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Synthesis of Eupomatilone-6 and Assignment of Its Absolute Configuration

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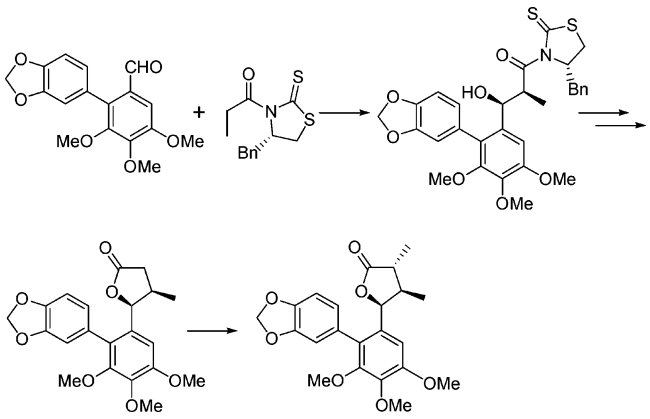

The Zn-mediated Barbier reaction of the biarylaldehyde **8** with crotyl bromide followed by hydroboration and oxidation provided the γ-butyrolactones **4** and **5**. The stereoselective installation of methyl group at C-3 by using LiHMDS and MeI completed the synthesis of racemic eupomatilone-6 (**2**) and its diastereomer **3**. The spectroscopic data of **2** was in full agreement with reported spectra of natural product, thus confirming the revised relative configuration of eupomatilone-6. Similarly, an optically active (3*R*,4*R*,5*S*)-isomer of eupomatilone-6 (**23**) was prepared in which the aldol reaction with thiazolidinethione as a chiral auxiliary was employed as a key step. On the basis of the spectroscopic data and optical rotation values of **23**, the absolute configuration of eupomatilone-6 was proposed.

In 1991, Taylor et al. isolated a series of novel lignans named as eupomatilones-1−7 from the shrubs *Eupomatia bennettii* F. Muell. Their relative configurations were elucidated by extensive NMR studies.[1] Eupomatilones are characterized by the biaryl system with a substituted γ-lactone ring attached to one of the aryl rings. Some of the eupomatilone molecules, including eupomatilone-6, exist as a mixture of fluctional atropisomers. Eupomatilones are the subject of intense synthetic activities.[2]

Earlier we reported the synthesis of a putative structure of eupomatilone-6 (**1**).[2b] The discrepancy in the spectral data of natural and synthetic eupomatilone-6 warranted revision of its relative stereochemistry as either 3α,4β,5β-configuration (**2**) or 3β,4α,5β-configuration (**3**). While the present work was in progress, Coleman and Gurrala[2d] reported the synthesis of racemic eupomatilone-6 and confirmed its relative stereochemistry as shown in structure **2**. Herein we disclosed a new synthetic strategy to prepare racemic eupomatilone-6 and then extended the protocol to synthesize optically active (+)-eupomatilone-6.

A retrosynthetic strategy for **2** and **3** is depicted in Figure 1. The stereoselective methylation at C-3 of the 4,5-disubstituted γ-butyrolactones **4** and **5** was envisaged to furnish 3,4,5-*trans-cis* and *trans-trans*-diastereomeric products (**2** and **3**).[3,4] The proposal to obtain both *cis*- and *trans*-4,5-disubstituted-γ-butyrolactones (**4** and **5**), respectively, from the *syn*- and *anti*-homoallylic alcohols **6** and **7** was envisioned as a straightforward proposition.[5] The proposed investigation on crotylation of the biaryl aldehyde **8**[2b] under Barbier[6]-type reaction conditions would give rise to both the requisite syn- and anti-products **6** and **7** (Scheme 1).

