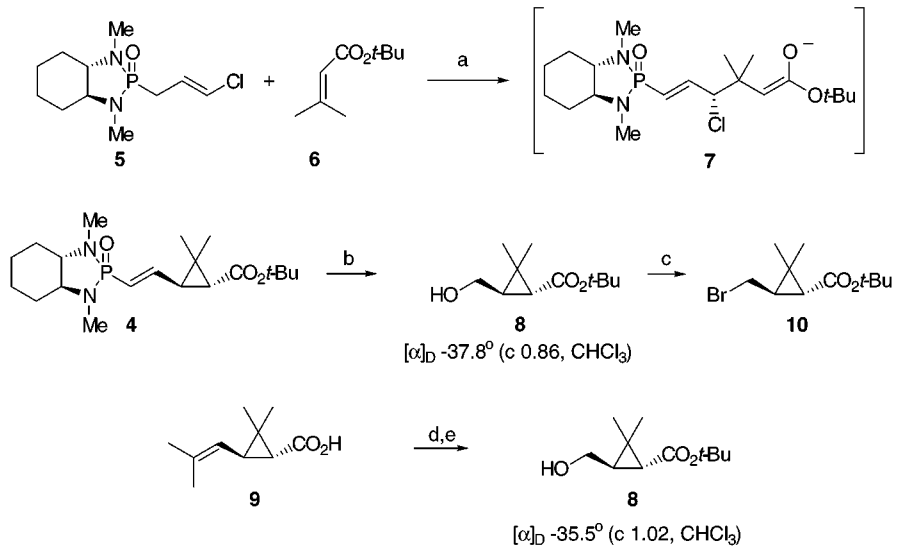
10.1021/jo990302n CCC: $18.00 
Published on Web 06/02/1999

**Scheme 1**[a]




[a] Reagents: (a) BuLi, $Et_2O$, −78 °C, 46% (b) Ozone, $CH_2Cl_2$, MeOH; $NaBH_4$, 83%. (c) $CBr_4$, $PPh_3$, MeCN, 73%. (d) *t*-Butyl trichloroacetimidate, $BF_3{\cdot}Et_2O$, $CH_2Cl_2$, cyclohexane (e) Ozone, $CH_2Cl_2$, MeOH; $NaBH_4$, 63% over 2 steps.

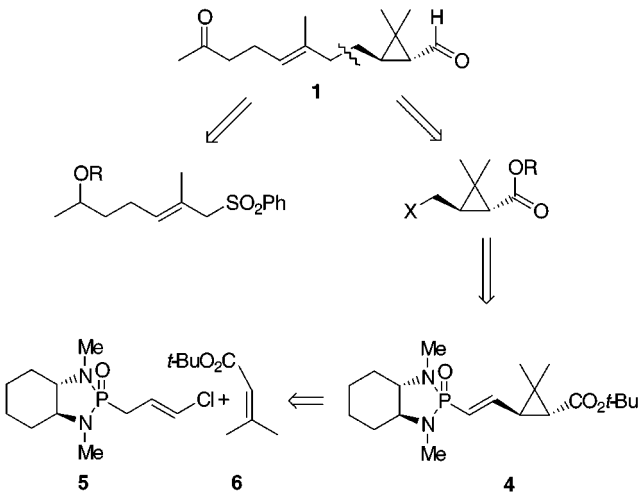



**Figure 2.**

The right-hand segment of the molecule, consisting of a trans tetrasubstituted cyclopropane, presented a certain challenge in view of the need to secure an enantioselective synthesis of an appropriately functionalized intermediate. Previous studies in our laboratories have demonstrated the utility of chloroallyl phosphonamides in the highly diastereoselective synthesis of polysubstituted cyclopropanes such as **4**.[8] The (*S*,*S*)-reagent **5**, shown in Figure 2, would be needed to generate the desired substitution pattern in the cyclopropane precursor intended for anthoplalone.

In the event, treatment of the readily available **5** with *n*-BuLi generated the corresponding chloroallyl anion, to which was added *tert*-butyl 3,3-dimethyl acrylate **6** as shown in Scheme 1. A diastereomerically pure cyclopropane adduct **4** was obtained in 46% yield. Unfortunately, attempts to optimize this yield were not successful. To ascertain the absolute stereochemistry of the adduct, we opted for an ozonolytic oxidative cleavage and reduction protocol, which led to the alcohol derivative **8**. An independent synthesis from the commercially available *trans*-chrysanthemic acid **9** confirmed the stereochemistry assigned to **8** based on the anticipated mode of attack[9] of the anion derived from **5**, followed by intramolecular enolate alkylation, as illustrated in Scheme 1. The alternative pathway to **4** via a carbene insertion mechanism, which is not expected to proceed with such high diastereoselectivity, cannot be excluded. Alcohol **8** was converted to the required bromide **10** using standard methods, providing us with the right-hand segment of the molecule.

The sulfone segment (Figure 2) was prepared from 6-methyl-5-hepten-2-ol **11** (Scheme 2). Protection under standard conditions,[10] followed by ozonolysis, afforded the corresponding aldehyde, which was subjected to a modified[11] Horner-Emmons olefination to give **13** as the pure *E*-isomer. Reduction with DIBAL-H afforded the allylic alcohol **14**, which was converted to the corresponding bromide **15**,[12] and the latter was transformed to the desired sulfone derivative **16** by treatment with sodium phenyl sulfinate. The potassium anion of **16**, generated with *t*-BuOK, was reacted with **10** in the presence of $n$-$Bu_4NI$ to afford the coupling product **17** in 61% yield after deprotection.

There remained the seemingly simple task of desulfonylating the allylic sulfone en route to the intended target **1**. It is at this step that we encountered difficulties in securing the desired trisubstituted *E* double bond. Using methods of desulfonylation that rely on electron transfer or radicals (Na/Hg, Li/$EtNH_2$, $SmI_2$−HMPA),[13] the reaction proceeded in good yield to generate a 1:1 mixture of two regioisomers (**18a** and **18b**). The isomer ratio was enriched to a mixture favoring the desired regioisomer

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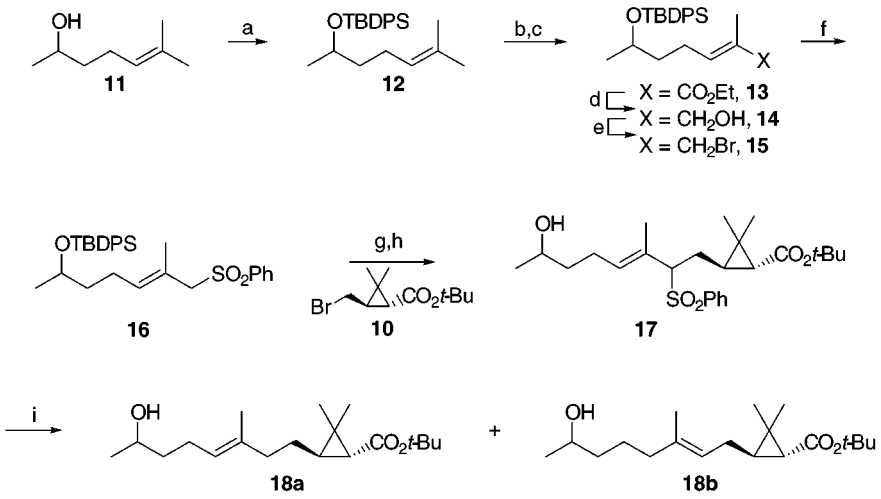
**Scheme 2**[a]




