Supporting Information

Isolation, Structure Elucidation and Total Synthesis of
Myrtuspirone A from *Myrtus communis*

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# Table of Contents

1. Experimental detail for isolation and elucidation of natural product ........................................... 3  
   1.1 General experimental procedure .................................................................................. 3  
   1.2 Isolation of myrtuspirone A (1) .............................................................................. 3  
   1.3 Chiral HPLC analysis of (±)-myrtuspirone A (1) ...................................................... 4  
   1.4 Physico-chemical data of myrtuspirone A (1) ........................................................... 4  
   1.5 $^1$H and $^{13}$C NMR data of 1 ............................................................................... 5  
   1.6 X-ray crystallographic study of myrtuspirone A (1) .................................................... 5  
   1.7 Calculation details for myrtuspirone A (1) ................................................................. 6  
   1.8 HRESIMS, UV, IR, NMR spectra of natural product myrtuspirone A (1) ............... 12  

2. Synthetic experimental procedures ................................................................................................. 16  
   2.1 General information ....................................................................................................... 16  
   2.2 General procedure for the synthesis of 4a-4k and (-)-4 ............................................. 17  
       2.2.1 Synthesis of 4 ..................................................................................................... 17  
       2.2.2 Procedure A: General procedure for the synthesis of 4a-4k ............................... 17  
       2.2.3 Procedure B: Synthesis of enantioenriched product (-)-4 ................................. 19  
   2.3 Synthesis of (±)-myrtuspirone A and (-)-myrtuspirone A .......................................... 27  

3. Synthetic $^1$H and $^{13}$C NMR spectra ......................................................................................... 29  

4. HPLC chromatogram of (-)-myrtuspirone A ........................................................................... 44  

5. Antibacterial activity assay ........................................................................................................... 45  
   5.1. Microorganisms ......................................................................................................... 45  
   5.2 Antibiotics and reagents ............................................................................................. 45  
   5.3 MIC determination ........................................................................................................ 45  
   5.4 In vitro antibacterial activities of myrtuspirone A (1) ..................................................... 45
1. Experimental detail for isolation and elucidation of natural product

1.1 General experimental procedure

IR spectra (KBr disks, in cm⁻¹) were obtained using a Jasco FT/IR-4600 Fourier Transform spectrometer (Jasco, Tokyo, Japan) or a Shimadzu IR Prestige 21 spectrometer (Shimadzu, Japan). UV spectra were recorded on a Jasco V-550 UV/Vis spectrometer (Jasco, Tokyo, Japan); λ_max (log ε) in nm. Optical rotations were measured on a Jasco P-2000 polarimeter (Jasco, Tokyo, Japan) with a 1 cm cell at setting temperature. Melting points were obtained on a Buchi melting point B-545 apparatus (Buchi Instrument, Switzerland) without correction. X-ray crystallographic analysis was carried out on an Agilent Gemini S Ultra CCD diffractometer with Cu Kα radiation (λ = 1.54178 Å). CD spectra were obtained on a ChirascanqCD (Applied Photophysics Limited, Surrey, United Kingdom) at room temperature. HRESIMS spectra were detected using an Agilent 6210 LC/MSD TOF-MS spectrometer (Agilent Technologies, CA, USA) or a Bruker Apex IV FTMS mass spectrometer. NMR spectra were measured with Bruker AV-600 or AV-500 spectrometer (Bruker, Fällanden, Switzerland). Column chromatographies (CC) were performed on silica gel (300–400 mesh, Qingdao Marine Chemical Plant, China), ODS (Merck, Darmstadt, Germany) and Sephadex LH-20 (Pharmacia, Uppsala, Sweden). Preparative thin layer chromatography (PTLC) separations were carried out 0.50 mm Yantai (China) silica gel plates. HPLC were carried out using Agilent 1260 Series instrument equipped with 1260 series multiple wavelength detector, as well as Cosmool 5C18-MS-II and chiral Phenomenex Lux cellulose-3 (4.6 × 250 mm) columns. Preparative HPLC were carried out using Agilent 1260 Series instrument and Cosmool 5C18-MS-II (250×20 mm; 250×10 mm) columns. All solvents used in CC and HPLC were analytical (Tianjin Fuyu Fine Chemical Company, Tianjin, China) and chromatographic grade (Fisher Scientific, NJ, USA), respectively.

1.2 Isolation of myrtuspirone A (1)

The leaves of Myrtus communis were collected in Shanghai City of China, in August of 2014. A voucher specimen (No. 2014082401) was deposited in the Institute of Traditional Chinese Medicine and Natural Products, College of Pharmacy, Jinan University, Guangzhou, P. R. China.

The air-dried and powdered leaves of M. Communis (8.0 kg) were percolated with 95% EtOH (24 h × 5) at room temperature. After filtration, the alcoholic extract was evaporated under
reduced pressure to give 1.2 kg crude extract, which was then suspended in H₂O and extracted with petroleum ether (PE, b.p. 60–90 °C). The petroleum ether solution was concentrated to give a residue (389 g), which was subjected to a silica gel column eluted with a gradient mixture of PE/EtOAc (100:0 → 0:100). Ten fractions (Frs. A–J) were collected and examined by TLC. Fr. F (19.0 g) was subjected to ODS column using CH₃OH-H₂O (70:30→100:0) as eluent to yield eight subfractions (Frs. F1–F8). The subfraction F6 was purified by reversed-phase semi-preparative HPLC (column: Cosmosil 5C18-MS-II 250×10 mm, flow rate: 3 mL/min; detection wavelength: 280 nm; mobile phase: 85% CH₃CN-H₂O) to afford 1 (25.3 mg, tR 30.3 min).

1.3 Chiral HPLC analysis of (±)-myrtuspirone A (1)

![Chromatogram for the Chiral HPLC analysis of (±)-1](image1)

**Figure S1** Chromatogram for the Chiral HPLC analysis of (±)-1; Conditions for analytical HPLC: Phenomenex Lux 5u Cellulose-3 (250 × 4.6 mm, 5 μm), 55:45 (MeCN: H₂O), 1.0 mL/min, 25°C, UV 280 nm.