Treatment of **8** with crotyl bromide in the presence of zinc and ammonium chloride gave an inseparable 1:1 mixture of *syn*- and *anti*-homoallylic alcohols **6** and **7**. However, subsequent hydroboration−oxidation of **6/7** by using $BH_3{\cdot}SMe_2$ and H_2O_2 followed by treatment with 2,2-dimethoxypropane and PPTS gave the acetonide derivatives **11** and **12**, which were separated by silica gel chromatography. The ^1H NMR spectral analyses, particularly the characteristic chemical shifts and coupling constants of benzylic proton at C-5, were useful in assigning the relative stereochemistries as depicted in structures **11** and **12**. For example, **11** revealed signals of benzylic proton of the equilibrating atropisomers as singlets at 4.77 and 4.87 ppm, whereas it appeared as

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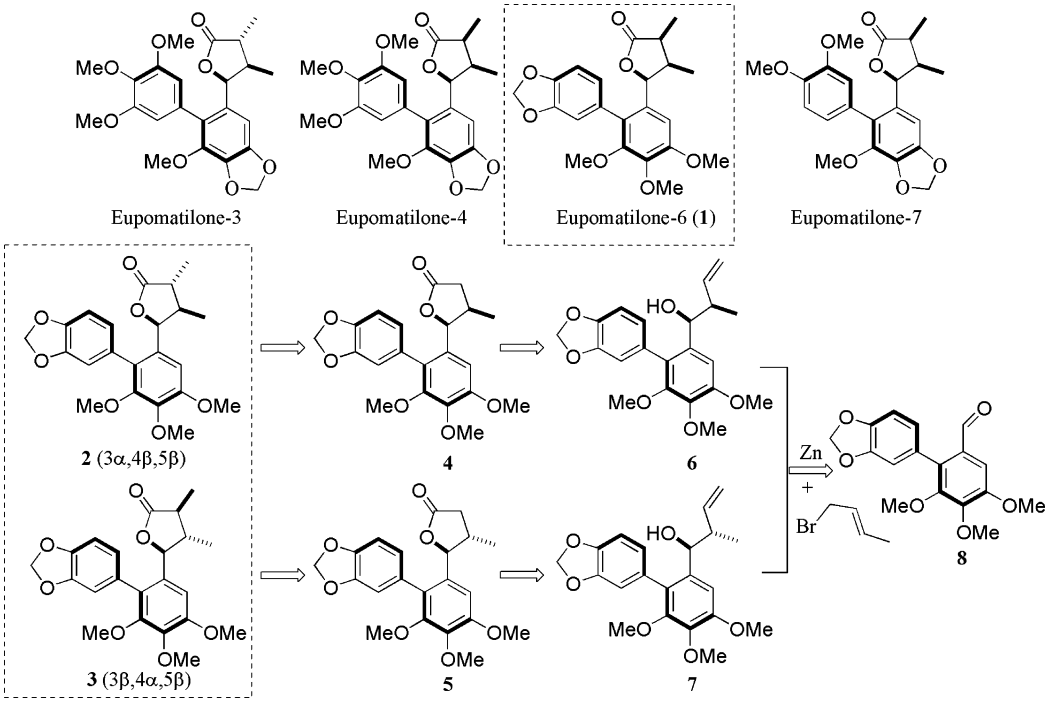
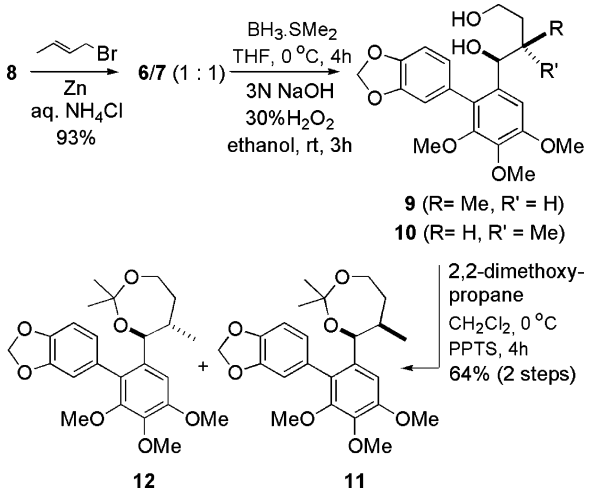


FIGURE 1. Representative natural eupomatilones and the alternative structures suggested for the eupomatilone-6 and the retrosynthetic strategy.

SCHEME 1. Synthesis of 1,4-Diols 9 and 10



doublets at 4.33 and 4.36 ppm with $J = 9.4$ Hz in the case of compound **12**.