[a] Reagents: (a) TBDPSCl, imidazole, DMF, quant. (b) Ozone, $CH_2Cl_2$, DMS (c) $(EtO)_2P(O)CH(Me)CO_2Et$, LiCl, MeCN, 89% over 2 steps. (d) DIBAL-H, toluene, 98%. (e) DMS, NBS, $CH_2Cl_2$, 67%. (f) $PhSO_2Na$, DMF, 89%. (g) *t*-BuOK, TBAI, THF; **10**, THF. (h) TBAF, THF, 61% over 2 steps. (i) Pd(dppp), $LiBHEt_3$, THF, 76% (3:1, **18a**/**18b**).

**18a** using Pd(dppp)/$LiEt_3BH$ as the desulfonylation reagent.[14] Variation of the protective group on the alcohol (MOM, MEM, TBDPS), or the nature of the hydride source, did not improve this ratio. The mixture of isomers was carried through to the final product as a 3:1 mixture (NMR) of double-bond regioisomers, but could not be separated at any stage.

In exploring other approaches to sulfone anion coupling, we prepared the *β*-hydroxysulfone intermediate **19** from the sulfone **16** and the aldehyde prepared from **8**. However, the sequential removal of the sulfone and hydroxyl groups was not successful, resulting in ring opening and elimination products.[15] When we attempted to "protect" the olefin by oxidizing it to the diol **20**, the desulfonylation led to the Julia elimination product even when the hydroxyls were protected.

Having access to the diene **21** by the elimination of the *β*-hydroxysulfone **19**, we attempted many conditions for the selective reduction of the olefin adjacent to the cyclopropane.[16] Treatment with diimide led to the slow and unselective reduction of both olefins. The use of other reducing systems (Rh/C, $PtO_2$, Wilkinson's catalyst) under a hydrogen atmosphere also failed to provide the desired precursor to **1**. In the hope of providing an anchor for the catalyst to favor the selective reduction of the undesired disubstituted double bond, we attempted the reaction with a variety of catalysts on the primary alcohol rather than the ester. Again, no selectivity was observed.

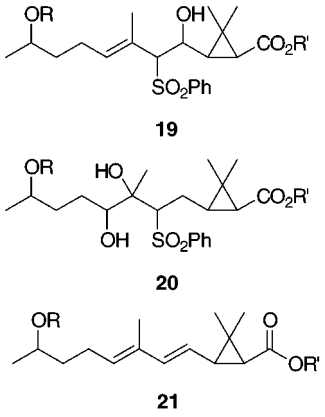



**Figure 3.**

After exploring several unproductive approaches, we concluded that the Julia coupling, through a different disconnection, might prove successful (Figure 4). Thus a sulfone anion coupling was envisaged with ketone **22** derived from an extension of the original intermediate **8**. This type of disconnection was also the basis of the Fukumoto synthesis.[5] However, previous work in this area did not augur well for the creation of the *E*-trisubstituted olefin using a phenyl sulfone union.[17] This prompted us to look at heteroaromatic sulfone anions to effect the coupling and subsequent elimination.

Recent work by Kende,[18] S. Julia,[19] and Kocienski[20] showed that heterocyclic sulfone anions offered an advantageous alternative to the classical phenyl sulfone,

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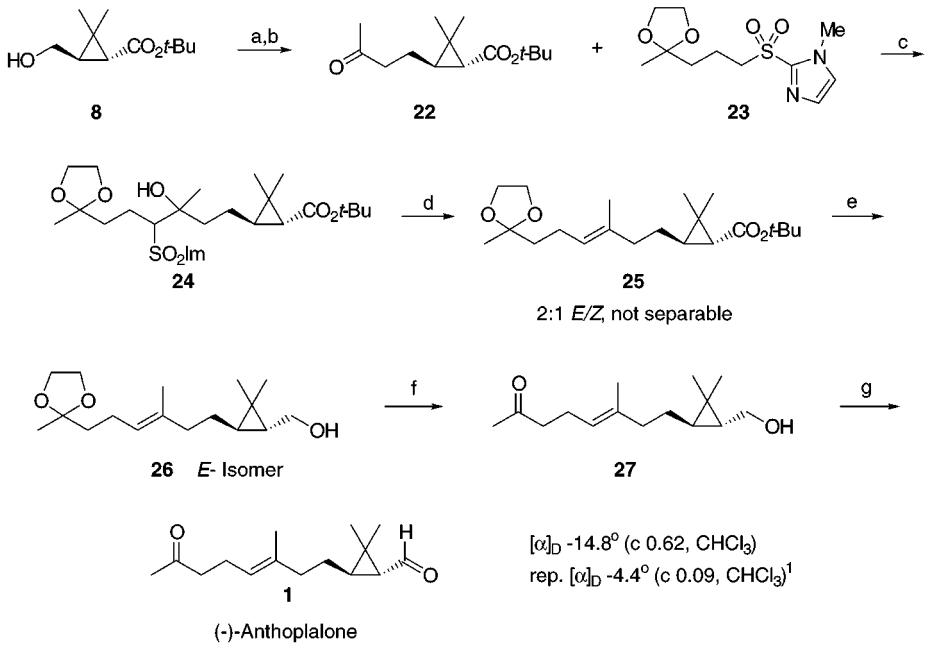
**Scheme 3**[a]




[a] Reagents: (a) DMSO, $(COCl)_2$, $Et_3N$, $CH_2Cl_2$; $Ph_3P{=}CHC(O)Me$. (b) $H_2$, $Pd(OH)_2/C$, EtOAc, 82% over 2 steps. (c) BuLi, THF, −78 °C, 1 h., 98%. (d) $SmI_2$, THF, 84%. (e) $LiAlH_4$, THF, 55 °C, 87%. Separation of E/Z isomers. (f) Amberlite (IR-120, $H^+$), MeOH, 79%. (g) TPAP, NMO, 4 Å sieves, $CH_2Cl_2$, 75%.

