

## An Efficient Total Synthesis of ( $\pm$ )-Sinulariol-B

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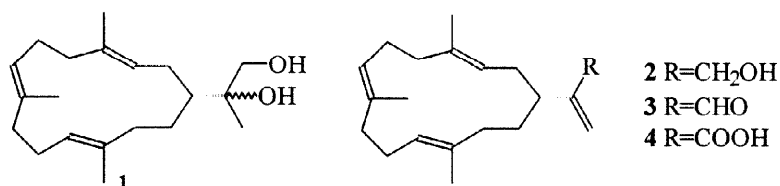
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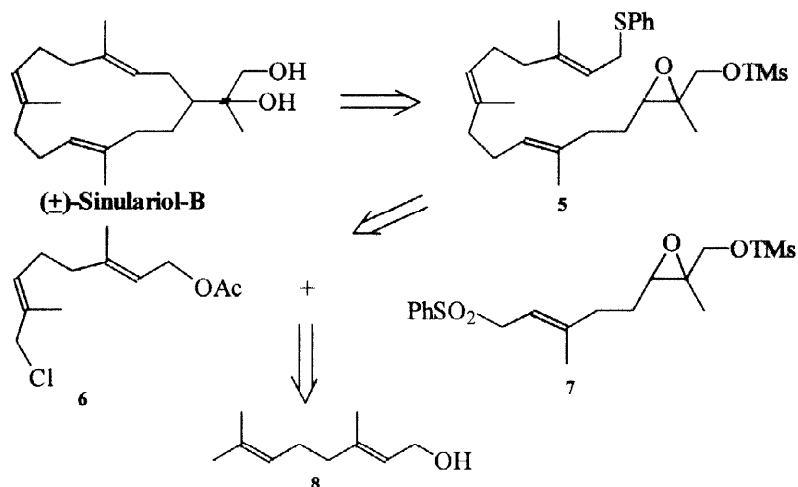
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**Abstract:** The first total synthesis of ( $\pm$ )-Sinulariol-B, a marine cembrandiol, was achieved in ten steps and ~10% overall yield from *E*-geraniol (**8**). The key steps were the coupling of sulfone **7** with allylic chloride **6** and the macrocyclization of precursor **5** by sulfone- and thioether-stabilized carbanionic alkylations, respectively. © 1998 Published by Elsevier Science Ltd. All rights reserved.

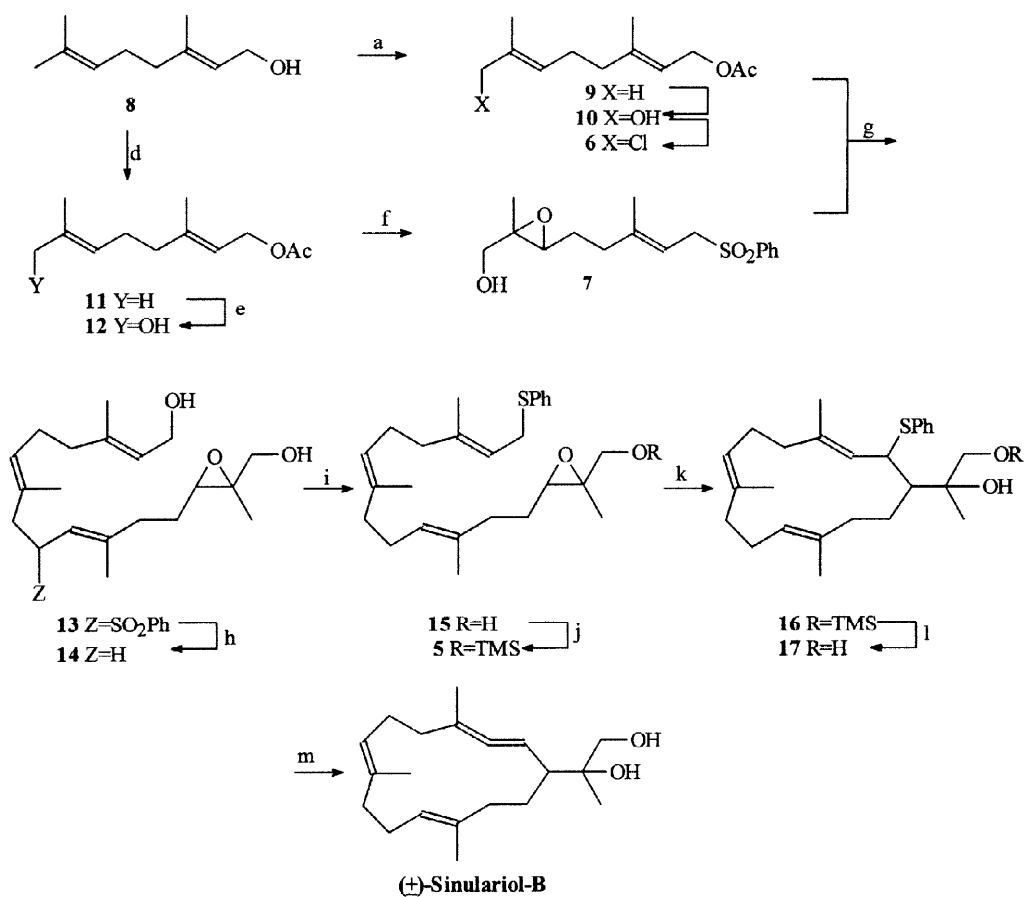
Cerbanoids, a 14-membered cyclic diterpene family, have become of interest to synthetic chemists and biologists because of their unusual structures and wide range of biological activities.<sup>1,2</sup> Sinulariol-B (**1**),<sup>3</sup> sinulaiol-D (**2**), sinularial-A (**3**) and sinularic acid-A (**4**),<sup>4</sup> four marine cembranoids (Chart), were isolated in 1987 and 1988 from the southern Japan soft coral *Sinularia mayi*. Their geometrical structures and configurations were confirmed to be 3*E*, 7*E*, 11*E*, and 1*R*, respectively. In order to lay a solid foundation for the asymmetric syntheses of **1-4**, the total synthesis of ( $\pm$ )-Sinulariol-B was studied. We have now achieved the first total synthesis of ( $\pm$ )-Sinulariol-B,<sup>5</sup> and here provide detail of this accomplishment.