The diol **9**, obtained by hydrolysis of **11**, was converted into the lactone derivative **4** by oxidation with NCS and TEMPO (Scheme 2).[2d,7] After screening several reagents, we observed that the diastereoselectivity of methylation at C-3 was highest with LiHMDS−MeI. The dialkylated product **13** was also isolated as a minor product. The spectral data of **2** was in complete agreement with the data published for the naturally occurring eupomatilone-6.[1,2d] Similarly, compound **12** was transformed by adopting the same strategy into diastereomeric eupomatilone **3** (Scheme 3). The ^{1}H NMR spectrum of **3** was substantially different from that of the natural eupomaltinone-6.

After successfully establishing the relative stereochemistry of racemic eupomatilone-6, we felt the need to design, on the basis of our new findings, the asymmetric synthetic protocol that would establish the absolute configuration of eupomatilone-6. It is pertinent to mention that eupomatilone-6 inherently exists in nature, as a mixture of atropisomers whose separation is still being precluded.

The titanium enolate of *N*-propionylthiazolidinethione **15** was reacted with the biarylaldehyde **8** to give **16**, whose free hydroxyl group was protected as TBS−ether **17**.[8] The reductive removal of the thiazolidinethione auxiliary from **17** with $NaBH_4$ in THF−EtOH gave **18**.[9] The Dess−Martin periodinane oxidation and consequent Wittig reaction with $PPh_3{=}CH_2$ gave the olefin derivative **19**, from which the TBS group was departed in the presence of 1 M solution *n*-Bu_4NF in THF to afford **20**. Compound **20** was subjected to successive hydroboration and oxidation to give the lactone derivative **22**. The chiral HPLC analysis (Chiracel-OD column) of **22** and **4** established the enantiomeric excess of 97%. The alkylation of **22** was executed by using essentially the same reaction (LiHMDS−MeI) as reported above to give (3*R*,4*R*,5*S*)-eupomatilone-6 (**23**), whose spectroscopic data was in full agreement with reported spectra (Scheme 4). The optical rotation observed {$[\alpha]^{25}_D$ 24.7 (*c* 0.5, $CHCl_3$)} for synthetic

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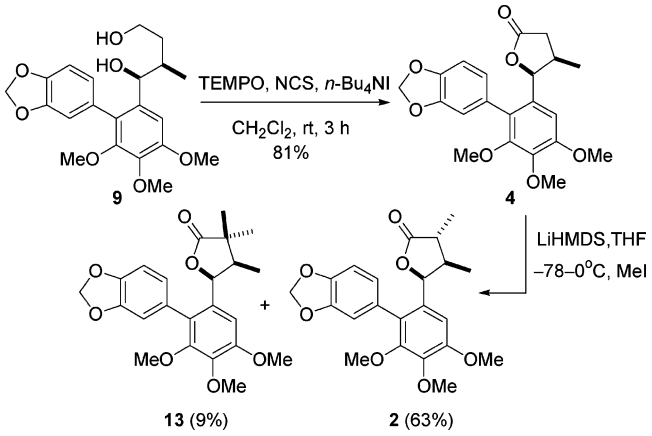
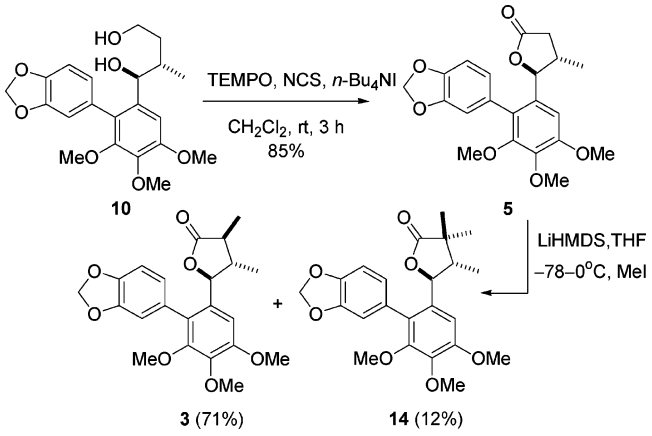
SCHEME 2. Synthesis of (±)-Eupomatilone-6 (2)



SCHEME 3. Synthesis of 3



product was in agreement with reported value {$[\alpha]^{25}_D$ −25.6 (*c* 0.5)}[1b] but with opposite sign. The minor quantity of dialkylated product (**24**) was also isolated and characterized.