1.4 Physico-chemical data of myrtuspirone A (1)

**Myrtuspirone A (1):** colourless blocks (CH₃OH); mp 204–205 °C; (+)-1 [α]D²⁶ = +93° (c 0.88, CH₃OH); (−)-1 [α]D²⁶ = −88° (c 0.91, CH₃OH); UV (CH₃OH) λmax (log e) 204 (4.19), 226
(4.28), 290 (4.25) nm; IR (KBr) \( \nu_{\text{max}} \) 3461, 2985, 2874, 1709, 1631, 1589, 1456, 1387, 1143, 1116, 971, 872 cm\(^{-1}\); CD (CH\(_3\)CN) for (+)-1: 214 (\( \Delta \epsilon \) -13.7), 232 (\( \Delta \epsilon \) +4.9), 285 (\( \Delta \epsilon \) -20.6), 311 (\( \Delta \epsilon \) +27.0) nm; for (-)-1: 214 (\( \Delta \epsilon \) +13.0), 232 (\( \Delta \epsilon \) -4.2), 286 (\( \Delta \epsilon \) +18.9), 311 (\( \Delta \epsilon \) -23.4) nm; HRESIMS \( m/z \) 445.2224 [M+H]\(^+\) (calcd for C\(_{25}\)H\(_{33}\)O\(_7\): 445.2221).

1.5 \(^1\)H and \(^{13}\)C NMR data of 1

| No. | \( \delta_H \) | \( \delta_C \) | No. | \( \delta_H \) | \( \delta_C \) |
|-----|-------------|-------------|-----|-------------|-------------|
| 1   | –           | –           | 13  | 1.10 d (6.7)| 19.4        |
| 2   | –           | 98.7        | 14  | 1.10 d (6.7)| 19.1        |
| 3   | 4.22 d (2.5)| 47.9        | 15  | 1.89 s      | 8.0         |
| 3a  | –           | 103.8       | 2'  | –           | 202.8       |
| 4   | –           | 155.1       | 3'  | –           | 59.0        |
| 5   | –           | 106.1       | 4'  | –           | 208.1       |
| 6   | –           | 163.0       | 5'  | –           | 55.7        |
| 7   | –           | 98.5        | 6'  | –           | 202.2       |
| 7a  | –           | 161.1       | 7'  | 1.46 s      | 22.4        |
| 8   | 2.12 m      | 29.3        | 8'  | 1.35 s      | 22.6        |
| 9   | 0.53 d (6.6)| 17.3        | 9'  | 1.23 s      | 24.1        |
| 10  | 1.00 d (7.0)| 21.8        | 10' | 1.31 s      | 23.9        |
| 11  | –           | 210.7       | 4-OH| 11.13 s     | –           |
| 12  | 3.92 septet (6.7)| 38.7 | 6-OH| 13.02 s     | –           |

1.6 X-ray crystallographic study of myrtuspirone A (1)

Crystallographic data for myrtuspirone A (1) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1875660. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or email: deposit@ccdc.cam.ac.uk).

Table S2 Crystal data and structure refinement for myrtuspirone A (1)

| Empirical formula       | C\(_{25}\)H\(_{32}\)O\(_7\) |
|-------------------------|-----------------------------|
| Formula weight          | 444.50                      |
| Temperature             | 150.00 (10)                 |
| Wavelength              | 1.54184 Å                   |
Crystal system, space group: monoclinic, P2₁/c

Unit cell dimensions:

\[ a = 16.02412(10) \text{ Å}, \alpha = 90.0 \text{ deg.} \]
\[ b = 12.70828(8) \text{ Å}, \beta = 93.7949(6) \text{ deg.} \]
\[ c = 11.36386(7) \text{ Å}, \gamma = 90.0 \text{ deg.} \]

Volume: \( 2309.05 (3) \text{ Å}^3 \)

Z, Calculated density: 4, 1.279 Mg/m³

Absorption coefficient \( \mu \): 0.762 mm⁻¹

\( F(000) \): 952.0

Crystal size: \( 0.31 \times 0.29 \times 0.22 \text{ mm} \)

2Θ range for data collection: 8.888 to 141.632 deg.

Limiting indices: \(-19 \leq h \leq 19, -15 \leq k \leq 15, -12 \leq l \leq 13\)

Reflections collected / unique: 26565 / 4409 [R(int) = 0.0232]

Max. and min. transmission: 1.00000 and 0.408

Data / restraints / parameters: 4409/13/294

Goodness-of-fit on \( F^2 \): 1.079

Final R indices [I>2sigma(I)]: \( R_1 = 0.0390, wR_2 = 0.0975 \)

R indices (all data): \( R_1 = 0.0410, wR_2 = 0.0991 \)

Largest diff. peak and hole: 0.50 and -0.28 e.Å⁻³

1.7 Calculation details for myrtuspirone A (1)

The conformational analysis of 3S-1 was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 56 conformers of 3S-1 with an energy cutoff of 10 kcal mol⁻¹ to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in acetonitrile by using Gaussian09 software,¹ and 8 conformers of 3S-1 were selected. All of the optimized stable conformers were used for TDDFT computation of the excited states at the same levels, with the consideration of the first 50 excitations. The overall ECD curves of 3S-1 were weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.2 eV), with a UV correction of 2 nm. The calculated ECD spectrum of 3S-1 was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.² The ECD spectra of 3R-1 was calculated using the same method.
Figure S2 Key molecular orbitals involved in important transitions regarding the ECD spectra of conformer 8 in acetonitrile at the B3LYP/6-31+G(d) level.

