Supporting Information
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Supporting Information

Biomimetic Total Synthesis of Scabellone B

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1. General experimental details

All reactions involving air or moisture sensitive reagents or intermediates were carried out under nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Yields refer to isolated compounds. Column chromatography was performed on silica gel (200-300 mesh). ¹H NMR spectra were recorded on a 400 MHz NMR spectrometer and ¹³C NMR spectra were recorded on a 100 MHz NMR spectrometer. Chemical shifts were reported in parts per million (ppm) with respect to the residual solvent signal CDCl₃ (¹H NMR: δ = 7.26; ¹³C NMR: δ = 77.16). Peak multiplicities were reported as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet.

2. Synthetic procedures:

2.1 Preparation of Trimethyl (2,3,6-trimethoxyphenyl) silane (8):

![Chemical structure of 7 and 8]

To solution of compound 7 (10.0 g, 59.49 mmol) in THF (50 mL) n-BuLi (2.5 M, 65.44 mmol) was added at 0°C. The mixture was stirred for 2 hours. TMSCl (7.1 g, 65.38 mmol) was added to the mixture. After 1 hour of stirring, the system was quenched with saturated NH₄Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous brine, and dried over anhydrous Na₂SO₄. The organic phase was concentrated by vacuum and purified by column chromatography, affording 8 as a colorless liquid (13.7 g, 96%): Rf (100% Petroleum ether) 0.2; IR (CCl₄) ν max: 2950, 2831, 1460, 1242, 1085, 856 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.89 (d, J = 8 Hz, 1H), 6.55 (d, J = 8 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.74 (s, 3H), 1.40 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 158.6, 154.6, 147.0, 121.2, 114.4, 105.4, 60.9, 56.3, 55.6, 1.4; HRMS (ESI⁺) m/z: [M+H]⁺ calcd for C₁₂H₂₀NaO₅Si, 241.1254; found, 241.1258.

2.2 Preparation of (E)-(4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,6-trimethoxyphenyl) trimethylsilane (9)

![Chemical structure of 8 and 9]
To solution of compound 8 (1.5 g, 6.24 mmol) in THF (20 mL), TMEDA (1.8 mL, 12.48 mmol) and n-BuLi (2.5 M, 7.49 mmol) were added at -78 °C. The mixture was stirred for 2 hours at 0 °C. Then, geranyl bromide (2.1 g, 9.98 mmol) was added as a colorless oil (1.80 g, 84%): Rf (100 % Petroleum ether) 0.3; IR (CCl4) νmax: 2933, 1457, 1376, 1098, 837 cm−1; 1H NMR (400 MHz, CDCl3) δ 6.44 (s, 1H), 5.33 (t, J = 4 Hz, 1H), 5.14 (t, J = 4 Hz, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.74 (s, 3H), 3.38 (d, J = 8 Hz, 2H), 2.10-2.12 (m, 2H), 2.07-2.08 (m, 2H), 1.77 (s, 3H), 1.69 (s, 3H), 1.62 (s, 3H), 0.32 (s, 9H); 13C NMR (100 MHz, CDCl3) δ 160.4, 158.5, 145.0, 137.9, 136.4, 131.6, 124.3, 122.7, 118.3, 106.6, 60.6, 60.3, 55.5, 39.9, 28.7, 26.9, 25.8, 17.8, 16.3, 1.5; HRMS (ESI+) m/z: [M+H]+ calcd for C22H37O3Si, 377.2506; found, 377.2498.