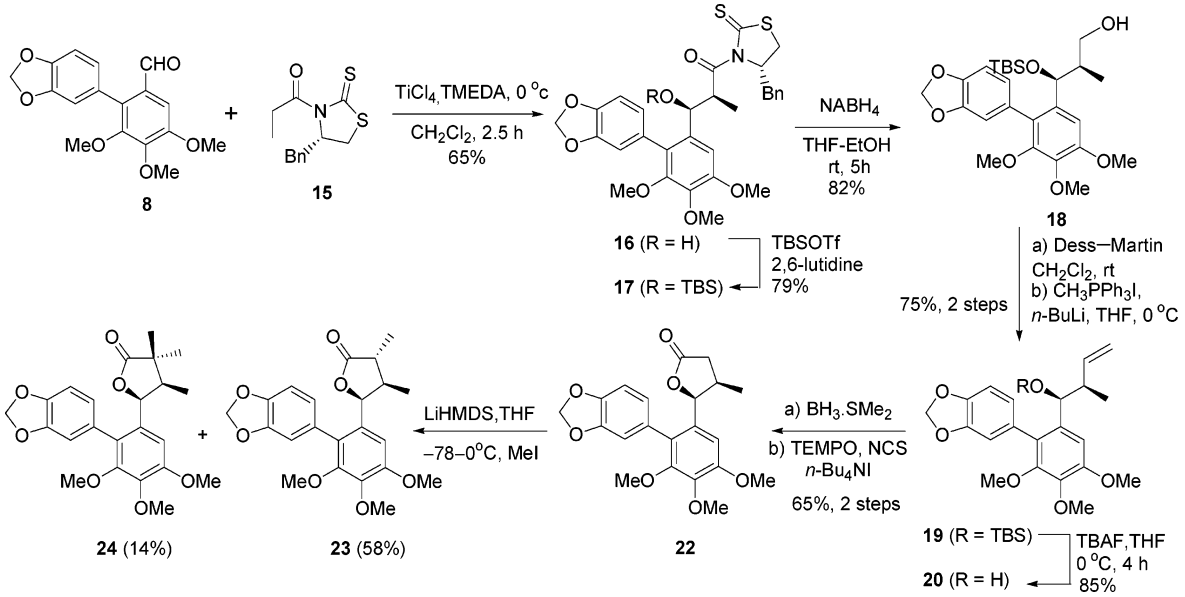
In summary, we have devised a four-step synthesis of eupomatilone-6 (**2**) and its diastereomer **3** that established the relative stereochemistry of the natural eupomatilone-6. Further studies on optically active (3*R*,4*R*,5*S*)-isomer (**23**) proposed the absolute configuration of naturally occurring eupomatilone-6 as (3*S*,4*S*,5*R*).

Experimental Section

Synthesis of *syn*-Lactone 4. A biphasic mixture of diol **9** (2 g, 5.1 mmol), TEMPO (80 mg, 0.51 mmol), *n*-Bu_4NI (190 mg, 0.51 mmol) and *N*-chlorosuccinimide (2.05 g, 15.4 mmol), aqueous $NaHCO_3$ (0.5M, 10 mL), and aqueous K_2CO_3 (0.05M, 10 mL) and CH_2Cl_2 (20 mL) was vigorously stirred for 3 h at room temperature. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The organic layer was washed with brine, dried, and evaporated. The residue was purified by silica gel column chromatography by eluting with light petroleum/ethyl acetate (4:1) to give **4** (1.6 g, 81%). IR ($CHCl_3$): 3020, 1776, 1599, 1483, 1324, 1215, 1080, 1042, 929, 757, 669 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 0.68 (d, J = 7.3 Hz, 3H), 0.70 (d, J = 7.3 Hz, 3H), 2.20−2.30 (m, 4H), 2.69 (dd, J = 7.8, 6.3 Hz, 1H), 2.72 (dd, J = 7.8, 6.3 Hz, 1H), 3.65 (s, 3H), 3.66 (s, 3H), 3.91 (s, 12H), 5.42 (d, J = 5.6 Hz, 1H), 5.51 (d, J = 5.6 Hz, 1H), 6.02−6.03 (m, 2H), 6.04−6.05 (m, 2H), 6.58 (dd, J = 7.9, 1.6 Hz, 1H), 6.62 (d, J = 1.6 Hz, 1H), 6.70 (dd, J = 7.9, 1.6 Hz, 1H), 6.73 (d, J = 1.6 Hz, 1H), 6.81 (s, 1H), 6.82 (s, 1H), 6.85 (d, J = 7.9 Hz, 1H), 6.88 (d, J = 7.9 Hz, 1H). ^{13}C NMR (75 MHz): 15.2 (q), 15.3 (q), 33.6 (d), 33.8 (d), 37.7 (t), 56.0 (q), 60.6 (q), 60.9 (q), 81.9 (d), 101.0 (t), 104.8 (d), 108.0 (d), 108.2 (d), 109.5 (d), 110.5 (d), 122.3 (d), 123.3 (d), 126.3 (s), 126.4 (s), 128.9 (s), 130.0 (s), 141.6 (s), 146.8 (s), 146.9 (s), 147.5 (s), 151.4 (s), 152.7 (s), 176.1 (s) ppm. Maldi top Calcd for $C_{21}H_{22}O_7$: 386.14, obsd: 387.16 (M^+ + 1), 409.13 (M^+ + Na). Anal. Calcd for $C_{21}H_{22}O_7$: C, 65.28; H, 5.74%. Found: C, 65.21; H, 5.53%.