Our strategy started from *E*-geraniol (**8**) as outlined in Scheme 1, and involved two key steps: (1) the coupling of sulfone **7** with allylic chloride **6** by sulfone-stabilized carbanionic alkylation, and (2) the macrocyclization of precursor **5** by intramolecular thioether-stabilized carbanionic alkylation.

**Scheme 1**

Its synthesis begins with *E*-geraniol (Scheme 2). Acetylation of *E*-geraniol (**8**) with  $\text{Ac}_2\text{O}^6$  in pyridine gave acetate **9** in 98% yield, which then was converted into alcohol **10** in 73% yield by selective oxidation of the terminal *E* methyl group with  $\text{SeO}_2/t\text{-BuOOH}$  according to the Sharpless procedure.<sup>7</sup> Reaction of alcohol **10** with the insoluble complex<sup>8</sup> of  $\text{NCS}$  and  $\text{Ph}_3\text{P}$  in dry THF yielded allylic chloride **6**. Sulfone **11** was prepared

**Scheme 2**

a)  $\text{Ac}_2\text{O}$ , Py, r.t., 98%; b)  $\text{SeO}_2$ , *t*-BuOOH,  $\text{CH}_2\text{Cl}_2$ , r.t., 73%; c)  $\text{Ph}_3\text{P}$ , NCS, THF, r.t., 85%, d),  $\text{PBr}_3$ ,  $\text{Et}_2\text{O}$  then  $\text{PhSO}_2\text{Na}$ , DMF, r.t., 75%; e)  $\text{Se}_2\text{O}$ , *t*-BuOOH,  $\text{CH}_2\text{Cl}_2$ , r.t., 78%; f)  $\text{VO}(\text{acac})_2$ , *t*-BuOOH, PhH, reflux, 96%; g) LDA,  $-78^\circ\text{C}$  then  $\text{K}_2\text{CO}_3$ -MeOH, r.t., 88%; h) Li-EtNH<sub>2</sub>,  $-78^\circ\text{C}$ , 78%; i)  $\text{Ph}_3\text{P}$ , NCS, THF, r.t., then PhSLi 64%; j) TMSCl, imidazole, DMF,  $50^\circ\text{C}$ , 98%; k) LDA,  $-78^\circ\text{C}$ , Dabco, 48%; l)  $n\text{-Bu}_4\text{N}^+\text{F}^-$ , ~100%; m) Li-EtNH<sub>2</sub>,  $-78^\circ\text{C}$ , 67%.

in 75% yield from *E*-geraniol (**8**) using the Grieco procedure,<sup>9</sup> which then was transformed into sulfonyl alcohol **12** in 78% yield by selective oxidation with  $\text{SeO}_2/t\text{-BuOOH}$ . Epoxidation **10** of the sulfonyl alcohol **12** with *t*-BuOOH in the presence of  $\text{VO}(\text{acac})_2$  gave epoxide **7** in 96% yield.