2.3 Preparation of (E)-1-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5-trimethoxybenzene (10)

To solution of compound 9 (1.9 g, 5.05 mmol) in EtOAc, KI (2.5 g, 15.6 mmol) and TMSCl (2.3 g, 21.8 mmol) were added. The mixture was stirred for 1.5 hours, quenched with saturated Na2SO4, and extracted with EtOAc. The organic layer was dried over anhydrous Na2SO4, concentrated by vacuum and purified by column chromatography, affording 10 as a colorless oil (1.41 g, 87%): Rf (1:100 Ethyl acetate: Petroleum ether) 0.4; IR (CCl4) νmax: 2932, 1541, 1220, 1148, 1056, 1010 cm−1; 1H NMR (400 MHz, CDCl3) δ 6.36 (d, J = 2.8 Hz, 1H), 6.30 (d, J = 2.8 Hz, 1H), 5.29 (t, J = 4 Hz, 1H), 5.10 (t, J = 4 Hz, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 3.35 (d, J = 8 Hz, 2H), 2.08-2.12 (m, 2H), 2.05-2.07 (m, 2H), 1.73 (s, 3H), 1.67 (s, 3H), 1.59 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 156.0, 153.4, 141.0, 136.2, 135.9, 131.5, 124.3, 122.8, 105.0, 97.8, 60.8, 55.8, 55.5, 39.8, 28.5, 26.8, 25.8, 17.8, 16.3; HRMS (ESI+) m/z: [M+H]+ calcd for C19H28NaO3, 305.2111; found, 305.2101.

2.4 Preparation of 6,6'-bis((E)-3,7-dimethylocta-2,6-dien-1-yl)-4,4'-dimethoxy-[1,1'-bi(cyclohexane)]-3,3',6,6'-tetraene-2,2',5,5'-tetraone (6)
To solution of 10 (100 mg, 0.33 mmol) in acetonitrile (16 mL), solution of CAN (723 mg, 1.32 mmol) in water (4 mL) was added slowly at -40°C. The solution was stirred 10 minutes at -40°C and extracted with EtOAc. The organic phase was dried over anhydrous Na₂SO₄, concentrated by vacuum and purified by column chromatography, affording 6 as a yellow oil (51.2 mg, 49%): \( R_f \) (1:5 Ethyl acetate: Petroleum ether) 0.4; IR (CCl₄) \( \nu_{max} \): 2930, 1717, 1558, 1276, 1232, 853 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 5.93 (s, 2H), 4.99 (t, \( J = 8 \) Hz, 2H), 4.85 (t, \( J = 8 \) Hz, 2H), 3.83 (s, 6H), 3.12-3.17 (m, 2H), 2.90-2.95 (m, 2H), 1.96-1.99 (m, 4H), 1.87-1.90 (m, 4H), 1.64 (s, 6H), 1.56 (s, 6H), 1.53 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 185.3, 181.2, 158.7, 143.5, 138.5, 138.4, 131.7, 123.9, 118.3, 107.3, 56.5, 39.7, 27.0, 26.5, 25.7, 17.8, 16.4; HRMS (ESI⁺) m/z: [M+H]⁺ calcd for C₃₅H₄₂NaO₆, 547.3054; found, 547.3047.

### 2.5 Preparation of scабellone A

The solution of 6 (40 mg, 0.073 mmol) in Pyridine (1 mL) was stirred for 2 d ays, concentrated by vacuum and purified by column chromatography, affording scабellone A as a brown oil (7 mg, 20%): \( R_f \) (1:2 Ethyl acetate: Petroleum ether) 0.2; IR (CCl₄) \( \nu_{max} \): 3427, 2921, 1636, 1457, 1275, 853 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.42 (s, 1H), 6.02 (s, 1H), 5.93 (d, \( J = 12 \) Hz, 1H), 5.60 (d, \( J = 12 \) Hz, 1H), 5.07 (t, \( J = 4 \) Hz, 1H), 5.00 (t, \( J = 4 \) Hz, 1H), 4.91 (t, \( J = 4 \) Hz, 1H), 4.48 (s, 1H), 3.85 (s, 6H), 3.07-3.12 (m, 1H), 2.95-3.01 (m, 1H), 2.10-2.12 (m, 2H), 1.93-1.97 (m, 2H), 1.84-1.87 (m, 2H), 1.73-1.75 (m, 2H), 1.64 (s, 6H), 1.55 (s, 6H), 1.43 (s, 3H), 1.36 (s,
2.6 Preparation of scabellone B

![Image of scabellone B preparation](image)