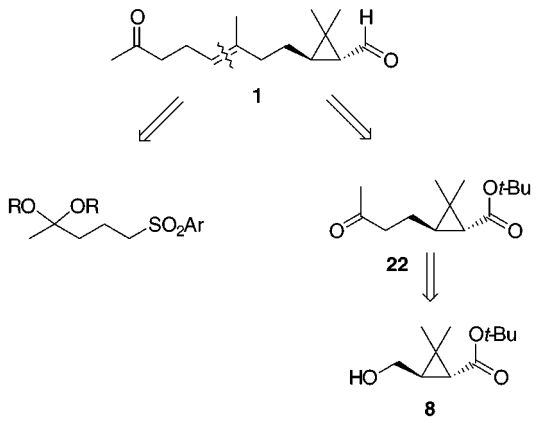



**Figure 4.**

since elimination to the olefin is highly facilitated. Work in this area has focused primarily on additions of sulfone anions to aldehydes. In fact, using benzothiazole sulfone anions on model ketones failed to provide the desired olefin in our hands in significant amount.

We then turned to an imidazole sulfone anion for the coupling to ketone **22**, since in such cases, reduction with $SmI_2$ need not be done in the presence of HMPA.[18,21] Furthermore, it has been shown that the presence of HMPA lowers the E/Z ratio in the cleavage vinyl sulfones.[22]

Thus, the required ketone **22** was prepared from alcohol **8** using a one-pot Swern oxidation/Wittig olefination protocol, to give the corresponding volatile enone, which was hydrogenated in the presence of $Pd(OH)_2/C$ to give ketone **22** (Scheme 3). The lithium anion of sulfone **23** was added to **22**, to give the corresponding $\beta$-hydroxysulfone **24** as a mixture of isomers. Monitoring of the temperature (−78 °C) was crucial, because this addition is reversible at higher temperatures.[23] Treatment of **24** with $SmI_2$ led to **25** as a 2:1 mixture of *E*/*Z*-isomers.[6n,s] Although this ratio constitutes an improvement of the originally reported ratio of 1:2.6 (*E*/*Z*),[5] it is still disappointing, even if one can ultimately resort to recycling the minor isomer.[24] Attempts to improve this ratio by

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varying the temperature and the use of additives ($MgBr_2$, $ZnCl_2$, ethylene glycol) were not met with success.

After reduction of ester **25** to primary alcohol **26** with LAH, the isomers could be separated by chromatography. The *E*-isomer was converted into the natural product by acidic deprotection of the ketal and oxidation of the primary alcohol with tetrapropylammonium perruthenate (TPAP).[25] Although the NMR spectral characteristics were identical to those reported,[1] the value of the optical rotation of our synthetic sample was found to be significantly greater than the one reported for the natural product.[1] This may be due to the low concentration and the small amount of sample available from natural sources.

## Conclusion

The total synthesis of enantiopure anthoplalone was accomplished in only nine steps and overall yield of 9% from readily available precursors. A number of connectivities were investigated utilizing various sulfone anion couplings to appropriately functionalized cyclopropanes, which are available in enantiopure form utilizing allylic phosphonamides as chiral reagents.[26] Securing the correct regioisomer or the *E*-geometry of the trisubstituted double bond proved to be a major challenge. Our total synthesis of (−)-anthoplalone also confirmed the absolute configuration as 2*R*, 3*R*.

## Experimental Section

**General Procedures.** All commercially available reagents were used without further purification. Solvents were distilled under positive pressure of dry nitrogen before use; THF and ether, from K/benzophenone; and $CH_2Cl_2$ and toluene, from $CaCl_2$. NMR ($^1H$, $^{13}C$, $^{31}P$) spectra were recorded on 300, 400, or 600 MHz spectrometers in $CDCl_3$, and DEPT experiments were performed routinely. Low- and high-resolution mass spectra were measured using fast atom bombardment (FAB) or electrospray techniques. Optical rotations were measured at the sodium line at ambient temperature. Flash column chromatography[27] was performed in the usual way using (40−60 $\mu$m) silica gel. Melting points are uncorrected.

**3(*R*)-[2-(1,3-Dimethyl-2-oxo-octahydro-2$\lambda^5$-benzo[1,3,2]-diazaphosphol-2-yl)-vinyl]-2,2-dimethylcyclopropane-1(*R*)carboxylic Acid *tert*-Butyl Ester (4).** To a solution of *n*-BuLi (0.334 mL, 0.836 mmol, 2.5 M solution in hexanes) in $Et_2O$ (4 mL) was added phosphonamide **5** (200 mg, 0.760 mmol) in $Et_2O$ at −78 °C under a nitrogen atmosphere. After 5 min, *tert*-butyl 3,3-dimethyl acrylate **6** (143 mg, 0.916 mmol) in $Et_2O$ was added. The solution was stirred for 16 h at −78 °C and then poured in a 1:1 mixture of aqueous $NH_4Cl$ and EtOAc (100 mL). The product was extracted with EtOAc (3 × 100 mL) and dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (95:5 EtOAc/MeOH) to give the title compound as a pale yellow oil (150 mg, 46%): $[\alpha]_D$ + 28.7 (*c* 1.82, $CHCl_3$); $^1H$ (400 MHz, $CDCl_3$) $\delta$ (ppm) 6.41 (1H, ddd, $J_1$ = 9.4 Hz, $J_2$ = 16.5 Hz, $J_3$ = 19.9 Hz), 5.53 (1H, dd, $J_1$ = 6.5 Hz, $J_2$ = 21.3 Hz), 2.76−2.70 (1H, m), 2.49−2.43 (6H, m), 2.44−2.38 (1H, m), 2.08 (1H, dd, $J_1$ = 5.3 Hz, $J_2$ = 9.3 Hz), 2.01−1.95 (2H, m), 1.83−1.78 (2H, m), 1.69 (1H, d, $J$ = 5.3 Hz), 1.43 (9H, s), 1.39−1.17 (3H, m), 1.22 (3H, s), 1.18 (3H, s), 1.13−1.00 (1H, m); $^{13}C$ (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 170.31, 150.87, 150.82, 120.90, 119.37, 80.62, 64.65, 64.57, 63.62, 63.56, 36.22, 36.17, 35.93, 29.35, 28.72, 28.67, 28.63, 28.56, 28.54, 28.11, 28.08, 28.00, 24.17, 24.08, 22.04, 20.08; $^{31}P$ (161.3 MHz, $CDCl_3$) $\delta$ (ppm) 32.80; LRMS 405 (M + Na), 383 (M + 1), 327 (M − 55); HRMS ($C_{20}H_{36}N_2O_3P$) calcd 383.24637, found 383.24500, $\sigma$ = 3.6 ppm.