Table S3 Key transitions and their related rotatory and oscillator strengths of conformer 8 of 3S-1 at the B3LYP/6-31+G(d) level in acetonitrile.

| No. | Energy (cm$^{-1}$) | Wavelength (nm) | R (length) | Osc. Strength | Major contribs |
|-----|-------------------|-----------------|------------|---------------|----------------|
| 1   | 27429.5           | 364.6           | 6.4967     | 0.007         | HOMO→LUMO (83%) |
| 2   | 28982.1           | 345             | 11.078     | 0.0236        | H-1→LUMO (62%), HOMO→LUMO (14%) |
| 3   | 30014.5           | 333.2           | 13.4355    | 0.0314        | HOMO→L+1 (94%)  |
| 4   | 30987.2           | 322.7           | -6.0379    | 0.0144        | H-1→L+1 (10%), HOMO→L+2 (75%)  |
| 5   | 31598.6           | 316.5           | 59.0673    | 0.0306        | H-2→LUMO (17%), H-2→L+1 (13%), H-1→L+1 (19%), H-1→L+2 (10%), HOMO→L+2 (18%) |
| 6   | 32351.9           | 309.1           | 11.9592    | 0.0027        | H-2→LUMO (41%), H-1→LUMO (18%), H-1→L+1 (15%) |
| 7   | 33581.9           | 297.8           | 7.9613     | 0.001         | H-3→LUMO (15%), H-3→L+1 (53%), H-3→L+2 |
|   | Value 1 | Value 2 | Value 3 | Value 4 | Description |
|---|---------|---------|---------|---------|-------------|
| 8 | 34224.8 | 292.2   | 103.26  | 0.0802  | H-5→LUMO (17%), H-2→L+2 (13%), H-2→L+3 (20%), H-1→L+1 (15%) |
| 9 | 35031.3 | 285.5   | -298.49 | 0.2013  | H-4→LUMO (16%), H-2→L+3 (16%), H-1→L+1 (29%) |
| 10| 35564.5 | 281.2   | 69.6763 | 0.085   | H-1→L+2 (53%), HOMO→L+3 (16%) |
| 11| 36012.9 | 277.7   | 33.7257 | 0.0419  | H-1→L+2 (10%), HOMO→L+3 (81%) |
| 12| 36012.9 | 262.4   | 6.632   | 0.0043  | H-1→L+3 (87%) |
| 13| 39044   | 256.1   | 2.6906  | 0.0003  | H-5→LUMO (33%), H-4→LUMO (17%), H-2→L+1 (23%) |
| 14| 39639.2 | 252.3   | 8.8377  | 0.0149  | H-3→LUMO (77%) |
| 15| 39966.7 | 250.2   | -7.6009 | 0.0332  | H-5→LUMO (11%), H-4→LUMO (13%), H-2→LUMO (10%), H-2→L+2 (21%), H-2→L+3 (23%) |
| 16| 40764.3 | 245.3   | 14.7566 | 0.0129  | H-4→LUMO (18%), H-2→L+1 (18%), H-2→L+2 (27%), H-2→L+3 (16%) |
| 17| 41184.6 | 242.8   | 1.1639  | 0.0015  | H-5→L+1 (25%), H-5→L+2 (21%), H-4→L+1 (13%), H-2→L+1 (12%) |
| 18| 42246   | 236.7   | 0.0207  | 0.0192  | H-5→LUMO (10%), H-4→L+1 (30%), H-4→L+2 (16%), H-3→L+1 (13%), H-3→L+2 (22%) |
| 19| 42515.4 | 235.2   | -3.7111 | 0.0133  | H-4→L+1 (13%), H-3→L+1 (22%), H-3→L+2 (39%) |
| 20| 42529.1 | 235.1   | 16.1843 | 0.0116  | HOMO→L+4 (51%), HOMO→L+5 (40%) |
| 21| 43986.6 | 227.3   | 32.0118 | 0.1124  | H-6→LUMO (12%), H-4→L+1 (20%), H-4→L+2 (23%), HOMO→L+5 (12%) |
| 22| 44260   | 225.9   | -17.883 | 0.0601  | H-1→L+4 (50%), H-1→L+5 (18%) |
| 23| 45114.1 | 221.7   | -3.0141 | 0.1375  | H-5→L+1 (12%), H-5→L+3 (11%), H-4→L+2 (11%), H-2→L+2 (11%), H-3→L+2 (39%) |
|   |   |   |   |   |
|---|---|---|---|---|
| 24 | 45398 | 220.3 | -35.621 | 0.0437 | H-4→L+3 (28%) |
|   |   |   |   |   | H-6→LUMO (61%), H-4→L+2 (11%) |
| 25 | 45612.6 | 219.2 | -19.964 | 0.0738 | HOMO→L+4 (19%), HOMO→L+5 (15%), HOMO→L+7 (12%) |