Synthesis of Eupomatilone-6 (2) and Its 3-Methylated Derivative 13. To a solution of **4** (0.50 g, 1.3 mmol) in anhydrous THF (5 mL) at −78 °C was added LiHMDS (1 M solution in THF, 1.55 mL). After 1 h, MeI (0.09 mL, 1.45 mmol) was added and stirring was continued for an additional 1 h at −78 °C. The reaction mixture was quenched with saturated ammonium chloride, extracted with ethyl acetate, dried over sodium sulfate, and concentrated. The crude residue was purified by silica gel chromatography by eluting with light petroleum/ethyl acetate (9:1) to give **13** (0.05 g, 9%) and **2** (0.33 g, 63%). Spectral data of eupomatilone-6 (**2**). IR ($CHCl_3$): 3429, 2932, 1773, 1596, 1457, 1406, 1326, 1226, 1197, 1127, 1040, 937, 754, 667 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 0.70 (d, J = 7.1 Hz,

SCHEME 4. Synthesis of (+)-Eupomatilone-6 (23)



3H), 0.73 (d, J = 7.1 Hz, 3H), 1.19 (d, J = 7.4 Hz, 3H), 1.20 (d, J = 7.4 Hz, 3H), 1.93−2.04 (m, 2H), 2.37 (sextet, J = 7.2 Hz, 2H), 3.63 (s, 3H), 3.64 (s, 3H), 3.89 (s, 6H), 3.90 (s, 6H), 5.53 (d, J = 6.9 Hz, 1H), 5.64 (d, J = 6.9 Hz, 1H), 6.01−6.03 (m, 4H), 6.59 (dd, J = 7.9, 1.6 Hz, 1H), 6.64 (d, J = 1.5 Hz, 1H), 6.66 (2s, 2H), 6.70 (dd, J = 7.9, 1.6 Hz, 1H), 6.72 (d, J = 1.5 Hz, 1H), 6.86 (d, J = 7.9 Hz, 1H), 6.88 (d, J = 7.9 Hz, 1H). ^{13}C NMR (125 MHz): 14.8 (q), 14.9 (q), 15.3 (q), 15.5 (q), 41.2 (d), 41.5 (d), 42.5 (d), 42.6 (d), 56.1 (q), 60.8 (q), 61.0 (q), 61.1 (q), 79.8 (d), 79.8 (d), 101.1 (t), 101.2 (t), 104.6 (d), 104.7 (d), 108.1 (d), 108.3 (d), 109.9 (d), 110.9 (d), 122.6 (d), 123.7 (d), 127.0 (s), 127.1 (s), 128.9 (s), 129.0 (s), 130.3 (s), 141.7 (s), 146.8 (s), 146.9 (s), 147.6 (s), 147.6 (s), 151.5 (s), 152.8 (s), 179.7 (s) ppm. Maldi top Calcd for $C_{22}H_{24}O_7$: 400.15, obsd: 400.57 (M^+), 401.57 (M^+ + 1), 423.57 (M^+ + Na). Anal. Calcd for $C_{22}H_{24}O_7$: C, 65.99; H, 6.04%. Found: C, 65.85; H, 5.91%.