**3(*R*)-Hydroxymethyl-2,2-dimethyl-cyclopropane-1(*R*)-carboxylic Acid *tert*-Butyl Ester (8).** The preceding compound **4** (547 mg, 1.43 mmol) was dissolved in $CH_2Cl_2$ (23 mL) and MeOH (26 mL). The solution was cooled to −78 °C, and ozone was bubbled until the solution turned blue. The solution was then flushed with nitrogen to remove excess ozone, and $NaBH_4$ (110 mg, 2.89 mmol) was added. The solution was then warmed to 0 °C and stirred until the aldehyde had disappeared by TLC analysis. Acetone (10 mL) was added, and the solvents were evaporated. The residue was dissolved in EtOAc, washed with aqueous $NH_4Cl$ and brine. The organic phase was dried with $Na_2SO_4$ and evaporated. The residue was purified by flash chromatography (1:1 EtOAc/hexanes) to give the title compound as a colorless oil (239 mg, 83%): $[\alpha]_D$ −38.7 (*c* 0.86, $CHCl_3$); $^1H$ (400 MHz, $CDCl_3$) $\delta$ (ppm) 3.65 (1H, dd, $J_1$ = 6.6 Hz, $J_2$ = 12.6 Hz), 3.48 (1H, dd, $J_1$ = 8.2 Hz, $J_2$ = 12.6 Hz), 2.60 (1H, broad), 1.58−1.53 (1H, m), 1.38 (9H, s), 1.25 (1H, d, $J$ = 5.5 Hz), 1.16 (3H, s), 1.12 (3H, s); $^{13}C$ (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 171.44, 80.15, 61.51, 33.54, 32.49, 28.07, 27.87, 26.36, 20.53; LRMS 201 (M + 1), 154, 107; HRMS calcd ($C_{11}H_{21}O_3$) 201.14906, found 201.14950, $\sigma$ = 3.6 ppm.

**Synthesis of 8 from Chrysanthemic Acid (9).** To a solution of chrysanthemic acid (180 mg, 1.07 mmol) in $CH_2Cl_2$ (5 mL) at 0 °C was added *tert*-butyl 2,2,2-trichloroacetimidate (0.47 mL, 2.1 mmol) in pentane (5 mL), followed by $BF_3 \cdot Et_2O$ (10 $\mu$L). After stirring for 12 h, $NaHCO_3$ (1 g) was added, the solids were filtered, and the solvents were evaporated. The product was purified by column chromatography (9:1 hexanes/EtOAc), and the product was carried directly into the next step.

A solution of the ester in a mixture of $CH_2Cl_2$ (4 mL) and EtOH (4 mL) was cooled to −78 °C, and ozone was bubbled until the solution turned blue. The solution was then flushed with nitrogen to remove excess ozone, and $NaBH_4$ (41 mg, 1.08 mmol) was added. The solution was warmed to 0 °C and stirred until the aldehyde had disappeared by TLC analysis. Acetone (5 mL) was added, and the solvents were evaporated. The residue was dissolved in EtOAc and washed with aqueous $NH_4Cl$ and brine. The organic phase was dried with $Na_2SO_4$ and evaporated. The residue was purified by flash chromatography (1:1 EtOAc/hexanes) to give the title compound as a colorless oil (134 mg, 63%): $[\alpha]_D$ −35.5 (*c* 1.02, $CHCl_3$); the NMR and MS data are identical to **8** prepared from phosphonamide **4**.

**3(*R*)-Bromomethyl-2,2-dimethylcyclopropane-1(*R*)-carboxylic Acid *tert*-Butyl Ester (10).** To a solution of **8** (60 mg, 0.30 mmol) and $CBr_4$ (124 mg, 0.38 mmol) in acetonitrile (7 mL) at 0 °C was added $PPh_3$ (118 mg, 0.45 mmol) in small portions under a nitrogen atmosphere, and the solution was warmed to room temperature and stirred for 3 h. The solvent was then evaporated and the residue purified by column chromatography (9:1 hexanes/EtOAc) to give the title compound as a volatile liquid (58 mg, 73%): $[\alpha]_D$ − 4.4 (*c* 0.77, $CHCl_3$); $^1H$ (400 MHz, $CDCl_3$) $\delta$ (ppm) 3.64 (1H, dd, $J_1$ = 6.5 Hz, $J_2$ = 10.5 Hz), 3.24 (1H, t, $J$ = 10.2 Hz), 1.84 (1H, ddd, $J_1$ = 5.4 Hz, $J_2$ = 6.5 Hz, $J_3$ = 9.9 Hz), 1.45 (9H, s), 1.36 (1H, d, $J$ = 5.3 Hz), 1.24 (3H, s), 1.23 (3H, s); $^{13}C$ (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 170.24, 80.46, 36.08, 33.55, 32.55, 28.84, 28.10, 20.32, 20.24; MS, the compound does not ionize with FAB and electrospray.

***tert*-Butyl-(1,5-dimethylhex-4-enyloxy)diphenylsilane (12).** To a solution of 6-methyl-5-hepten-2-ol **11** (4.0 g, 31 mmol) and imidazole (4.6 g, 68 mmol) in DMF (150 mL) was added TBDPSCl (8.9 mL, 34.1 mmol) under a nitrogen atmosphere, and the solution was stirred overnight for 18 h. Water was added to the solution, and the product was extracted with ether. The organic layer was washed with brine, dried with $Na_2SO_4$, and evaporated. The residue was purified by flash chromatography (hexanes) to give the title compound as a colorless oil (11.3 g, quantitative): $^1H$ (400 MHz, $CDCl_3$)

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$\delta$ (ppm) 7.76−7.68 (4H, m), 7.48−7.36 (6H, m), 5.03−4.98 (1H, m), 3.92−3.85 (1H, m), 2.04−1.93 (2H, m), 1.67 (3H, d, $J$ = 0.8 Hz), 1.57 (3H, d, $J$ = 0.8 Hz), 1.55−1.42 (2H, m), 1.10 (3H, d, $J$ = 5.9 Hz), 1.09 (9H, s); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 135.83, 135.82, 134.87, 134.49, 131.17, 129.34, 129.28, 127.37, 127.29, 124.35, 69.27, 39.49, 26.96, 25.59, 23.89, 23.08, 19.20, 17.50; LRMS 365 (M − H), 309 (M − *t*-Bu), 289 (M − Ph); HRMS calcd ($C_{24}H_{33}OSi$) (M − H) 365.23007, found 365.23100, $\sigma$ = −2.5 ppm.

**6-(*tert*-Butyldiphenylsilanyloxy)-2-methylhept-2(*E*)-enoic Acid Ethyl Ester (13).** Compound **12** (3 g, 8.19 mmol) was dissolved in 150 mL of $CH_2Cl_2$ and cooled to −78 °C. Ozone was bubbled in the solution until the blue color persisted, at which time nitrogen was passed through the solution to remove the excess ozone. Dimethyl sulfide (4 mL) was added, the solution was warmed to room temperature, and the solvents were evaporated to give the crude aldehyde as a yellowish oil, which was used in the next step without further purification.