| 26 | 45767.4 | 218.5 | 5.8767 | 0.0104 | H-1→L+4 (30%), H-1→L+5 (57%) |
| 27 | 46223.1 | 216.3 | -2.3752 | 0.0124 | H-5→L+1 (18%), H-5→L+2 (40%), H-4→L+3 (26%) |
| 28 | 46439.3 | 215.3 | -13.791 | 0.0488 | HOMO→L+7 (67%) |
| 29 | 46784.5 | 213.7 | 4.9799 | 0.0123 | H-5→L+3 (16%), H-3→L+3 (66%) |
| 30 | 47083.7 | 212.4 | -7.8792 | 0.0227 | H-5→L+3 (15%), H-3→L+3 (17%), HOMO→L+6 (50%) |
| 31 | 47155.5 | 212.1 | 10.4063 | 0.0194 | H-5→L+3 (38%), H-3→L+3 (12%), HOMO→L+6 (27%) |
| 32 | 48246.8 | 207.3 | 0.875 | 0.0184 | H-6→L+1 (63%), H-6→L+2 (19%) |
| 33 | 48433.1 | 206.5 | -3.2849 | 0.0033 | HOMO→L+8 (87%) |
| 34 | 49401 | 202.4 | 0.349 | 0.0022 | H-1→L+7 (60%), HOMO→L+9 (25%) |
| 35 | 49485.7 | 202.1 | -1.666 | 0.0071 | H-1→L+6 (66%) |
| 36 | 49665.5 | 201.3 | 0.7281 | 0.0051 | H-1→L+6 (15%), H-1→L+7 (25%), HOMO→L+9 (50%) |
| 37 | 49826.9 | 200.7 | 28.1785 | 0.0704 | H-6→L+1 (17%), H-6→L+2 (47%) |
| 38 | 50505.2 | 198 | 32.3571 | 0.0398 | H-8→LUMO (48%), H-7→LUMO (14%), HOMO→L+10 (10%) |
| 39 | 50644.7 | 197.5 | -10.267 | 0.0752 | H-8→LUMO (15%), HOMO→L+10 (42%) |
| 40 | 50816.5 | 196.8 | -13.803 | 0.0046 | H-3→L+4 (55%), H-3→L+5 (34%) |
| 41 | 51027.8 | 196 | -13.683 | 0.0055 | HOMO→L+11 (53%), HOMO→L+12 (13%), HOMO→L+13 (15%) |
| 42 | 51196.4 | 195.3 | -3.5898 | 0.0016 | H-7→LUMO (17%), H-7→L+1 (31%), H-7→L+2 (11%), HOMO→L+12 (14%) |
| 43 | 51314.2 | 194.9 | 8.8944 | 0.0178 | H-2→L+4 (14%), HOMO→L+11 (10%), HOMO→L+12 (29%) |
| 44 | 51380.3 | 194.6 | -3.4504 | 0.0048 | H-1→L+8 (84%) |
|   | Atomic | Atomic | Coordinates (Angstroms) |   |
|---|---|---|---|---|
| 1 | 8 | 0 | 2.825775 | 0.539713 | -2.18109 |
| 2 | 8 | 0 | 5.550259 | -0.615011 | 1.066591 |
| 3 | 8 | 0 | 1.179739 | -0.570661 | 2.094231 |
| 4 | 8 | 0 | 0.891869 | -0.960261 | -0.99429 |
| 5 | 8 | 0 | -3.56286 | -2.54352 | -1.26069 |
| 6 | 6 | 0 | -3.14027 | -0.436 | -0.13534 |
| 7 | 8 | 0 | -5.36857 | -1.20756 | -0.19125 |
| 8 | 8 | 0 | -2.48604 | 1.59339 | 0.993823 |
| 9 | 6 | 0 | -2.13141 | 0.509682 | 0.235868 |
| 10 | 6 | 0 | -0.81356 | 0.322204 | -0.14518 |
| 11 | 6 | 0 | -1.35057 | -1.84288 | -1.20027 |
| 12 | 1 | 0 | -1.68561 | 2.063647 | 1.27327 |
| 13 | 6 | 0 | -0.46352 | -0.86095 | -0.8022 |
| 14 | 6 | 0 | -4.58009 | -0.30485 | 0.165367 |
| 15 | 6 | 0 | 1.531176 | 0.077776 | -0.20798 |
| 16 | 6 | 0 | -2.70087 | -1.5979 | -0.86804 |
| 17 | 1 | 0 | -4.46974 | -2.25862 | -0.93471 |
| 18 | 6 | 0 | 2.804701 | 0.513725 | -0.96886 |
| 19 | 6 | 0 | -0.94455 | -3.10287 | -1.91764 |
| 20 | 1 | 0 | -1.43402 | -3.17255 | -2.89635 |
| 21 | 1 | 0 | 0.137151 | -3.13082 | -2.07062 |
| 22 | 1 | 0 | -1.24403 | -3.99334 | -1.35224 |
| 23 | 6 | 0 | 4.04726 | 0.836182 | -0.12421 |
| 24 | 6 | 0 | 3.753298 | 1.98759 | 0.885905 |
| 25 | 1 | 0 | 2.928551 | 1.771368 | 1.572648 |
| 26 | 1 | 0 | 4.6504 | 2.166805 | 1.486551 |
| 27 | 1 | 0 | 3.514711 | 2.907441 | 0.342128 |
| 28 | 6 | 0 | 1.926782 | -0.61674 | 1.137392 |
| 29 | 6 | 0 | 4.40114 | -0.40267 | 0.741247 |