Alkylation of the anion of sulfone **7** with allylic chloride **6** took place smoothly in the dry THF at  $-78^\circ\text{C}$  and the acetyl group was removed from the product without damage to the rest of the molecule by treatment with anhydrous  $\text{K}_2\text{CO}_3$  in the dry MeOH at room temperature to give sulfonyl diol **13** in 88% yield. The sulfonyl group was reductively removed from sulfonyl diol **13** by reaction with Li-EtNH<sub>2</sub><sup>11</sup> at  $-78^\circ\text{C}$  to yield diol **14** in 78% yield. Thioether **15** was prepared in 64% yield from **14** by treatment with NCS- $\text{Ph}_3\text{P}$  complex and PhSLi in dry THF at room temperature in one pot, the hydroxy group of **15** was protected with TMSCL<sup>12</sup> to yield cyclization precursor **5** quantitatively.

With cyclization precursor **5** in hand, we next turned to the key step for the proposed synthesis—an intramolecular  $\text{S}_{\text{N}}2$  reaction of thioether-stabilized carbanion. Slow addition of **5** over 30 h in dry THF to a cooled ( $-78^\circ\text{C}$ ), well-stirred solution of LDA and Dabco<sup>13</sup> in dry THF gave intermediate **16** in 48% yield. After deprotection of **16** in usual way the (thiophenyl) diol was obtained in ~100% yield, which then was reduced with Li-EtNH<sub>2</sub> at  $-78^\circ\text{C}$  to yield ( $\pm$ )-sinulariol-B in 67% yield.

The spectral data of synthetic ( $\pm$ )-sinulariol-B thus obtained was coincided with those of natural sinulariol-B. Thus, we succeeded in obtaining ( $\pm$ )-sinulariol-B in ten steps and ~10% overall yield from *E*-geraniol. We believe that our strategy for synthesis of ( $\pm$ )-sinulariol-B makes possible for the asymmetric synthesis<sup>14</sup> of sinulariol-B, sinulariol-D, sinulariol-A and sinularic acid-A by means of asymmetric Sharpless epoxidation.<sup>15</sup>

## EXPERIMENTAL

**General:** Melting points were determined on a kolfer apparatus, and uncorrected. IR spectra were recorded on a FT-170SX spectrometer. <sup>1</sup>HNMR specter was measured on a varian FT-80A or Bruker AM-400 spectrometer using  $\text{CDCl}_3$  as solvent and TMS as an internal standard. MS spectra were obtained on a VGZAB-HS spectrometer (EI, 70eV). All solvents were distilled prior to use. All anhydrous solvents were achieved by standard methods. All reactions were conducted under an argon atmosphere unless otherwise noted, and monitored by TLC. All products prepared were purified by flash column chromatography on silica gel (200-300 mesh). *E*-Geraniol was purchased from Aldrich Chemical Company, INC.

**3,7-Dimethyl-2(*E*), 6-octadien-1-yl acetate (**9**).** A mixture of *E*-geraniol **8** (2.0 g, 12.9 mmol) and acetic anhydride  $\text{Ac}_2\text{O}$  (1.83 mL, 19.4 mmol) in pyridine (15 mL) was stirred at room temperature for 6 h, then poured into water and extracted with ether (3×50 mL). The combined ether layer was washed

successively with 2N HCl, 10% NaHCO<sub>3</sub>, water and brine, then dried on MgSO<sub>4</sub> and concentrated. The resulting oil was purified by flash column chromatography on silica gel using petroleum ether-acetone (30:1, v/v) as eluent to yield acetate **9** (2.49 g, 98%) as a colorless oil. <sup>1</sup>HNMR (80 MHz, CDCl<sub>3</sub>): δ 1.68 (s, 6H, 2CH<sub>3</sub>), 1.70 (s, 3H, CH<sub>3</sub>), 2.04 (s, 3H, CH<sub>3</sub>CO), 2.00–2.40 (m, 4H, 2CH<sub>2</sub>), 4.59 (d, 2H, J=7.2Hz, CH<sub>2</sub>OAc), 4.90–5.30 (m, 2H, 2CH=).

Anal. calcd. for C<sub>12</sub>H<sub>20</sub>O<sub>2</sub>: C, 73.43; H, 10.27; found C, 73.69; H, 10.19.