To a suspension of dry LiCl (1.39 g, 32.8 mmol) and triethyl 2-phosphonopropionate (6.98 mL, 32.8 mmol) in MeCN (80 mL) was added DBU (3.65 mL, 24.1 mmol). The mixture was stirred at room temperature until it became homogeneous. Then the aldehyde in MeCN (25 mL) was added to the solution at 0 °C. The solution was stirred until the reaction was complete (∼3 h), the solvent was removed under reduced pressure, the residue was dissolved in $CH_2Cl_2$, washed with water and brine, and dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by flash chromatography (15:1 hexanes/EtOAc) to give the title compound as a colorless oil (3.09 g, 89%): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.71−7.67 (4H, m), 7.46−7.36 (6H, m), 6.71−6.65 (1H, m), 4.19 (2H, q, $J$ = 7.1 Hz), 3.94−3.86 (1H, m), 2.26−2.13 (2H, m), 1.78 (3H, d, $J$ = 1.3 Hz), 1.64−1.49 (2H, m), 1.30 (3H, t, $J$ = 7.2 Hz), 1.10 (3H, d, $J$ = 6.1 Hz), 1.07 (9H, s); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 168.11, 141.94, 135.78, 135.73, 134.56, 134.19, 129.47, 129.39, 127.64, 127.45, 127.35, 68.98, 60.26, 37.92, 26.92, 24.45, 23.04, 19.17, 14.22, 12.17; LRMS 423 (M − H), 367 (M − *t*-Bu); HRMS calcd ($C_{26}H_{35}O_3Si$) 423.23553, found 423.23330, $\sigma$ = 5.3 ppm.

**6-(*tert*-Butyldiphenylsilanyloxy)-2-methylhept-2(*E*)-en-1-ol (14).** To a solution of ester **13** (2.4 g, 5.7 mmol) in toluene (60 mL) at −78 °C was added DIBAL-H (12.4 mmol, 1.5 M solution in toluene) under a nitrogen atmosphere. The solution was stirred at that temperature for 30 min, then at room temperature for 1 h, and cooled to 0 °C, and MeOH (20 mL) was added *slowly*. The solution was stirred for 1 h, and the translucent solid was filtered off and washed with boiling THF (200 mL). The solvents were then evaporated and the residue was purified by flash chromatography (95:5 hexanes/EtOAc) to give the title compound as a colorless oil (2.15 g, 98%): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.73−7.70 (4H, m), 7.46−7.28 (6H, m), 5.29−5.25 (1H, m), 3.95 (2H, s), 3.92−3.85 (1H, m), 2.18−1.97 (2H, m), 1.62 (3H, s), 1.59−1.42 (2H, m), 1.41 (1H, s), 1.12 (3H, d, $J$ = 6.1 Hz), 1.08 (9H, s); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 135.83, 135.81, 134.74, 134.60, 134.43, 129.40, 129.34, 127.39, 127.32, 126.01, 69.11, 68.84, 39.06, 26.96, 23.42, 23.06, 19.18, 13.47; LRMS 381 (M − 1), 239 (TBDPS); HRMS calcd ($C_{24}H_{33}O_2Si$) 381.22498, found 381.22370, $\sigma$ = 3.3 ppm.

**(6-Bromo-1,5-dimethylhex-4(*E*)-enyloxy)-*tert*-butyldiphenylsilane (15).** To a solution of NBS (1.52 g, 8.57 mmol) in $CH_2Cl_2$ (25 mL) was added DMS (0.75 mL, 10.3 mmol) very slowly at 0 °C under a nitrogen atmosphere. The mixture was cooled to −20 °C, **14** (2.18 g, 5.71 mmol) in $CH_2Cl_2$ (8 mL) was added dropwise, the temperature was raised to 0 °C, and the solution was stirred for 3 h. The solution was then diluted with pentane and washed with cold water and cold brine. The organic phase was dried with $Na_2SO_4$ and evaporated, and the residue was rapidly purified by flash chromatography (9:1 hexanes/EtOAc) to give the title compound as a colorless oil (1.70 g, 67%): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.70−7.67 (4H, m), 7.46−7.27 (6H, m), 5.45−5.42 (1H, m), 3.92 (2H, s), 3.90−3.81 (1H, m), 2.10−1.93 (2H, m), 1.69 (3H, t, $J$ = 0.7 Hz), 1.57−1.40 (2H, m), 1.08 (3H, d, $J$ = 6.1 Hz), 1.06 (9H, s); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 135.80, 135.77, 134.63, 134.29, 131.73, 131.24, 129.34, 127.41, 127.32, 68.95, 41.75, 38.49, 26.93, 24.09, 23.05, 19.16, 14.43; LRMS 445 (M + 1), 389 (M − *t*-Bu), 365 (M − Br); HMRS calcd ($C_{24}H_{32}OSi^{79}Br$) 443.14059, found 443.14150, $\sigma$ = −2.0 ppm.

**(6-Benzenesulfonyl-1.5-dimethylhex-4(*E*)-enyloxy)-*tert*-butyldiphenylsilane (16).** To a solution of **15** (1.54 g, 3.46 mmol) in DMF (85 mL) was added sodium benzene sulfinate (1.13 g, 6.89 mmol) under a nitrogen atmosphere. The solution was stirred for 15 h at room temperature, ether was added, followed by successive washes with water and brine, and the organic layer was dried with $Na_2SO_4$. After evaporation of the solvent, the residue was purified by flash chromatography (5:1 hexanes/EtOAc) to give the title compound as a colorless oil (1.56 g, 89%): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.82−7.81 (2H, m), 7.71−7.66 (3H, m), 7.60−7.56 (1H, m), 7.50−7.36 (9H, m), 4.89−4.85 (1H, m), 3.78−3.70 (1H, m), 3.67 (2H, s), 2.00−1.83 (2H, m), 1.71 (3H, d, $J$ = 1.2 Hz), 1.36−1.17 (2H, m), 1.07 (9H, s), 1.04 (3H, d, $J$ = 8.5 Hz); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 138.18, 136.07, 135.79, 135.75, 134.56, 134.28, 133.37, 129.50, 129.43, 128.74, 128.43, 127.46, 127.37, 123.15, 68.85, 66.12, 38.33, 26.95, 24.05, 23.00, 19.18, 16.14; LRMS 507 (M + 1), 429 (M − Ph); HRMS ($C_{30}H_{39}O_3SiS$) calcd 507.23892, found 507.23731, $\sigma$ = 3.2 ppm.

**3(*R*)-(2-Benzenesulfonyl-7-hydroxy-3-methyloct-3(*E*)-enyl)-2,2-dimethylcyclopropane-1(*R*)-carboxylic Acid *tert*-Butyl Ester (17).** To a solution of **16** (192 mg, 0.380 mmol) and tetrabutylammonium iodide (84 mg, 0.228 mmol) in THF (3 mL) was added *t*-BuOK (0.418 mmol, 1 M solution in THF) under a nitrogen atmosphere at −78 °C. After 10 min, bromide **10** (50 mg, 0.190 mmol) in THF (3 mL) was added dropwise to the yellow solution, which was left to slowly warm to room temperature overnight, and brine was added. The solution was then extracted with EtOAc, and the organic phase was dried with $Na_2SO_4$ and evaporated. The residue was purified by flash chromatography (9:1 hexanes/EtOAc) to give a mixture of starting sulfone and addition product.