Methylation of *anti*-Lactone 5. Compound **5** (0.5 g, 1.29 mmol) was subjected to essentially the same reaction conditions to produce **14** (0.068 g, 12%) and **3** (0.37 g, 71%). Spectral data of compound **3**. IR ($CHCl_3$): 3429, 2932, 1772, 1596, 1457, 1406, 1326, 1226, 1197, 1127, 1040, 937, 754 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.87 (d, J = 6.0 Hz, 3H), 0.89 (d, J = 6.0 Hz, 3H), 1.23 (s, 3H), 1.26 (s, 3H), 1.92−2.24 (m, 4H), 3.62 (s, 3H), 3.63 (s, 3H), 3.91 (s, 12H), 4.78 (d, J = 9.4 Hz, 1H), 4.80 (d, J = 9.4 Hz, 1H), 6.01−6.03 (m, 4H), 6.61−6.73 (m, 6H), 6.83−6.87 (m, 2H). ^{13}C NMR (50 MHz): 12.9 (q), 14.3 (q), 43.3 (d), 47.6 (d), 56.1 (q), 60.8 (q), 60.9 (q), 61.0 (q), 82.5 (d), 82.6 (d), 101.1 (2t), 105.1 (d), 105.1 (d), 107.8 (d), 108.1 (d), 110.5 (d), 111.4 (d), 123.3 (d), 124.3 (d), 128.8 (s), 128.9 (s), 129.9 (s), 130.6 (s), 130.8 (s), 142.6 (s), 146.8 (s), 146.9 (s), 147.3 (s), 147.5 (s), 151.2 (s), 151.2 (s), 153.3 (s), 178.4 (s), 178.5 (s) ppm. Maldi top Calcd for $C_{22}H_{24}O_7$: 400.15, obsd: 400.57 (M^+), 401.57 (M^+ + 1), 423.57 (M^+ + Na). Anal. Calcd for $C_{22}H_{24}O_7$: C, 65.99; H, 6.04%. Found: C, 66.15; H, 6.07%.

Synthesis of 16 by Aldol Reaction between Biaryl Aldehyde (8) and Thiazolidine Thione (15). To a solution of *N*-propionylthiazolidinethione (**15**, 9.2 g, 34.7 mmol) in dry CH_2Cl_2 (90 mL) at 0 °C were added $TiCl_4$ (6.3 g, 33.4 mmol) and TMEDA (8.9 g, 87 mmol) and stirred for 20 min. To this dark red enolate solution was added biaryl aldehyde **8** (10.0 g, 31.6 mmol) in dry CH_2Cl_2 (30 mL) and stirring was continued for an additional 2 h at 0 °C. The reaction was quenched with aqueous NH_4Cl (60 mL), and the layers were separated. The aqueous layer was extracted with ethyl acetate. The combined organic layer was dried over sodium sulfate, filtered, and concentrated. Purification of the residue by column chromatography on silica gel with light petroleum/ethyl acetate (4:1) as eluent gave **16** (12 g, 65%). $[\alpha]^{25}_D$ +133 (c 1.0, $CHCl_3$). IR ($CHCl_3$): 3400, 3019, 1672, 1597, 1456, 1341, 1215, 1041, 938, 759, 668 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.23 (d, J = 7.0 Hz, 3H), 1.27 (d, J = 7.0 Hz, 3H), 2.79 (d, J = 11.4 Hz, 1H), 2.80 (d, J = 11.4 Hz, 1H), 2.87−3.19 (m, 8H), 3.56 (s, 3H), 3.58 (s, 3H), 3.86 (s, 6H), 3.94 (s, 6H), 4.31−4.39 (m, 2H), 4.72−4.89 (m, 4H), 5.94 (d, J = 1.3 Hz, 1H), 5.96 (d, J = 1.3 Hz, 1H), 6.02 (d, J = 1.5 Hz, 1H), 6.08 (d, J = 1.5 Hz, 1H), 6.59−6.66 (m, 4H), 6.78 (d, J = 7.7 Hz, 1H), 6.99 (d, J = 7.8 Hz, 1H), 6.98 (s, 1H), 6.99 (s, 1H), 7.19−7.39 (m, 10H). ^{13}C NMR (50 MHz): 11.3 (q), 11.5 (q), 32.4 (t), 32.5 (t), 36.2 (t), 44.4 (d), 55.8 (q), 60.5 (q), 60.7 (q), 60.8 (q), 68.7 (d), 68.8 (d), 71.5 (d), 71.7 (d), 100.7 (t), 101.0 (t), 105.2 (d), 105.3 (d), 107.4 (d), 108.2 (d), 110.0 (d), 111.6 (d), 122.4 (d), 124.1 (d), 127.0 (d), 127.2 (s), 128.7 (d), 128.8 (s), 129.1 (d), 134.7 (s), 134.8 (s), 136.1 (s), 141.3 (s), 141.3 (s), 146.4 (s), 146.5 (s), 147.0 (s), 147.3 (s), 151.0 (s), 151.1 (s), 152.5 (s), 152.5 (s), 178.2 (s), 178.3 (s), 200.2 (s), 200.5 (s) ppm. Anal. Calcd for $C_{30}H_{31}NO_7S_2$: C, 61.94; H, 5.37; N, 2.41; S, 11.02%. Found: C, 62.02; H, 5.54; N, 2.40; S, 11.29%.