**3,7-Dimethyl-8-hydroxy-2(E),6(E)-octadien-1-yl acetate (10)**. To a suspension of SeO<sub>2</sub> (27 mg), salicylic acid (170 mg) and 80% *t*-BuOOH (5 mL) in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) was added acetate **9** (2.4 g) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL). After being stirred at 25 °C for 25 h, the reaction mixture was diluted with ether (150 mL) and washed successively with 10% KOH, saturated NaHSO<sub>3</sub>, water and brine, then dried on MgSO<sub>4</sub>, and concentrated. The resulting oil was purified by flash column chromatography on silica gel using petroleum ether-acetone (10:1, v/v) as eluent to give alcohol **10** (1.27 g, 73% based on the consumed starting material) as a colorless oil. IR (film): ν<sub>max</sub> 3437, 1738, 1670, 1021; <sup>1</sup>HNMR (80 MHz, CDCl<sub>3</sub>): δ 1.68 (s, 3H, CH<sub>3</sub>), 1.70 (s, 3H, CH<sub>3</sub>), 2.04 (s, 3H, CH<sub>3</sub>CO), 2.00–2.40 (m, 4H, 2CH<sub>2</sub>), 3.97 (s, 2H, OCH<sub>2</sub>), 4.59 (d, 2H, J=7.2Hz, CH<sub>2</sub>OAc), 4.90–5.30 (m, 2H, 2CH=).

Anal. calcd. for C<sub>12</sub>H<sub>20</sub>O<sub>3</sub>: C, 67.89; H, 9.50; found C, 67.61; H, 9.53.

**3,7-Dimethyl-8-Chloro-2(E),6(E)-octadien-1-yl acetate (6)**. Triphenylphosphine Ph<sub>3</sub>P (1.69 g, 6.4 mmol, 1.14 equiv) in THF (10 mL) was added dropwise to a stirring solution of *N*-Chlorosuccinimide NCS (860 mg, 6.4 mmol, 1.14 equiv) in THF (10 mL) under an atmosphere of argon. After 30 min alcohol **10** (1.2g, 5.7mmol) in THF (10 mL) was added slowly over 5 min to the resulting suspension of solids, and the mixture was stirred at room temperature until it became clear and homogeneous (about 2.5 h). The resulting dark mixture was diluted with ether (100 mL), washed successively with saturated aqueous NaHCO<sub>3</sub>, water and brine, then dried on MgSO<sub>4</sub>, and concentrated. Flash column chromatography over silica gel using petroleum ether-acetone (20:1, v/v) as eluent gave chloride **6** (1.11 g, 85%) as a colorless oil. <sup>1</sup>HNMR (80 MHz, CDCl<sub>3</sub>): δ 1.70 (s, 3H, CH<sub>3</sub>), 1.72 (s, 3H, CH<sub>3</sub>), 2.02 (s, 3H, CH<sub>3</sub>CO), 1.88–2.20 (m, 4H, 2CH<sub>2</sub>), 3.96 (s, 2H, CH<sub>2</sub>Cl), 4.55 (d, 2H, J=7.2Hz, CH<sub>2</sub>OAc), 5.00–5.40 (m, 2H, 2CH=).

Anal. calcd. for C<sub>12</sub>H<sub>19</sub>ClO<sub>2</sub>: C, 62.47; H, 8.30; found C, 62.15; H, 8.38.

**3,7-Dimethyl-1-(phenylsulfonyl)-2(E), 6(E)-octadiene (11)**. Phosphorus tribromide PBr<sub>3</sub> (1.35 mL, 14.2 mmol) was added dropwise into a dry ethereal solution (100mL) of *E*-geraniol **8** (2.0 g, 12.9 mmol) under ice-bath cooling, and the mixture was stirred for 3 h at room temperature. After the reaction was quenched with saturated aqueous NaHCO<sub>3</sub>, the ether layer was washed twice with brine, dried over MgSO<sub>4</sub>, and concentrated to give an oil. The oil was added into sodium benzenesulfinate PhSO<sub>2</sub>Na (2.12 g, 12.9 mmol) dissolved in dry DMF (30 mL), and the mixture was stirred at room temperature under argon in the dark for 20 h. After addition of brine, the organic substances were extracted with ether, and the usual workup gave an oil. Flash column chromatography on silica gel using petroleum ether-acetone (10:1, v/v) as eluent gave sulfone **11** (2.7 g, 75%) as a colorless oil. IR (film): ν<sub>max</sub> 1655, 1585, 1300, 1140; <sup>1</sup>HNMR (80 MHz, CDCl<sub>3</sub>): δ 1.31 (s, 3H, CH<sub>3</sub>), 1.57 (s, 3H, CH<sub>3</sub>), 1.68 (s, 3H, CH<sub>3</sub>), 1.90–2.20 (m, 4H, 2CH<sub>2</sub>), 3.79 (d, 2H,

$J=7.9\text{Hz}$ ,  $\text{CH}_2\text{SO}_2$ ), 3.90–5.40 (m, 2H, 2CH=), 7.40–8.00 (m, 5H, ArH).