Table S4 Cartesian coordinates of conformer 8 of 3S-1

Standard orientation:

| Center Number | Atomic Number | Atomic Type | X | Y | Z |
|---------------|---------------|-------------|---|---|---|
| 1             | 8             | 0           | 2.825775 | 0.539713 | -2.18109 |
| 2             | 8             | 0           | 5.550259 | -0.615011 | 1.066591 |
| 3             | 8             | 0           | 1.179739 | -0.570661 | 2.094231 |
| 4             | 8             | 0           | 0.891869 | -0.960261 | -0.99429 |
| 5             | 8             | 0           | -3.56286 | -2.54352 | -1.26069 |
| 6             | 6             | 0           | -3.14027 | -0.436 | -0.13534 |
| 7             | 8             | 0           | -5.36857 | -1.20756 | -0.19125 |
| 8             | 8             | 0           | -2.48604 | 1.59339 | 0.993823 |
| 9             | 6             | 0           | -2.13141 | 0.509682 | 0.235868 |
| 10            | 6             | 0           | -0.81356 | 0.322204 | -0.14518 |
| 11            | 6             | 0           | -1.35057 | -1.84288 | -1.20027 |
| 12            | 1             | 0           | -1.68561 | 2.063647 | 1.27327 |
| 13            | 6             | 0           | -0.46352 | -0.86095 | -0.8022 |
| 14            | 6             | 0           | -4.58009 | -0.30485 | 0.165367 |
| 15            | 6             | 0           | 1.531176 | 0.077776 | -0.20798 |
| 16            | 6             | 0           | -2.70087 | -1.5979 | -0.86804 |
| 17            | 1             | 0           | -4.46974 | -2.25862 | -0.93471 |
| 18            | 6             | 0           | 2.804701 | 0.513725 | -0.96886 |
| 19            | 6             | 0           | -0.94455 | -3.10287 | -1.91764 |
| 20            | 1             | 0           | -1.43402 | -3.17255 | -2.89635 |
| 21            | 1             | 0           | 0.137151 | -3.13082 | -2.07062 |
| 22            | 1             | 0           | -1.24403 | -3.99334 | -1.35224 |
| 23            | 6             | 0           | 4.04726 | 0.836182 | -0.12421 |
| 24            | 6             | 0           | 3.753298 | 1.98759 | 0.885905 |
| 25            | 1             | 0           | 2.928551 | 1.771368 | 1.572648 |
| 26            | 1             | 0           | 4.6504 | 2.166805 | 1.486551 |
| 27            | 1             | 0           | 3.514711 | 2.907441 | 0.342128 |
| 28            | 6             | 0           | 1.926782 | -0.61674 | 1.137392 |
| 29            | 6             | 0           | 4.40114 | -0.40267 | 0.741247 |
|   |   |   |          |          |          |
|---|---|---|----------|----------|----------|
| 30| 6 | 0 | -5.19286 | 0.87839  | 0.915876 |
| 31| 1 | 0 | -4.61344 | 1.777124 | 0.700969 |
| 32| 6 | 0 | 0.431345 | 1.181528 | 0.025497 |
| 33| 1 | 0 | 0.546227 | 1.531041 | 1.059402 |
| 34| 6 | 0 | 3.274992 | -2.53682 | 0.162784 |
| 35| 1 | 0 | 4.23919  | -3.04933 | 0.234963 |
| 36| 1 | 0 | 2.477552 | -3.24301 | 0.414269 |
| 37| 1 | 0 | 3.125643 | -2.21683 | -0.87159 |
| 38| 6 | 0 | 3.267713 | -1.3573  | 1.18636 |
| 39| 6 | 0 | 0.507341 | 2.429157 | -0.91905 |
| 40| 1 | 0 | 1.564119 | 2.725712 | -0.95997 |
| 41| 6 | 0 | -6.64839 | 1.110006 | 0.482769 |
| 42| 1 | 0 | -7.04951 | 1.984396 | 1.009286 |
| 43| 1 | 0 | -7.27884 | 0.246396 | 0.712609 |
| 44| 1 | 0 | -6.72146 | 1.298834 | -0.59443 |
| 45| 6 | 0 | 5.227904 | 1.224515 | -1.02251 |
| 46| 1 | 0 | 6.110867 | 1.422033 | -0.41048 |
| 47| 1 | 0 | 4.981767 | 2.120087 | -1.60096 |
| 48| 1 | 0 | 5.468956 | 0.42635  | -1.72955 |
| 49| 6 | 0 | -5.10624 | 0.604507 | 2.435467 |
| 50| 1 | 0 | -5.52778 | 1.452308 | 2.988556 |
| 51| 1 | 0 | -4.07279 | 0.465421 | 2.766791 |
| 52| 1 | 0 | -5.68147 | -0.29191 | 2.69603 |
| 53| 6 | 0 | 3.540658 | -1.89724 | 2.597769 |
| 54| 1 | 0 | 2.769235 | -2.61986 | 2.878391 |
| 55| 1 | 0 | 3.534079 | -1.09558 | 3.342353 |
| 56| 1 | 0 | 4.518022 | -2.38439 | 2.62201 |
| 57| 6 | 0 | 0.03939  | 2.159934 | -2.35833 |
| 58| 1 | 0 | -1.02929 | 1.918562 | -2.38291 |
| 59| 1 | 0 | 0.193747 | 3.055894 | -2.9716 |
| 60| 1 | 0 | 0.589679 | 1.337934 | -2.82275 |
| 61| 6 | 0 | -0.2549  | 3.629346 | -0.3287 |
| 62| 1 | 0 | 0.036302 | 3.83187  | 0.711731 |
| 63| 1 | 0 | -1.33982 | 3.479438 | -0.36879 |
| 64| 1 | 0 | -0.03856 | 4.534817 | -0.90754 |
1.8 HRESIMS, UV, IR, NMR spectra of natural product myrtuspirone A (1)

**Figure S3** HRESIMS spectrum of myrtuspirone A (1)

**Figure S4** UV spectrum of myrtuspirone A (1)
Figure S5 IR spectrum of myrtuspirone A (1)

Figure S6 $^1$H NMR spectrum of myrtuspirone A (1)
Figure S7 $^{13}$C NMR spectrum of myrtuspirone A (1)

Figure S8 $^1$H-$^1$H COSY spectrum of myrtuspirone A (1)
Figure S9 HSQC spectrum of myrtestirone A (1)

Figure S10 HMBC spectrum of myrtestirone A (1)
2. Synthetic experimental procedures

2.1 General information

Unless otherwise mentioned, all reactions were carried out under a nitrogen atmosphere under anhydrous conditions and all reagents were purchased from commercial suppliers without further purification. Solvent purification was conducted according to *Purification of Laboratory Chemicals* (Peerrin, D. D.; Armarego, W. L. and Perrins, D. R., Pergamon Press: Oxford, 1980). Yields refer to chromatographically and spectroscopically (\(^1\text{H NMR}\)) homogeneous materials, unless otherwise stated. Reactions were monitored by Thin Layer Chromatography on plates (GF254) using UV light as visualizing agent, an ethanolic solution of phosphomolybdic acid, or basic aqueous potassium permanganate (KMnO$_4$), and heat as developing agents. For the experiment apparatus, see part 1.1.

*Figure S11* NOESY spectrum of myrtepirone A (1)
2.2 General procedure for the synthesis of 4, 4a-4k and (-)-4

2.2.1 Synthesis of 4

To a solution of compound 3\(^\text{[3]}\) (2 g, 10.2 mmol) in CH\(_2\)Cl\(_2\) (51 mL) under argon was added compound 2\(^\text{[3]}\) (3.61 g, 15.3 mmol, 1.5 equiv.), and the resulting solution was stirred at 25 °C. After the reaction was finished according to TLC, the mixture was cooled down to −10 °C. Then tetrahydrofuran (THF; 173 mL) and N-iodosuccinimide (NIS; 25.5 mL, 2.5 equiv., 1M in THF) were added. The mixture was stirred for about 1 h and quenched with saturated aqueous sodium thiosulfate (10 mL). Next the mixture was extracted with ethyl acetate (3×10 mL) and the combined organic layers were dried over Na\(_2\)SO\(_4\), filtered and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (2.5%-5% hexane/ethyl acetate) to afford the compound 4 (3.56 g, 63%) as white solid.