Synthesis of 18. Compound **17** (5 g, 7.2 mmol) and $NaBH_4$ (540 mg, 14.3 mmol) in THF (25 mL) and EtOH (5 mL) were stirred at room temperature for 5 h. Excess borohydride was quenched at 0 °C with diluted HCl and concentrated. The residue was partioned between water−ether, and the organic layer was separated and washed with 1 M NaOH, H_2O, and brine, dried over sodium sulfate, and concentrated. The crude was purified on silica gel by using light petroleum/ethyl acetate (4:1) as an eluent to give **18** (2.91 g, 82%). $[\alpha]^{25}_D$ −8.5 (c 1.05, $CHCl_3$). IR ($CHCl_3$): 3389, 2930, 1598, 1481, 1402, 1384, 1322, 1232, 1125, 1040, 939, 872, 838, 757 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ −0.15 (s, 3H), −0.15 (s, 3H), 0.01 (s, 6H), 0.75 (d, J = 6.9 Hz, 3H), 0.78 (d, J = 6.9 Hz, 3H), 0.92 (s, 18H), 1.53−1.68 (br m, 2H), 3.33 (s, 2H), 3.36 (s, 2H), 3.62 (s, 3H), 3.63 (s, 3H), 3.89 (s, 6H), 3.90 (s, 6H), 4.80 (d, J = 2.7 Hz, 1H), 4.89 (d, J = 2.7 Hz, 1H), 6.01−6.04 (m, 4H), 6.60 (dd, J = 7.8, 1.7 Hz, 1H), 6.63−6.67 (m, 3H), 6.85 (d, J = 7.8 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.93 (s, 2H). ^{13}C NMR (50 MHz): −5.2 (q), −4.5 (q), 9.6 (q), 18.0 (s), 25.8 (q), 42.4 (d), 42.6 (d), 55.6 (q), 60.7 (q), 60.8 (q), 60.9 (q), 65.8 (t), 70.7 (d), 100.9 (t), 106.3 (d), 107.8 (d), 107.9 (d), 109.9 (d), 111.4 (d), 122.5 (d), 124.0 (d), 126.0 (s), 129.6 (s), 129.7 (s), 137.7 (s), 137.8 (s), 140.6 (s), 146.4 (s), 146.5 (s), 147.3 (s), 147.4 (s), 150.9 (s), 152.0 (s) ppm. Maldi top Calcd for $C_{26}H_{38}O_7Si$: 490.24, obsd: 513.57 (M^+ + Na). Anal. Calcd for $C_{26}H_{38}O_7Si$: C, 63.64; H, 7.81%. Found: C, 63.81; H, 7.76%.