Anal. calcd. for  $\text{C}_{16}\text{H}_{22}\text{SO}_2$ : C, 69.03; H, 7.96; found C, 69.53; H, 7.88.

**3,7-Dimethyl-1-(phenylsulfonyl)-8-hydroxy-2(E),6(E)-octadiene (12).** To a suspension of  $\text{SeO}_2$  (21 mg, 0.18 mmol), salicylic acid (129 mg, 0.93 mmol) and 80% *t*-BuOOH (3.7 mL, 33.6 mmol) in  $\text{CH}_2\text{Cl}_2$  (20 mL) was added sulfone **11** (2.6 g, 9.3 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL). After being stirred at 25 °C for 25 h, the reaction mixture was poured into water and extracted with ether (3×20 mL). The combined organic layers were washed successively with 10% KOH, saturated  $\text{NaHSO}_3$ , water and brine, then dried on  $\text{MgSO}_4$ , and concentrated to give an oil. Flash column chromatography on silica gel using petroleum ether-acetone (8:1, v/v) as eluent yielded alcohol **12** (1.70 g, 78% based on the consumed starting material) as a colorless oil. IR (film):  $\nu_{\text{max}}$  3440, 1658, 1587, 1312, 1150;  $^1\text{H}$ NMR (80 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.36 (s, 3H,  $\text{CH}_3$ ), 1.64 (s, 3H,  $\text{CH}_3$ ), 1.90–2.40 (m, 4H, 2 $\text{CH}_2$ ), 3.78 (d, 2H,  $J=7.9$  Hz,  $\text{CH}_2\text{SO}_2$ ), 3.98 (s, 2H,  $\text{OCH}_2$ ), 5.00–5.45 (m, 2H, 2CH=), 7.40–8.00 (m, 5H, ArH); EIMS  $m/z$ : 294 ( $\text{M}^+$ , 1%), 279 (5), 276 (3), 212 (45), 77(100).

Anal. calcd. for  $\text{C}_{16}\text{H}_{22}\text{SO}_3$ : C, 65.28; H, 7.53; found C, 65.82; H, 7.47.

**3,7-Dimethyl-1-(phenylsulfonyl)-6,7-epoxy-8-hydroxy-2(E)-octene (7).** To a solution of allylic alcohol **12** (1.5 g, 5.1 mmol) and a catalytic amount of vanadyl acetonate  $\text{VO}(\text{acac})_2$  in refluxing benzene (40 mL) was added dropwise 3.4 M anhydrous TBHP-toluene solution (2 mL, 6.8 mmol). After 1 h at reflux, the reaction mixture was cooled to room temperature, then dilution with ether (100 mL), and washed with brine. Evaporation of the solvent followed by flashed column chromatography on silica gel using petroleum ether-acetone (4:1, v/v) as eluent afforded epoxide **7** (1.52 g, 96%) as a colorless oil. IR (film):  $\nu_{\text{max}}$  3400, 1650, 1250, 1150;  $^1\text{H}$ NMR (80 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.29 (s, 3H,  $\text{CH}_3$ ), 1.38 (s, 3H,  $\text{CH}_3$ ), 1.50–2.40 (m, 4H, 2 $\text{CH}_2$ ), 2.97 (t, 1H,  $J=6.1$  Hz, epoxy H), 3.61 (brs, 2H,  $\text{OCH}_2$ ), 3.80 (d, 2H,  $J=7.9$  Hz,  $\text{CH}_2\text{SO}_2$ ), 5.24 (t, 1H,  $J=7.9$  Hz, CH=), 7.40–8.00 (m, 4H, ArH); EIMS  $m/z$ : 310 ( $\text{M}^+$ , 0.6%), 295 (1), 292 (3), 151 (15), 141 (100), 77 (81).

Anal. calcd. for  $\text{C}_{16}\text{H}_{22}\text{SO}_4$ : C, 61.91; H, 7.14; found C, 62.45, H, 7.05.