The mixture was dissolved in 15 mL of THF and cooled to 0 °C, and TBAF (0.760 mmol, 1 M solution in THF) was added under a nitrogen atmosphere. The solution was stirred for 10 h at room temperature, after which aqueous $NH_4Cl$ was added. The solution was then extracted with EtOAc, the organic phase was dried with $Na_2SO_4$ and evaporated, and the residue was purified by flash chromatography (2:1 hexanes/EtOAc) to give the title compound as a colorless oil as a mixture of isomers (104 mg, 61%): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.80−7.78 (2H, m), 7.61−7.58 (1H, m), 7.52−7.47 (2H, m), 5.21−5.16 (0.5H, m), 5.15−5.10 (0.5H, m), 3.62−3.52 (1H, m), 3.51−3.44 (1H, m), 2.25−2.17 (0.5H, m), 2.07−1.92 (2H, m), 1.89−1.76 (0.5H, m), 1.68−1.65 (4H, m), 1.39 (5H, s), 1.38 (4H, s), 1.31−1.22 (4H, m), 1.15−1.03 (10H, m); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 171.32, 171.28, 137.95, 137.92, 135.79, 135.69, 133.27, 128.67, 128.64, 126.64, 126.61, 126.48, 80.08, 80.05, 80.00, 67.08, 67.05, 67.01, 51.93, 37.96, 37.94, 37.91, 37.89, 34.29, 34.27, 33.29, 33.24, 29.70, 29.59, 29.54, 29.07, 28.99, 28.12, 28.11, 27.68, 27.56, 25.90, 25.88, 25.40, 24.66, 24.53, 24.43, 24.36, 24.33, 24.31, 23.88, 23.42, 23.39, 23.36, 23.34, 21.58, 20.96, 20.37, 20.32, 20.30, 20.13, 13.96, 13.81, 13.68, 13.55, 13.49; HRMS calcd ($C_{25}H_{39}O_5S$) 451.25183, found 451.25410, $\sigma$ = −5.0 ppm.

**3(*R*)-(7-Hydroxy-3-methyloct-3(*E*)-enyl)-2,2-dimethylcyclopropane-1(*R*)-carboxylic Acid *tert*-Butyl Ester (18a and 18b).** To a solution of sulfone **17** (50 mg, 0.111 mmol) in THF (6 mL) was added $PdCl_2$(dppp) (2 mg, 0.003 mmol), and the solution was cooled to 0 °C under a nitrogen atmosphere. The solution was stirred for a few minutes, and $LiBHEt_3$ (0.333 mmol, 1 M solution in THF) was added dropwise, upon which the solution turned red. The reaction was stirred for 3 h at that temperature, and 5% NaOH (2 mL) followed by KCN (10 mg) were added. The solution was then diluted with brine and extracted with ether. The organic phase was dried with $Na_2SO_4$ and evaporated, and the residue was purified by flash chromatography (9:1 hexanes/EtOAc) to give the title compounds as a colorless oil (26 mg, mixture of 2 regioisomers, 76%): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 5.15−5.12 (1H, m), 3.80−3.77 (1H, m), 2.11−1.99 (4H, m), 1.68 (1H, s), 1.61 (2.25H, s),

1.57 (0.75H, s) 1.52−1.40 (5H, m), 1.43 (9H, s), 1.19 (3H, d, $J$ = 6.2 Hz), 1.18 (3H, s), 1.12 (3H, s), 1.07 (1H, d, $J$ = 5.5 Hz); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 172.18, 135.09, 135.05, 124.33, 124.26, 123.77, 123.22, 79.63, 67.89, 67.72, 39.10, 39.08, 38.67, 33.96, 32.63, 32.59, 32.40, 32.37, 31.57, 29.56, 28.19, 26.92, 26.84, 26.69, 24.27, 24.23, 23.90, 23.79, 23.40, 23.35, 23.16, 21.29, 21.20, 20.70, 15.85, 15.81; LRMS 311 (M + 1), 237 (M − O*t*-Bu); HRMS calcd ($C_{19}H_{35}O_3$) 311.25861, found 311.26023, $\sigma$ = 0.3 ppm.

**2,2-Dimethyl-3(*R*)-(3-oxobutyl)cyclopropane-1(*R*)-carboxylic acid *tert*-Butyl Ester (22).** To a solution of oxalyl chloride (0.151 mL, 1.73 mmol) in $CH_2Cl_2$ (5 mL) at −78 °C was added dropwise DMSO (0.237 mL, 3.35 mmol) under a nitrogen atmosphere. A solution of **8** (239 mg, 1.20 mmol) in $CH_2Cl_2$ (5 mL) was added dropwise via cannula. The solution was stirred 30 min, and $Et_3N$ (0.635 mL, 4.54 mmol) was added dropwise. Then the mixture was warmed to room temperature and stirred for 90 min. A solution of 1-triphenylphosphoranylidene-2-propanone (1.53 g, 4.78 mmol) in $CH_2Cl_2$ (10 mL) was added. After stirring for 24 h, a further 1.53 g of Wittig reagent was added, and the solution was stirred for another 24 h. The solvent was removed under reduced pressure, and the residue purified by flash chromatography (9:1 hexanes/EtOAc). The compound was carried into the next step directly because of its volatility.

To a solution of the enone in EtOAc (15 mL) was added $Pd(OH)_2$ (85 mg, 10% w/w), and the flask was evacuated prior to placing it under $H_2$ atmosphere. The suspension was stirred for 4 h, the catalyst was filtered off, and the solvent was evaporated to give the desired ketone (237 mg) as a colorless and volatile liquid: $[\alpha]_D$ −25.3 (*c* 0.63, $CHCl_3$); $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 2.44 (2H, t, $J$ = 7.6 Hz), 2.08 (3H, s), 1.62−1.49 (2H, m), 1.39−1.34 (1H, m), 1.36 (9H, s), 1.10 (3H, s), 1.07 (3H, s), 1.03 (1H, d, $J$ = 5.5 Hz); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 208.29, 171.74, 79.75, 43.22, 33.80, 31.64, 29.93, 28.08, 26.74, 22.51, 21.03, 20.51; LRMS (M + 1) 241; HMRS calcd ($C_{14}H_{25}O_3$) 241.18037, found 241.17960, $\sigma$ = 3.2 ppm.