Synthesis of 19. A suspension of alcohol **18** (2.0 g, 4.1 mmol) and Dess−Martin periodinane (2.08 g, 4.9 mmol) in CH_2Cl_2 (10 mL) was stirred at 0 °C for 1.5 h, filtered through Celite, and concentrated to procure the aldehyde (1.8 g, 90%). To a suspension of methyltriphenylphosphonium iodide (7.4 g, 18.3 mmol) in anhydrous THF (30 mL) at 0 °C was added *n*-BuLi (23 mL of 1.6 M in hexane). The mixture was stirred for 1 h at room temperature and then transferred into the above prepared aldehyde solution in THF (10 mL) maintained at 0 °C. The reaction mixture was allowed to attain room temperature and was further stirred for 12 h. The reaction was quenched with saturated aqueous NH_4Cl, extracted with ethyl acetate, dried (Na_2SO_4), and concentrated. Purification of the residue on silica gel by using light petroleum/ethyl acetate (19:1) furnished **19** (1.49 g, 75%). $[\alpha]^{25}_D$ −8.1 (c 1, $CHCl_3$). IR ($CHCl_3$): 3379, 2932, 2856, 1597, 1481, 1401, 1322, 1195, 1157, 1083, 1040, 938, 837, 775 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ −0.19 (s, 3H), −0.18 (s, 3H), −0.06 (s, 6H), 0.88−0.91 (m, 6H), 0.89 (s, 18H), 2.11−2.25 (m, 2H), 3.63 (s, 6H), 3.89 (s, 6H), 3.90 (s, 6H), 4.52 (d, J = 3.6 Hz, 1H), 4.57 (d, J = 3.6 Hz, 1H), 4.67 (ddd, J = 17.2, 1.8, 1.3 Hz, 2H), 4.82 (br. ddd, J = 10.2, 1.7, 0.9 Hz, 2H), 5.58 (ddd, J = 17.2, 10.2, 7.3 Hz, 1H), 5.60 (ddd, J = 17.2, 10.2, 7.3 Hz, 1H), 6.01−6.04 (m, 4H), 6.60−6.69 (m, 4H), 6.84−6.95 (m, 4H). ^{13}C NMR (50 MHz): −4.9 (q), −4.6 (q), 12.3 (q), 12.4 (q), 18.2 (s), 25.8 (q), 44.7 (d), 44.8 (d), 55.7 (q), 60.7 (q), 60.9 (q), 61.0 (q), 74.3 (d), 100.9 (t), 106.2 (d), 106.3 (d), 107.8 (d), 107.9 (d), 109.9 (d), 111.8 (d), 113.6 (t), 115.3 (d), 120.0 (s), 122.5 (d), 124.4 (d), 126.4 (s), 129.4 (d), 129.7 (s), 129.9 (s), 138.2 (s), 140.6 (s), 142.5 (d), 142.6 (d), 146.4 (s), 146.5 (s), 147.3 (s), 150.8 (s), 152.0 (s) ppm. Anal. Calcd for $C_{27}H_{38}O_6$ Si: C, 66.63; H, 7.87%. Found: C, 66.87; H, 7.78%.

Synthesis of (+)-Eupomatilone-6 (23) and 3-Methyl Derivative 24. To solution of **22** (0.10 g, 0.258 mmol) in anhydrous THF (1 mL) at −78 °C, 1 M LiHMDS solution in THF (0.3 mL) was added. After 1 h, MeI (0.02 mL, 0.32 mmol) was added and stirring was continued for an additional 1 h. The reaction mixture was quenched with saturated ammonium chloride, extracted with ethyl acetate, dried over sodium sulfate, and concentrated. The crude residue was purified by silica gel chromatography by eluting with light petroleum/ethyl acetate (9:1) to give **24** (0.015 g, 14%) and **23** (0.06 g, 58%).

23 $[\alpha]^{25}_D$ +24.7 (c 0.5, $CHCl_3$) Lit.[1b] {$[\alpha]^{25}_D$ −25.6 (c 0.5)}.

24 $[\alpha]^{25}_D$ −40.8 (c 0.5, $CHCl_3$).

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Supporting Information Available: Experimental procedures, analytical and/or spectral data for all new compounds (**5**−**7**, **9**−**14**, **17**), NMR spectra of **2**−**5**, **11**−**14**, and HPLC chromatograms for **2**, **23**, **4**, **22**. This material is available free of charge via the Internet at http://pubs.acs.org.

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