**2,6,10,14-Tetramethyl-2,3-epoxy-8-(phenylsulfonyl)-6(E),10(E),14(E)-hexadecatrien-1,16-diol (13).** To a cooled (-78 °C), well-stirred solution of 1.6 M LDA-hexane (3.15 mL, 5 mmol) in anhydrous THF (40 mL) was added dropwise sulfone **7** (750 mg, 2.4 mmol) in dry THF (5 mL) under argon atmosphere. After 30 min, allylic chloride **6** (558 mg, 2.4 mmol) in dry THF (5 mL) was added. The reaction mixture was allowed to warm to room temperature in 5 h and then saturated aqueous  $\text{NH}_4\text{Cl}$  (20 mL) was added. The usual workup gave an oil, which was added to anhydrous  $\text{K}_2\text{CO}_3$  (1 g) suspended in dry methanol (20 mL), and the mixture was stirred at room temperature for 30 min. After addition of water, the organic substances were extracted with ethyl acetate (3×30 mL). The pooled extracts were washed with water and brine, then dried on  $\text{MgSO}_4$ , and concentrated. The resulting oil was passed through a short pad of silica gel using petroleum ether-acetone (2:1, v/v) as eluent to give sulfonyl diol **13** (980 mg, 88%) as a colorless oil. IR (film):  $\nu_{\text{max}}$  3421, 1640, 1252, 1151;  $^1\text{H}$ NMR (80 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.30 (s, 3H,  $\text{CH}_3$ ), 1.37 (s, 3H,  $\text{CH}_3$ ), 1.64 (s, 3H,  $\text{CH}_3$ ), 1.68 (s, 3H,  $\text{CH}_3$ ), 1.40–2.40 (m, 10H, 5 $\text{CH}_2$ ), 2.98 (t, 1H,  $J=6.0$  Hz, epoxy H), 3.64 (brs, 2H,  $\text{OCH}_2$ ), 3.78 (m, 1H,  $\text{CHSO}_2$ ), 4.14 (d, 2H,  $J=7.1$  Hz,  $\text{OCH}_2$ ), 4.80–5.40 (m, 3H, 3CH=), 7.00–8.00 (m, 5H, ArH); EIMS  $m/z$ : 462 ( $\text{M}^+$ , <1%), 477 (<1), 444 (2), 135(14), 107 (27), 93 (56), 43 (100), 41 (39).

Anal. calcd. for  $C_{26}H_{38}O_5S$ : C, 67.50; H, 8.28; found C, 67.28, H, 8.30.

**2,6,10,14-Tetramethyl-2,3-epoxy-6(E),10(E),14(E)-hexadecatrien-1,16-diol (14).** Sulfonyl diol **13** (950 mg, 2.05 mmol) in dry THF (2 mL) was added at  $-78\text{ }^\circ\text{C}$  to the solution of lithium wire (820 mg, 117 mmol) dissolved in dry ethylamine  $\text{EtNH}_2$  (20 mL, dried over sodium). The mixture was stirred at  $-78\text{ }^\circ\text{C}$  for 3.5 h and some solid  $\text{NH}_4\text{Cl}$  and some methanol were added. The solution was allowed to warm to room temperature, then poured into water, and extracted with ethyl acetate ( $3\times 20\text{ mL}$ ). The combined organic layers were washed with water and brine, then dried on  $\text{MgSO}_4$ , and concentrated to give an oil, which was purified by flash column chromatography on silica gel using petroleum ether-acetone (4:1, v/v) as eluent to yield diol **14** (516 mg, 78%) as a colorless oil. IR (film):  $\nu_{\text{max}}$  3440br, 1644, 1250, 1020, 920;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.30 (s, 3H,  $\text{CH}_3$ ), 1.63 (s, 6H,  $2\text{CH}_3$ ), 1.67 (s, 6H,  $2\text{CH}_3$ ), 1.40–2.45 (m, 12H,  $6\text{CH}_2$ ), 3.01 (t, 1H,  $J=6.1\text{ Hz}$ , epoxy H), 3.66 (d, 2H,  $J=12.1\text{ Hz}$ ,  $\text{OCH}_2$ ), 4.15 (d, 2H,  $J=7.0\text{ Hz}$ ,  $\text{OCH}_2$ ), 5.08 (t, 1H,  $J=6.8\text{ Hz}$ ,  $\text{CH}=\text{}$ ), 5.16 (t, 1H,  $J=6.7\text{ Hz}$ ,  $\text{CH}=\text{}$ ), 5.41 (t, 1H,  $J=6.9\text{ Hz}$ ,  $\text{CH}=\text{}$ ); EIMS  $m/z$ : 322 ( $\text{M}^+$ ,  $<1\%$ ), 288 ( $<1$ ), 135 (14), 123 (18), 95 (58), 69 (51), 43 (100), 41 (38).

Anal. calcd. for  $C_{20}H_{34}O_3$ : C, 74.49; H, 10.63; found C, 74.11, H, 10.74.

