Supporting Information to:

Alkaloids from *Melochia chamaedrys*

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Materials and Methods

Reduction of 2
Alkaloid 2 (20 mg) was treated with NaBH₄ (2 mg) in MeOH (2 mL) for 1 h. The reaction mixture was evaporated and subjected to preparative TLC eluting with CHCl₃:MeOH (96:4) to give 3 (12 mg) as colorless needles. m.p. 65.2 – 66.2 °C; ¹H-NMR (CDCl₃, 400 MHz): δ = 4.86 (1H, m, H-8), 3.93 (3H, s, Me-18), 2.97 (1H, m, H-5), 2.48 (3H, s, Me-17), 2.06/1.92 (2H, m, H-7), 1.90/1.69 (2H, m, H-6), 0.87 (3H, s, Me-16); ¹³C-NMR (CDCl₃, 100 MHz): δ = 168.3 (C-4), 147.4 (C-3), 143.8 (C-4’), 142.2 (C-2), 128.7 (C-8’), 66.0 (C-8), 60.5 (C-18), 32.2 (C-7), 31.8 (C-9), 31.7 (C-5), 23.1 (C-6), 25.6-29.7 (C-10-15), 14.2 (C-16), 14.1 (C-17); EI-MS: m/z =321 [M]+, and 4 (2.4 mg) as an oil; ¹H-NMR (CDCl₃, 400 MHz): δ = 4.76 (1H, m, H-8), 3.75 (3H, s, Me-18), 2.87 (1H, m, H-5), 2.35 (3H, s, Me-17), 2.04/1.90 (2H, m, H-7), 1.92/1.60 (2H, m, H-6), 0.85 (3H, s, Me-16); ¹³C-NMR (CDCl₃, 100 MHz): δ = 168.4 (C-4), 147.0 (C-3), 144.1 (C-4’), 142.0 (C-2), 128.3 (C-8’), 66.5 (C-8), 60.6 (C-18), 32.1 (C-7), 31.8 (C-9), 32.7 (C-5), 23.0 (C-6), 25.0-30.0 (C-10-15), 14.1 (C-16), 14.0 (C-17); EI-MS: m/z =321 [M]+.

Methylation of 3 and 4
Compound 3 (10 mg) was treated with diazomethane in Et₂O for 24 hours to give 5 (8.5 mg) as an oil; ¹H-NMR (CDCl₃, 400 MHz): δ = 4.18 (1H, m, H-8), 3.75(3H, s, Me-18), 2.85 (1H, m, H-5), 2.34 (3H, s, Me-17), 2.0/1.95 (2H, m, H-7), 1.92/1.70 (2H, m, H-6), 0.91 (3H, s, Me-16); ¹³C-NMR (CDCl₃, 100 MHz): δ = 167.5 (C-4), 147.7 (C-3), 144.1 (C-4’), 142.4 (C-2), 127.6 (C-8’), 75.1 (C-8), 58.5 (C-18), 56.4 (C-19), 31.8 (C-7), 31.6 (C-5), 23.4 (C-6), 25.0-30.1 (C-10-15), 14.3 (C-16), 14.1 (C-17); EI-MS: m/z = 335 [M]+.
Compound 4 (1.5 mg) was treated with diazomethane in Et₂O for 24 hours to give 6 (1.4 mg) as oil; ¹H-NMR (CDCl₃, 400 MHz): δ = 4.20 (1H, m, H-8), 3.74 (3H, s, Me-18), 2.85 (1H, m, H-5), 2.37 (3H, s, Me-17), 2.06/1.95 (2H, m, H-7), 1.90/1.70 (2H, m, H-6), 0.90 (3H, s, Me-16); ¹³C-NMR (CDCl₃, 100 MHz): δ 168.2 (C-4), 147.2 (C-3), 144.1 (C-4’), 142.1 (C-2), 128.2 (C-8’), 75.9 (C-8), 58.5 (C-18), 56.4 (C-19), 31.8 (C-7), 31.6 (C-5), 23.4 (C-6), 25.0-30.0 (C-10-15), 14.5 (C-16), 14.1 (C-17); EI-MS: m/z = 335 [M⁺].