To solution of 6 (100 mg, 0.18 mmol) in DCM (5 mL), Et$_3$N (47 mg, 0.54 mmol) was added. After 5 minutes stirring, the system was concentrated by vacuum and purified by column chromatography, affording scabellone B as a purple oil (95 mg, 95%): $R_f$ (1:5 Ethyl acetate: Petroleum ether) 0.3; IR (CCl$_4$) $\nu_{\text{max}}$: 3467, 2922, 1684, 1594, 1221, 750 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.40 (s, 1H), 6.00 (d, $J$ = 8 Hz, 1H), 5.79 (s, 1H), 5.50 (s, 1H), 5.27 (d, $J$ = 8 Hz, 1H), 5.05 (m, 1H), 5.00 (t, $J$ = 4 Hz, 1H), 4.93 (t, $J$ = 4 Hz, 1H), 3.88 (s, 3H), 3.79 (s, 3H), 3.57 (m, 1H), 3.36 (dd, $J$ = 12 Hz, 1H), 1.94-1.98 (m, 4H), 1.92-1.94 (m, 2H), 1.92 (s, 3H), 1.85-1.87 (m, 2H), 1.62 (s, 3H), 1.59 (s, 3H), 1.56 (s, 3H), 1.50 (s, 3H), 1.49 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 182.7, 178.9, 158.0, 151.5, 150.2, 144.5, 139.3, 137.7, 137.2, 131.9, 131.8, 130.9, 127.0, 124.4, 124.0, 123.7, 117.0, 111.2, 107.4, 98.5, 67.8, 56.3, 56.2, 40.0, 39.9, 26.7, 26.5, 26.3, 25.7, 25.7, 17.7, 17.6, 17.4, 16.7; HRMS (ESI$^+$) $m/z$: [M+H]$^+$ calcd for C$_{34}$H$_{42}$NaO$_6$, 547.3054; found, 547.3046.

2.7 Preparation of scabellone C/D

![Image of scabellone C/D preparation](image)

To solution of 6 (100 mg, 0.18 mmol) in pyridine (5 mL), CuCl (0.9 mg, 0.09 mmol) was added and stirred for 4 days. The mixture was concentrated by vacuum and purified by column chromatography, affording scabellone C (42 mg, 42%) and
**Scabellone D** (21 mg, 21%).

**Scabellone C** as a purple oil: $R_f$ (1:5 Ethyl acetate: Petroleum ether) 0.5; IR (CCl$_4$) $\nu_{max}$: 2924, 1653, 1557, 1138, 749 cm$^{-1}; ^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.45 (s, 1H), 6.10 (d, $J$ = 12 Hz, 1H), 6.05 (d, $J$ = 12 Hz, 1H), 5.89 (s, 1H), 5.59 (d, $J$ = 8 Hz, 1H), 5.35 (d, $J$ = 12 Hz, 1H), 5.15 (t, $J$ = 4 Hz, 1H), 4.94(t, $J$ = 4 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 2.17-2.20 (m, 2H), 2.08-2.14 (m, 2H), 1.94-1.99 (m, 2H), 1.92-1.95 (m, 2H), 1.93 (s, 3H), 1.91-1.93 (m, 1H), 1.73-1.76 (m, 1H), 1.68 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H), 1.51 (s, 3H), 1.49 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 185.5, 179.1, 158.4, 153.1, 151.7, 144.5, 138.4, 134.0, 131.9, 131.9, 131.5, 126.7, 124.3, 123.9, 123.7, 120.3, 117.1, 107.7, 107.2, 101.3, 77.9, 67.8, 56.4, 56.3, 41.3, 39.9, 26.3, 25.8, 25.7, 24.7, 23.3, 17.8, 17.8, 17.3; HRMS (ESI$^+$) m/z: [M+H]$^+$ calcd for C$_{34}$H$_{40}$NaO$_6$, 545.2898; found, 545.2899.