**2, 6, 10, 14-Tetramethyl-2, 3-epoxy-16-(thiophenyl)-6(E), 10(E), 14(E)-hexadecatrien-1-ol (15).** Triphenylphosphine  $\text{Ph}_3\text{P}$  (464 mg, 1.77 mmol, 1.14 equiv) in THF (5 mL) was added dropwise to a stirring solution of *N*-Chlorosuccinimide NCS (236 mg, 1.77 mmol, 1.14 equiv) in THF (5 mL) under argon atmosphere. After 30 min, diol **14** (500 mg, 1.55 mmol) in THF (5 mL) was added dropwise in 5 min to the resulting suspension, and the mixture was stirred at room temperature until it become clear and homogeneous (about 2 h), and then sodium thiophenoxide  $\text{PhSLi}$  (410 mg, 3.1 mmol) in THF (2 mL) was added. After 2 h, the reaction mixture was poured into water and extracted with ether ( $3\times 20\text{ mL}$ ). The combined organic layers were washed successively with 2N KOH, water and brine, then dried on  $\text{MgSO}_4$ , and concentrated to yield oil, which was purified by flash column chromatography on silica gel using petroleum ether-acetone (20:1, v/v) as eluent to yield diol **15** (410 mg, 64%) as a colorless oil. IR (film):  $\nu_{\text{max}}$  3640br, 1644, 1450, 1399, 1160, 720, 690;  $^1\text{H NMR}$  (80 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.29 (s, 3H,  $\text{CH}_3$ ), 1.60 (s, 3H,  $\text{CH}_3$ ), 1.64 (s, 3H,  $\text{CH}_3$ ), 1.66 (s, 3H,  $\text{CH}_3$ ), 1.40–2.40 (m, 12H,  $6\text{CH}_2$ ), 3.02 (t, 1H,  $J=6.1\text{ Hz}$ , epoxy H), 3.51 (d, 2H,  $J=7.6\text{ Hz}$ ,  $\text{CH}_2\text{S}$ ), 3.65 (brs, 2H,  $\text{OCH}_2$ ), 4.90–5.40 (m, 3H,  $3\text{CH}=\text{}$ ), 7.20–7.50 (m, 5H, ArH); EIMS  $m/z$ : 322 ( $\text{M}^+$ , 1%), 287 (M- $\text{H}_2\text{O}$ -SPh, 2), 161 (18), 135 (25), 107 (36), 93 (100), 81 (93).

Anal. calcd. for  $C_{26}H_{38}SO_2$ : C, 75.31; H, 9.24; found C, 75.13, H, 9.28.

**2, 6, 10, 14-Tetramethyl-1-(trimethylsiloxy)-2, 3-epoxy-16-(thiophenyl)-6(E), 10(E), 14(E)-hexadecatriene (5).** To a mixture of **15** (300 mg, 0.72 mmol) and imidazole (108 mg, 1.59 mmol, 2.2 equiv) in dry DMF (2 mL) was added trimethylchlorosilane (0.1 mL, 0.8 mmol, 1.1 equiv). After being stirred at  $50\text{ }^\circ\text{C}$  for 10h under an atmosphere of argon, the reaction mixture was cooled to room temperature, then diluted with brine, and extracted with ether ( $3\times 20\text{ mL}$ ). The combined organic layers were washed successively with 10%  $\text{NaHCO}_3$ , water and brine, then dried on  $\text{MgSO}_4$ , and concentrated. The resulting oil was purified by flash column chromatography on silica gel using petroleum ether-acetone (30:1, v/v) as eluent to yield **5** (345 mg, 98%) as a colorless oil. IR (film):  $\nu_{\text{max}}$  1650, 1458, 1401, 1150, 720, 690;  $^1\text{H NMR}$  (400 MHz,

CDCl<sub>3</sub>):  $\delta$  0.03 (s, 9H, 3CH<sub>3</sub>), 1.31 (s, 3H, CH<sub>3</sub>), 1.62 (s, 3H, CH<sub>3</sub>), 1.66 (s, 6H, 2CH<sub>3</sub>), 1.40-2.24 (m, 12H, 6CH<sub>2</sub>), 3.01 (t, 1H, J=6.1Hz, epoxy H), 3.52 (d, J=8.32 Hz, 2H, CH<sub>2</sub>S), 3.62 and 3.80 (each 1H, d, J=12.3 Hz, OCH<sub>2</sub>), 5.08 (t, 1H, J=6.8Hz, CH=), 5.15 (t, 1H, J=6.7Hz, CH=), 5.31 (t, 1H, J=6.8Hz, CH=), 7.25-7.40 (m, 5H, ArH); EIMS m/z: 486 (M<sup>+</sup>, 2%), 471 (1), 456 (2), 377 (3), 161 (20), 135 (21), 93 (100), 55 (38).