**1-Methyl-2-[3-(2-methyl-[1,3]dioxolan-2-yl)propane-1-sulfonyl]-1*H*-imidazole (23).** To a suspension of NaH (636 mg of a 60% dispersion in oil, 15.9 mmol) in DMF (20 mL) was added slowly a solution of 2-mercapto-1-methylimidazole (2.1 g, 18.3 mmol) in DMF (20 mL) at 0 °C. After the evolution of gas had ceased, the commercially available 5-chloro-2-pentanone ethylene ketal (2.0 g, 12.2 mmol) was added dropwise. The solution was stirred at room temperature for 12 h and quenched with $H_2O$ (30 mL). The product was then extracted with ether, and the organic phase was then successively washed with $H_2O$, saturated $NaHCO_3$, and brine. The organic phase was dried with $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (2:1 EtOAc/hexanes) to give a yellowish oil (1.2 g, 41%): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 6.98 (1H, d, $J$ = 1.3 Hz), 6.85 (1H, d, $J$ = 1.3 Hz), 3.87−3.81 (4H, m), 3.55 (3H, s), 3.06−3.00 (2H, m), 1.71−1.68 (4H, m), 1.23 (3H, s); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 141.61, 129.07, 121.93, 109.55, 64.50, 37.70, 34.37, 33.06, 24.22, 23.75; LRMS 243 (M + 1), 154, 129 (M − imidazole); HRMS calcd ($C_{11}H_{19}N_2O_2S$) 243.11673, found 243.11630, $\sigma$ = 1.8 ppm.

To a suspension of this product (1.15 g, 4.8 mmol) and $NaHCO_3$ (2.4 g, 28.8 mmol) in $CH_2Cl_2$ (50 mL) was added MCPBA (2.5 g, 14.4 mmol). The solution was stirred at room temperature for 3 h and then poured into a 1:1 mixture of saturated $NaHCO_3$ and 10% aqueous $Na_2S_2O_3$. The product was extracted with $CH_2Cl_2$, and the organic phase was washed with brine, dried ($MgSO_4$), and evaporated. The crude product was purified by flash chromatography (2:1 EtOAc/hexanes) to give the title compound as a white solid (1.12 g, 85% yield): mp 44−45 °C ($Et_2O$, pentane); $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.09 (1H, d, $J$ = 0.9 Hz), 6.98 (1H, d, $J$ = 0.7 Hz), 3.94 (3H, s), 3.93−3.85 (4H, m), 3.48−3.44 (2H, m), 1.91−1.87 (2H, m), 1.73 (2H, t, $J$ = 7.5 Hz), 1.25 (3H, s); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 141.68, 128.97, 125.47, 109.19, 64.56, 55.89, 36.86, 34.40, 23.75, 16.86; LRMS 275 (M + 1), 231, 136, 87; HRMS calcd ($C_{11}H_{19}N_2O_4S$) 275.10657, found 275.10700, $\sigma$ = −1.6 ppm. Anal. Calcd ($C_{11}H_{18}N_2O_4S$): C 48.16, H 6.61, N 10.21, S 11.69. Found: C 48.07, H 6.72, N 10.14, 11.62.

**3(*R*)-[3-Hydroxy-3-methyl-6-(2-methyl[1,3]dioxolan-2-yl)-4-(1-methyl-1*H*-imidazole-2-sulfonyl)hexyl]-2,2-dimethylcyclopropane-1(*R*)-carboxylic Acid *tert*-Butyl Ester (24).** To a solution of sulfone **23** (356 mg, 1.30 mmol) in THF (4 mL) was slowly added BuLi (1.43 mmol, 2.5 M solution in hexane) at −78 °C under a nitrogen atmosphere. Ketone **22** (104 mg, 0.430 mmol) in THF (4 mL) was added slowly, and the solution was stirred at −78 °C for 1 h. Then the reaction was stopped by adding saturated $NH_4Cl$ (5 mL) at −78 °C, and the mixture was allowed to warm to room temperature. The product was extracted with EtOAc, and the organic phase was washed with brine, dried with $MgSO_4$, and evaporated. The residue was purified by flash chromatography (3:1 hexanes/EtOAc) to give the title compound as an inseparable mixture of isomers (217 mg, 98%): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.11 (0.4H, s) 7.10 (0.6H, s), 6.98 (0.4H, s), 6.97 (0.6H, s), 4.18 (1H, broad), 3.96 (1.5H, s), 3.95 (1.5H, s) 3.89−3.80 (4H, m), 3.67−3.65 (0.6H, m), 3.53−3.50 (0.4H, m), 2.03−1.79 (3H, m), 1.74−1.44 (5H, m), 1.41 (4H, s) 1.40 (5H, s), 1.38−1.32 (3H, m), 1.20−1.05 (11H, m); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 171.96, 142.70, 142.18, 128.87, 128.82, 128.71, 125.53, 109.10, 109.02, 79.72, 74.57, 74.53, 74.37, 74.31, 73.45, 73.41, 72.23, 72.15, 64.45, 64.41, 60.26, 41.26, 41.19, 39.17, 39.10, 38.22, 37.83, 35.19, 35.13, 33.96, 33.88, 33.83, 33.80, 32.44, 32.40, 32.28, 28.16, 28.04, 26.85, 26.81, 26.77, 25.81, 25.76, 23.94, 23.88, 23.45, 22.51, 22.47, 22.01, 21.96, 21.14, 21.02, 20.76, 20.68; LRMS 515 (M + 1); HRMS calcd ($C_{25}H_{43}N_2O_7S$) 515.27911, found 515.27760, $\sigma$ = 1.8 ppm.

**2,2-Dimethyl-3(*R*)-[3-methyl-6-(2-methyl-[1,3]dioxolan-2-yl)hex-3-enyl]cyclopropane-1(*R*)-carboxylic Acid *tert*-Butyl Ester (25).** Under a nitrogen atmosphere were placed metallic Sm (246 mg, 1.64 mmol) and $EtI_2$ (369 mg, 1.31 mmol). Nitrogen was passed for 5 min, THF (10 mL) was added, and the solution was stirred until a deep blue color persisted (45−60 min), after which the hydroxy sulfone **24** (217 mg, 0.422 mmol) in THF (10 mL) was added dropwise. The reaction was complete within 20 min, and the solution was poured in 10% aqueous $Na_2S_2O_3$. The product was extracted with EtOAc, and the organic phase was washed with brine, dried with $MgSO_4$, and evaporated. The residue was purified by flash chromatography (5:1 hexanes/EtOAc) to give the title compound as an inseparable mixture of isomers (125 mg, 84%, 2:1 *E*/*Z*): $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 5.12−5.08 (1H, m), 3.94−3.88 (4H, m), 2.10−1.99 (4H, m), 1.65−1.60 (3H, m), 1.57 (2H, s), 1.48−1.33 (2H, m), 1.44 (3H, s), 1.43 (6H, s), 1.30 (3H, s), 1.22−1.18 (1H, m), 1.17 (1H, s), 1.16 (2H, s), 1.13 (1H, s), 1.10 (2H, s), 1.07 (0.33H, d, $J$ = 5.4 Hz), 1.05 (0.66H, d, $J$ = 5.6 Hz); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 172.12, 172.06, 134.85, 134.67, 124.75, 124.14, 109.75, 109.69, 79.61, 79.55, 64.48, 39.31, 39.19, 38.91, 33.86, 32.41, 31.47, 28.14, 26.99, 26.91, 26.78, 23.66, 23.35, 22.52, 22.37, 21.17, 21.04, 20.71, 20.67, 15.78; LRMS 353 (M + 1), 297 (M − *t*-Bu), 279 (M − O*t*-Bu); HRMS calcd ($C_{21}H_{37}O_4$) 353.26920, found 353.27010, $\sigma$ = −2.6 ppm.