2.2.2 Procedure A: General procedure for the synthesis of 4a-4k
Note: The compounds 3a-3h and 2a-2d were synthesized according to our previous work\textsuperscript{[3]}.

To a solution of compound 3a-3h\textsuperscript{[3]} (0.2 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (1 mL) under argon was added compound 2 or 2a-2d\textsuperscript{[3]} (0.3 mmol, 1.5 equiv.), and the resulting solution was stirred at 25 °C. After the reaction was finished according to TLC, the mixture was cooled down to −10 °C. Then tetrahydrofuran (THF; 4.5 mL) and N-iodosuccinimide (NIS; 0.5 mL, 2.5 equiv, 1M in THF) were added. The mixture was stirred for about 1 h and quenched with saturated aqueous sodium thiosulfate (10 mL). Next the mixture was extracted with ethyl acetate (3×10 mL) and the combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated in vacuo. The crude residue was purified by silica gel column chromatography to afford the compound 4a-4k.
2.2.3 Procedure B: Synthesis of enantioenriched product (-)-4

(11aS)-3,7-Bis[3,5-bis(trifluoromethyl)phenyl]-10,11,12,13-tetrahydro-5-hydroxy-diindenophosphocin 5-oxide [(S)-C1; 377 mg, 0.51 mmol, 0.1 equiv.], aluminum fluoride (AlF$_3$; 428.5 mg, 5.1 mmol, 1 equiv.) under argon were added to a solution of compound 3 (1.0 g, 5.1 mmol) and 3 Å MS (1.8 g) in toluene (87 mL). The resulting mixture was stirred for 30 min at 20 °C and cooled down to −70 °C. Compound 2 (1.81 g, 7.65 mmol, 1.5 equiv., 0.5 M in toluene) was added, and the resulting mixture was stirred at −70 °C until all the starting material was consumed (TLC). Tetrahydrofuran (THF; 90 mL) was added and N-iodosuccinimide (NIS; 2.88 g, 12.75 mmol, 2.5 equiv.) in THF (20 mL) was added. Then the mixture was warmed up to −10 °C and stirred for about 1 h. Then the mixture was quenched with saturated aqueous sodium thiosulfate (30 mL) and saturated aqueous sodium chloride (100 mL). The mixture was extracted with ethyl acetate (3×30 mL) and the combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (2.5%-5% hexane/ethyl acetate) to afford the title compound (-)-4 (1.42 g, 55%) as white solid.

Compound (-)-4: white solid, mp = 192-193 °C; according to procedure B;

$R_f$ = 0.45 (hexane/ethyl acetate = 4/1);

$[\alpha]_D^{22} = -126.4$ (c = 0.1 in MeOH);

IR (film) $\lambda_{\text{max}}$ 3428, 2986, 2936, 2875, 1707, 1626, 1605, 1578, 1470, 1422, 1393, 1221, 1099, 943, 872;
\textbf{1H NMR} (500 MHz, CDCl$_3$) $\delta$ 13.19 (s, 1H), 7.18 (s, 1H), 4.25 (s, 1H), 3.89 – 3.81 (m, 1H), 2.28 – 2.23 (m, 1H), 1.58 (s, 3H), 1.37 (s, 3H), 1.36 (s, 3H), 1.33 (s, 3H), 1.18 (t, $J$ = 6.9 Hz, 6H), 1.13 (d, $J$ = 7.0 Hz, 3H), 0.64 (d, $J$ = 6.7 Hz, 3H);

\textbf{13C NMR} (125 MHz, CDCl$_3$) $\delta$ 210.8, 207.7, 202.5, 201.5, 162.2, 161.8, 158.7, 106.7, 105.5, 98.6, 59.8, 56.6, 56.5, 49.6, 39.5, 29.2, 24.6, 23.6, 22.8, 22.6, 21.8, 19.3, 19.2, 17.4;

\textbf{HRMS} (ESI) calcd for C$_{24}$H$_{29}$IO$_7$ [(M-H)$-$] Exact Mass: 555.0885; found: 555.0886.

**Compound 5**: white solid, mp = 166-168 °C;

$R_f$ = 0.37 (hexane/ethyl acetate = 4/1);

\textbf{IR (film)} $\lambda_{\text{max}}$ 3420, 2984, 2937, 2875, 1714, 1656, 1599, 1463, 1383, 1244, 1155, 978, 871;

\textbf{1H NMR} (400 MHz, CDCl$_3$) $\delta$ 12.69 (s, 1H), 8.21 (s, 1H), 5.99 (s, 1H), 4.02 (d, $J$ = 1.8 Hz, 1H), 3.88 (m, 1H), 2.15 (dd, $J$ = 13.6, 6.8 Hz, 1H), 1.54 (s, 3H), 1.43 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.20 (d, $J$ = 5.4 Hz, 3H), 1.18 (d, $J$ = 6.6 Hz, 3H), 1.16 (d, $J$ = 7.2 Hz, 3H), 0.65 (d, $J$ = 6.6 Hz, 3H);

\textbf{13C NMR} (100 MHz, CDCl$_3$) $\delta$ 211.0, 208.8, 203.3, 202.5, 162.9, 162.0, 161.2, 105.5, 105.3, 99.7, 90.5, 59.8, 56.5, 49.2, 39.4, 29.7, 24.7, 23.9, 22.8, 22.6, 21.8, 19.3, 19.2, 17.3;

\textbf{HRMS} (ESI) calcd for C$_{24}$H$_{31}$O$_7$ [(M+H)$^+$] Exact Mass: 431.2064; found: 431.2081.