Anal. calcd. for C<sub>29</sub>H<sub>46</sub>O<sub>2</sub>SSi: C, 71.55; H, 9.51; found C, 71.89, H, 9.41.

**2-[4,8,12-Trimethyl-2-(thiophenyl)-3(E),7(E),11(E)-cyclotetradecatrien-1-yl]-propan-1,2-diol (17).**

To a mixture of 1.6M LDA-hexane solution (0.9 mL, 1.45 mmol) and Dabco (52 mg, 0.48mmol) in anhydrous THF (30 mL) was added precursor **5** (200 mg, 0.41 mmol) in dry THF (30 mL) at -78°C via syringe pump over 34 h under an atmosphere of argon. After 3 h, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature, and then poured into saturated aqueous NH<sub>4</sub>Cl and extracted with ether (3 × 80 mL). The extracts were washed with water and brine, then dried on MgSO<sub>4</sub>, and concentrated to give crude product **16**, to which was added *n*-Bu<sub>4</sub>N<sup>+</sup>F<sup>-</sup> (200 mg) in THF (2 mL). After being stirred at room temperature for 20 h under argon, the reaction mixture was diluted with ethyl acetate (50 mL), and washed with water and brine, then dried over MgSO<sub>4</sub>, and concentrated. The resulting oil was purified by flash column chromatography on silica gel using petroleum ether-acetone (8:1, v/v) as eluent to yield **17** (82 mg, 48% from **5**) as a colorless needles. mp. 90.5-92°C. IR (KBr):  $\nu_{\max}$  3360-3100br, 1665, 1385, 890, 840, 690, 660; <sup>1</sup>HNMR (80 MHz, CDCl<sub>3</sub>):  $\delta$  1.07 (s, 3H, CH<sub>3</sub>), 1.30 (s, 3H, CH<sub>3</sub>), 1.52 (s, 3H, CH<sub>3</sub>), 1.54 (s, 3H, CH<sub>3</sub>), 1.40-2.10 (m, 13H, CH, 6CH<sub>2</sub>), 3.54 (d, 1H, J=11.8Hz, CH<sub>2</sub>O), 3.65 (d, 1H, J=11.8 Hz, CH<sub>2</sub>O), 3.81 (dd, 1H, J=8.6 and 10.8 Hz, CHSPH), 4.70-5.30 (m, 3H, 3CH=), 7.20-7.50 (m, 5H, ArH); EIMS m/z: 414 (M<sup>+</sup>, 2%), 305 (8), 304 (4), 287 (5), 153 (20), 93 (48), 81 (100), 71 (74).

Anal. calcd. for C<sub>26</sub>H<sub>38</sub>O<sub>2</sub>S: C, 75.31; H, 9.24; found C, 75.45, H, 9.12.

**2-[4,8,12-Trimethyl-3(E),7(E),11(E)-cyclotetradecatrien-1-yl]-propan-1,2-diol(1).** The mixture of **17** (60 mg, 0.144 mmol) in dry THF (1 mL) was added at -78 °C to a solution of lithium (80 mg, 12 mmol) dissolved in dry EtNH<sub>2</sub> (10 mL, dried over sodium). The mixture was stirred at -78 °C for 3.5 h and a little amount of NH<sub>4</sub>Cl and methanol were added. The solution was allowed to warm to room temperature, then poured into water, and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with water and brine, then dried over MgSO<sub>4</sub>, and concentrated to give a crude product, which was purified by flash column chromatography on silica gel using petroleum ether-acetone (4:1, v/v) as eluent to yield (±)-sinulariol-B (**1**) (30 mg, 67%) as colorless needles. mp. 55.5-58°C (lit<sup>3</sup>, 61-63°C); IR (KBr):  $\nu_{\max}$  3260br, 1650, 1384,1370; <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.15 (s, 3H, CH<sub>3</sub>), 1.58 (s, 6H, 2CH<sub>3</sub>), 1.60 (s, 3H, CH<sub>3</sub>), 1.50-2.30 (m, 15H, 7CH<sub>2</sub>, CH), 3.42 (d, 1H, J=11.1Hz, OCH<sub>2</sub>), 3.54 (d, 1H, J=11.1Hz, OCH<sub>2</sub>), 4.91 (t, 1H, J=6.8Hz, CH=), 4.99 (t, 1H, J=6.7Hz, CH=), 5.10 (t, 1H, J=6.8Hz, CH=); EIMS m/z: 306(M<sup>+</sup>, 8%), 291 (15), 288 (6), 275 (45), 257 (42), 189 (35), 93 (70), 40 (100).

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