**Scabellone D** as a purple oil: $R_f$ (1:5 Ethyl acetate: Petroleum ether) 0.6; IR (CCl$_4$) $\nu_{max}$: 2924, 1684, 1578, 1222, 750 cm$^{-1}; ^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.44 (s, 1H), 6.08 (d, $J$ = 8 Hz, 1H), 6.03(d, $J$ = 12 Hz , 1H), 5.89 (s, 1H), 5.55 (d, $J$ = 12 Hz, 1H), 5.33 (d, $J$ = 8 Hz, 1H), 5.12 (t, $J$ = 4 Hz, 1H), 4.93(t, $J$ = 4 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 2.14-2.20 (m, 2H), 1.94-1.99 (m, 2H), 1.92-1.94 (m, 2H), 1.93 (s, 3H), 1.80-1.87 (m, 2H), 1.63 (s, 3H), 1.59 (s, 3H), 1.57 (s, 3H), 1.55 (s, 3H), 1.51 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 185.4, 179.1, 158.3, 152.9, 151.8, 144.5, 138.3, 133.9, 131.9, 131.7, 131.5, 127.4, 124.3, 123.7, 123.7, 120.8, 117.1, 107.7, 107.3, 101.1, 77.7, 67.8, 56.4, 56.2, 39.9, 38.4, 26.3, 26.0, 25.8, 25.7, 22.4, 17.8, 17.6, 17.3; HRMS (ESI$^+$) m/z: [M+H]$^+$ calcd for C$_{34}$H$_{40}$NaO$_6$, 545.2898; found, 545.2913.

### 2.8 Generation of scabellone C/D from scabellone A

![Diagram of scabellone A and C/D synthesis]

To solution of scabellone A (10 mg, 0.018 mmol) in CDCl$_3$ (5 mL), CuCl (0.1 mg, 0.01 mmol) was added and stirred for 3 days. The mixture was concentrated by vacuum and purified by column chromatography, affording scabellone C (5.6 mg, 56%) and scabellone D (1.5 mg, 15%).
3. Copies of $^1$H NMR and $^{13}$C NMR spectra

$^1$H NMR Copy for trimethyl (2,3,6-trimethoxyphenyl) silane (8).

$^{13}$C NMR Copy for trimethyl (2,3,6-trimethoxyphenyl) silane (8).
$^1$H NMR Copy for (E)-(4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,6-trimethoxyphenyl) trimethylsilane (9).

$^{13}$C NMR Copy for (E)-(4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,6-trimethoxyphenyl) trimethylsilane (9).
$^1$H NMR Copy for (E)-1-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5-trimethoxybenzene (10).

$^{13}$C NMR Copy for (E)-1-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5-trimethoxybenzene (10).
$^1$H NMR Copy for 6,6'-bis((E)-3,7-dimethylocta-2,6-dien-1-yl)-4,4'-dimethoxy-[1,1'-bi(cyclohexane)]-3,3',6,6'-tetraene-2,2',5,5'-tetraone (6).

$^{13}$C NMR Copy for 6,6'-bis((E)-3,7-dimethylocta-2,6-dien-1-yl)-4,4'-dimethoxy-[1,1'-bi(cyclohexane)]-3,3',6,6'-tetraene-2,2',5,5'-tetraone (6).
$^1$H NMR Copy for scabellone A (1).

$^1$H NMR Copy for scabellone B (2).
$^{13}$C NMR Copy for scabellone B (2).
$^1$H NMR Copy for scabellone C (3)
$^{13}$C NMR Copy for scabellone C (3).

$^1$H NMR Copy for scabellone D (4)
4. **Comparison the $^1$H NMR and $^{13}$C NMR spectra with Copp’s spectra**

(In all spectra below, the top ones are from our synthetic compounds, and the bottom ones are from Copp’s report)

$^1$H NMR Copy for scabellone A (1)
$^1$H NMR Copy for scabellone B (2)

$^{13}$C NMR Copy for scabellone B (2)
$^1$H NMR Copy for scabellone C (3)

$^{13}$C NMR Copy for scabellone C (3)
$^1$H NMR Copy for scabellone D (4)