**Compound 4a**: 75.9 mg, 65% yield, 7 h, white solid, mp = 156-158 °C, according to procedure A;

$R_f$ = 0.55 (hexane/ethyl acetate = 4/1);
IR (film) \( \lambda_{\text{max}} \): 3437, 2961, 2871, 1712, 1619, 1585, 1458, 1419, 1388, 1219, 1143, 873;

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 13.29 (s, 1H), 7.07 (s, 1H), 4.27 (d, \( J = 1.9 \) Hz, 1H), 3.09 (m, 2H), 2.28 (m, 1H), 1.60 (m, 3H), 1.60 (s, 3H), 1.39 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.15 (d, \( J = 7.0 \) Hz, 3H), 0.96 (s, 3H), 0.94 (s, 3H), 0.66 (d, \( J = 6.6 \) Hz, 3H);

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \): 207.7, 206.8, 202.5, 201.5, 162.2, 161.7, 158.9, 106.6, 106.2, 98.6, 59.8, 56.5, 49.6, 42.4, 33.3, 29.1, 27.9, 24.6, 23.6, 22.8, 22.6, 22.5, 21.9, 17.4;

HRMS (ESI) calcd for C\(_{26}\)H\(_{33}\)IO\(_7\) ([M+H]+) Exact Mass: 585.1344; found: 585.1347.

Compound 4b: 85.8 mg, 69% yield, 7 h, yellow solid, mp = 147-149 °C, according to procedure A;

\( R_f = 0.38 \) (hexane/ethyl acetate = 4/1);

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \): 13.06 (s, 1H), 7.21 (m, 2H), 7.05 (m, 2H), 4.41 (s, 2H), 4.27 (d, \( J = 2.1 \) Hz, 1H), 2.26 (m, 1H), 1.60 (s, 3H), 1.40 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.14 (d, \( J = 7.1 \) Hz, 3H), 0.67 (d, \( J = 6.6 \) Hz, 3H);

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \): 207.6, 203.1, 202.4, 201.5, 163.5, 162.8, 161.7, 160.3, 159.0, 131.4, 131.3, 130.3, 130.2, 115.4, 115.2, 106.9, 106.0, 98.6, 59.9, 56.6, 56.5, 49.8, 49.3, 29.3, 24.6, 23.5, 22.7, 22.6, 21.8, 17.5;

HRMS (ESI) calcd for C\(_{28}\)H\(_{28}\)FIO\(_7\) ([M+H]+) Exact Mass: 623.0937; found: 623.0937.

Compound 4c: 76.7 mg, 65% yield, 7 h, yellow solid, mp = 192-194 °C, according to procedure A;
$R_f = 0.37$ (hexane/ethyl acetate = 4/1);

IR (film) $\lambda_{\text{max}}$ 3442, 2981, 2942, 2877, 1712, 1632, 1599, 1574, 1458, 1377, 1289, 1090, 876;

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 10.08 (s, 1H), 8.23 (s, 1H), 7.63 (dd, $J = 8.1, 6.5$ Hz, 3H), 7.52 (m, 2H), 4.29 (d, $J = 2.2$ Hz, 1H), 2.32 (m, 1H), 1.62 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.14 (d, $J = 7.1$ Hz, 3H), 0.71 (d, $J = 6.6$ Hz, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 207.5, 202.6, 201.5, 198.3, 163.5, 160.0, 158.8, 139.7, 132.4, 128.8, 128.0, 106.8, 105.9, 94.8, 59.9, 56.5, 56.2, 49.4, 29.1, 24.5, 23.5, 22.9, 22.6, 21.7, 17.6;

HRMS (ESI) calcd for C$_{27}$H$_{27}$IO$_7$ [(M+H)$^+$] Exact Mass: 591.0874; found: 591.0871.

Compound 4d: 80.9 mg, 67% yield, 7 h, white solid, mp = 167-168 °C, according to procedure A;

$R_f = 0.42$ (hexane/ethyl acetate = 4/1);

IR (film) $\lambda_{\text{max}}$ 3432, 3032, 2936, 2877, 1712, 1630, 1613, 1460, 1390, 1225, 1143, 1092, 870;

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 13.10 (s, 1H), 7.37 (m, 3H), 7.26 (m, 2H), 7.14 (s, 1H), 4.44 (s, 2H), 4.27 (d, $J = 2.2$ Hz, 1H), 2.27 (m, 1H), 1.60 (s, 3H), 1.40 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.14 (d, $J = 7.0$ Hz, 3H), 0.67 (d, $J = 6.6$ Hz, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 207.7, 203.4, 202.5, 201.5, 198.7, 162.7, 161.7, 159.2, 134.7, 129.9, 128.5, 126.9, 106.8, 106.2, 98.6, 59.9, 56.5, 50.2, 49.6, 29.2, 24.6, 23.6, 22.8, 22.6, 21.9, 17.5;

HRMS (ESI) calcd for C$_{27}$H$_{27}$IO$_7$ [(M+H)$^+$] Exact Mass: 605.1031; found: 605.1035.

Compound 4e: 77.2 mg, 68% yield, 7 h, white solid, mp = 129-131 °C, according to procedure A;

$R_f = 0.52$ (hexane/ethyl acetate = 4/1);
IR (film) $\lambda_{\text{max}}$ 3482, 2964, 2939, 2867, 1700, 1613, 1579, 1414, 1382, 1279, 1146, 1025, 876;

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 13.30 (s, 1H), 6.99 (s, 1H), 4.27 (d, $J = 1.9$ Hz, 1H), 4.16 (m, 1H), 2.38 (m, 2H), 2.28 (m, 3H), 1.99 (m, 1H), 1.89 (m, 1H), 1.60 (s, 3H), 1.39 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.16 (d, $J = 7.1$ Hz, 3H), 0.66 (d, $J = 6.6$ Hz, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 207.8, 206.5, 202.5, 201.6, 162.3, 161.9, 158.8, 106.6, 105.2, 98.6, 59.8, 56.5, 56.3, 49.6, 46.5, 29.2, 24.9, 24.7, 24.6, 23.6, 22.8, 22.6, 21.8, 17.6, 17.4;

HRMS (ESI) calcd for C$_{25}$H$_{29}$IO$_7^+ [(M+H)$^+$] Exact Mass: 569.1031; found: 569.1054.