Determination of the absolute configuration of C-8 of 3 by Horeau’s method:

To 5 µmol of 3, ca. 6 µmol of racemic α-phenylbutyric anhydride and 30 µL dry pyridine were added. This solution was kept for 1 h at room temperature. After standing with 10 µL of water for 30 min, usual work-up gave an enantiomeric excess of (−)-2-phenylbutyric acid. A solution of diazomethane in diethyl ether (50 µL) was added until a permanent yellow color was formed. The solution was concentrated under an N₂ stream to ca. half its original volume, which was used for gas chromatography. A 25 m fused silica capillary column with heptakis(2,6-di-O-methyl-3-pentyl)-β-CD¹⁹ diluted with polysiloxane OV 1701 (1:1w/w) at 85 °C column temperature was used in a Varian 3800 gas chromatograph, equipped with FID, for the separation of the enantiomeric excess of 2-phenylbutyric acid methyl ester. An excess of 7.5% of the enantiomer (R) was observed. The modified Horeau’s rule for chiral GC (see ref. [20] in the main text), indicated the (R) configuration for C-8 in 3.

X-ray crystallographic analysis of 3
Crystallization of 3 from MeOH afforded crystals suitable for single-crystal X-ray diffraction. The structure of 3 (see Fig. 2 in the main text) was solved by direct methods (SHELXS-97) and additional atoms were located in the difference Fourier map and refined from F² (SHELXS-97).

Crystal data: C₁₉H₃₁NO₃.H₂O, M= 339.46, orthorhombic, space group P₂₁2₁2₁(No.19), a = 4.7572(2) Å, b = 15.3749 (7) Å, c = 26.7675 (11) Å, V = 1977.81 (15) Å³, T = 293 (2) K, Z = 4, Dc = 1.152 g/cm⁻³, µ = 0.079 mm⁻¹, 3.06 < θ < 25.5, F(0000) = 744; 10985 reflections measured, 2154 unique (Rint = 0.0996). The final wR² = 0.1423 (all data), R₁ [I > σ(I)] = 0.0544, GoF = 0.95. CCDC No 281011.

Table 1S Minimal inhibitory concentration (µg /mL) for compounds 1 and 3 – 6.

<table>
<thead>
<tr>
<th>Gram-positive bacteria</th>
<th>1</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Control¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em> ATCC 6538p</td>
<td>50.0</td>
<td>25.0</td>
<td>-</td>
<td>12.5</td>
<td>25.0</td>
<td>6.25</td>
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<td><em>Staphylococcus epidermidis</em> ATCC 12228</td>
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<td>25.0</td>
<td>-</td>
<td>12.5</td>
<td>-</td>
<td>3.12</td>
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<tr>
<td><em>Bacillus subtilis</em> ATCC 6633</td>
<td>75.0</td>
<td>nd</td>
<td>50.0</td>
<td>12.5</td>
<td>25.0</td>
<td>1.56</td>
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<tr>
<td>Gram-negative bacteria</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Salmonella setubal</em> ATCC 19796</td>
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<td>50.0</td>
<td>50.0</td>
<td>12.5</td>
<td>-</td>
<td>6.25</td>
</tr>
<tr>
<td><em>Escherichia coli</em> ATCC 25792</td>
<td>12.5</td>
<td>12.5</td>
<td>-</td>
<td>12.5</td>
<td>-</td>
<td>6.25</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> ATCC 10031</td>
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<td>75.0</td>
<td>-</td>
<td>12.5</td>
<td>-</td>
<td>3.12</td>
</tr>
<tr>
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<td>25.0</td>
<td>-</td>
<td>12.5</td>
<td>-</td>
<td>1.56</td>
</tr>
<tr>
<td>Yeasts</td>
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<tr>
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<td>-</td>
<td>5.15</td>
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<tr>
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<td>-</td>
<td>25.0</td>
<td>-</td>
<td>10.3</td>
</tr>
<tr>
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<td>nd</td>
<td>-</td>
<td>nd</td>
<td>-</td>
<td>10.3</td>
</tr>
</tbody>
</table>

¹ Standard antibiotic chloramphenicol for bacteria and nystatin for yeast.
nd = not determined (MIC was greater than 100 µg /mL); - = not determined (not enough compound available)