**{2,2-Dimethyl-3(*R*)-[3-methyl-6-(2-methyl-[1,3]dioxolan-2-yl)-hex-3(*E*)-enyl]-cyclopropyl}-1(*R*)-methanol (26).** To a suspension of LAH (32 mg, 0.842 mmol) in THF (2 mL) was added ester **25** (68 mg, 0.193 mmol) in THF (3 mL) at 0 °C under a nitrogen atmosphere. The reaction mixture was heated to 55 °C for 5 h and then quenched at 0 °C by carefully adding water (1 mL), 2 M NaOH (2 mL), and water (2 mL). The solid was filtered off, brine was added, and the product was extracted with EtOAc. The organic phase was dried with $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (7:1 petroleum ether/EtOAc) to give the title compound as a colorless oil (48 mg, 87%). The *E*/*Z*-isomers can be separated with the above conditions to give the pure *E*-isomer (30 mg): $[\alpha]_D$ +0.7 (*c* 0.93, $CHCl_3$); $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 5.13 (1H, dt, $J_1$ = 1.1 Hz, $J_2$ = 7.0 Hz), 3.99−3.89 (4H, m), 3.65 (1H, dd, $J_1$ = 6.9 Hz, $J_2$ = 11.4 Hz), 3.51 (1H, dd, $J_1$ = 8.3 Hz, $J_2$ = 11.4 Hz), 2.12−2.02 (2H, m), 2.03 (2H, t, $J$ = 7.3 Hz), 1.69−1.63 (2H, m), 1.60 (3H, s), 1.56−1.44 (2H, m), 1.32 (3H, s), 1.29 (1H, broad), 1.08 (3H, s), 1.06 (3H, s), 0.59−0.52 (1H, m), 0.34−0.28 (1H, m); $^{13}$C (100.4 MHz,

$CDCl_3$) $\delta$ (ppm) 135.15, 124.05, 109.77, 64.50, 63.79, 39.91, 38.94, 32.83, 29.11, 27.08, 23.66, 22.49, 21.71, 21.61, 19.75, 15.68; LRMS 283 (M + 1), 265 (M − OH), 115; HRMS calcd ($C_{17}H_{29}O_3$) 281.21167, found 281.21090, $\sigma = -2.7$ ppm.

**8(*R*)-(3(*R*)-Hydroxymethyl-2,2-dimethylcyclopropyl)-6-methyloct-5(*E*)-en-2-one (27).** To a solution of ketal **26** (28 mg, 0.099 mmol) in MeOH (3 mL) was added Amberlite (IR-120, $H^+$). The solution was stirred at room temperature for 4 h, and the resin was filtered off. The solvent was evaporated, and the residue was purified by flash chromatography (5:1 petroleum ether/EtOAc) to give the title compound as a colorless oil (19 mg, 79%): $[\alpha]_D$ +0.2 (*c* 0.61, $CHCl_3$); $^1$H (400 MHz, $CDCl_3$) $\delta$ (ppm) 5.10−5.06 (1H, m), 3.65 (1H, dd, $J_1 = 6.9$ Hz, $J_2 = 11.4$ Hz), 3.53 (1H, dd, $J_1 = 8.2$ Hz, $J_2 = 11.4$ Hz), 2.46 (2H, t, $J = 7.5$ Hz), 2.31−2.23 (2H, m), 2.13 (3H, s), 2.02 (2H, t, $J = 8.4$ Hz), 1.60 (3H, s), 1.53−1.47 (1H, m), 1.37−1.27 (1H, m), 1.25−1.23 (1H, broad), 1.08 (3H, s), 1.06 (3H, s), 0.58−0.52 (1H, m), 0.32−0.27 (1H, m); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 208.72, 136.34, 122.65, 63.78, 43.57, 39.89, 32.83, 29.78, 29.08, 27.03, 22.27, 21.71, 21.61, 19.78, 15.75; LRMS 239 (M + 1), 221 (M − OH); HRMS calcd ($C_{15}H_{27}O_2$) 239.2011, found 239.20000, $\sigma = +4.6$ ppm.

**(−)-Anthoplalone (1).** To a solution of alcohol **27** (17 mg, 0.071 mmol) and 4 Å molecular sieves (16 mg) in $CH_2Cl_2$ was added *N*-methylmorpholine oxide (16 mg, 0.137 mmol), followed by a catalytic amount of TPAP under a nitrogen atmosphere. After 15 min, the solution was loaded directly on a silica gel column, and purification by flash chromatography (100% $CH_2Cl_2$) gave the title compound (12.6 mg, 75%) as a pale yellow oil: $[\alpha]_D$ −14.8 (*c* 0.62, $CHCl_3$); $^1$H (600 MHz, $CDCl_3$) 9.30 (1H, d, $J = 5.7$ Hz), 5.08−5.02 (1H, m), 2.47 (2H, t, $J = 7.3$ Hz), 2.27 (2H, q, $J = 7.2$ Hz), 2.15 (3H, s), 2.05−2.02 (2H, m), 1.62 (3H, s), 1.61−1.55 (2H, m), 1.47−1.45 (1H, m), 1.39 (1H, t, $J = 5.2$ Hz), 1.30 (3H, s), 1.19 (3H, s); $^{13}$C (100.4 MHz, $CDCl_3$) $\delta$ (ppm) 208.57, 201.56, 135.25, 123.32, 43.47, 43.28, 39.08, 35.35, 30.80, 29.79, 26.49, 22.22, 22.09, 21.23, 15.73; LRMS 345 (M + thioglycerol), 237 (M + 1); HRMS calcd ($C_{15}H_{25}O_2$) 237.18546, found 237.18470, $\sigma = +3.2$ ppm. Also obtained: COSY, NOESY, HMQC.

**Acknowledgment.** We thank NSERC for financial assistance through the Medicinal Chemistry Chair Program. L.-D.C. thanks Servier Laboratories for a fellowship.

**Supporting Information Available:** $^1$H and $^{13}$C NMR spectra for **1**, **4** (also $^{31}$P NMR), **8**, **10**, **12**−**18**, and **22**−**27**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO990302N