Compound 4f: 82.6 mg, 71% yield, 7 h, white solid, mp = 215-217 °C, according to procedure A; $R_f = 0.50$ (hexane/ethyl acetate = 5/1);

IR (film) $\lambda_{\text{max}}$ 3429, 2958, 2839, 2866, 1709, 1625, 1602, 1577, 1460, 1388, 1219, 1092, 867;

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 13.23 (s, 1H), 7.09 (s, 1H), 4.27 (d, $J = 2.1$ Hz, 1H), 4.02 (m, 1H), 2.28 (m, 1H), 1.91 (m, 4H), 1.72 (m, 2H), 1.64 (m, 2H), 1.60 (s, 3H), 1.39 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.16 (d, $J = 7.1$ Hz, 3H), 0.66 (d, $J = 6.6$ Hz, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 209.3, 207.7, 202.6, 201.6, 162.1, 161.7, 158.7, 106.6, 106.0, 98.6, 59.8, 56.5, 56.3, 49.6, 30.3, 30.14, 29.2, 26.1, 26.1, 24.6, 23.6, 22.8, 22.6, 21.9, 17.5;

HRMS (ESI) calcd for C$_{26}$H$_{30}$INaO$_7^+ [(M+Na)$^+$] Exact Mass: 605.1007; found: 605.1010.

Compound 4g: 83.4 mg, 70% yield, 7 h, white solid, mp = 215-217 °C, according to procedure A; $R_f = 0.53$ (hexane/ethyl acetate = 5/1);

IR (film) $\lambda_{\text{max}}$ 3437, 2936, 2848, 1709, 1619, 1582, 1461, 1416, 1386, 1250, 1148, 1090, 870;
$^1\text{H NMR}$ (300 MHz, CDCl$_3$) $\delta$ 13.29 (s, 1H), 7.09 (s, 1H), 4.26 (d, $J = 2.2$ Hz, 1H), 3.58 (m, 1H), 2.28 (m, 1H), 1.84 (m, 5H), 1.60 (s, 3H), 1.50 (m, 2H), 1.41 (m, 3H), 1.39 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.15 (d, $J = 7.1$ Hz, 3H), 0.66 (d, $J = 6.6$ Hz, 3H);

$^{13}\text{C NMR}$ (100 MHz, CDCl$_3$) $\delta$ 209.8, 207.7, 202.5, 201.5, 162.1, 162.0, 158.6, 106.7, 105.7, 98.6, 59.8, 56.6, 56.5, 49.9, 49.7, 29.5, 29.2, 26.05, 26.0, 24.6, 23.6, 22.8, 22.6, 21.8, 17.5;

HRMS (ESI) calcd for C$_{27}$H$_{33}$I O$_7$ [(M+H)$^+$] Exact Mass: 597.1344; found: 597.1347.

Compound 4h: 50.2 mg, 43% yield, 2.5 h, white solid, mp = 160-162 °C, according to procedure A;

$R_f = 0.52$ (hexane/ethyl acetate = 5/1);

IR (film) $\lambda_{max}$ 3411, 2955, 2871, 1706, 1622, 1585, 1458, 1421, 1371, 1230, 1151, 878;

$^1\text{H NMR}$ (400 MHz, CDCl$_3$) $\delta$ 13.73 (s, 1H), 6.49 (s, 1H), 4.22 (dd, $J = 8.3$, 5.2 Hz, 1H), 2.96 (d, $J = 6.6$ Hz, 2H), 2.26 (m, 1H), 1.66 (m, 2H), 1.51 (s, 3H), 1.47 (s, 3H), 1.43 (s, 3H), 1.39 (s, 3H), 1.30 (m, 1H), 0.99 (s, 3H), 0.98 (s, 3H), 0.94 (d, $J = 6.2$ Hz, 3H), 0.90 (d, $J = 6.3$ Hz, 3H);

$^{13}\text{C NMR}$ (100 MHz, CDCl$_3$) $\delta$ 207.5, 206.0, 202.3, 201.3, 162.3, 161.5, 158.4, 109.5, 106.3, 96.5, 60.3, 56.7, 53.0, 44.1, 40.9, 26.0, 25.3, 24.9, 23.4, 23.3, 22.9, 22.8, 22.0, 21.8, 21.7;

HRMS (ESI) calcd for C$_{26}$H$_{33}$I O$_7$ [(M+H)$^+$] Exact Mass: 585.1344; found: 585.1351.

Note: Compound 4h were isolated in lower yield because the amount of the byproduct generated from the double-Michael addition increased. The structure of the byproduct is:
Compound 4i: 52.2 mg, 45% yield, 2.5 h, white solid, mp = 147-149°C, according to procedure A; 
\( R_f = 0.43 \) (hexane/ethyl acetate = 5/1);

**IR (film)** \( \lambda_{\text{max}} \) 3485, 2987, 2945, 1700, 1616, 1577, 1433, 1362, 1253, 1141, 1016, 966;

**\(^1\)H NMR** (400 MHz, CDCl\(_3\)) \( \delta \) 13.43 (s, 1H), 6.83 (s, 1H), 4.17 (m, 2H), 2.79 (m, 1H), 2.39 (m, 2H), 2.29 (m, 2H), 1.99 (m, 1H), 1.86 (m, 5H), 1.72 (m, 1H), 1.63 (m, 1H), 1.49 (s, 3H), 1.44 (s, 3H), 1.42 (s, 3H), 1.38 (s, 3H);

**\(^{13}\)C NMR** (100 MHz, CDCl\(_3\)) \( \delta \) 207.7, 206.5, 202.1, 201.2, 162.6, 161.7, 158.8, 107.5, 105.1, 96.4, 60.5, 56.5, 56.3, 50.0, 46.4, 37.0, 27.8, 26.4, 25.3, 24.9, 24.6, 24.1, 21.9, 21.8, 18.2, 17.6;

**HRMS** (ESI) calcd for C\(_{26}\)H\(_{29}\)IO\(_7\) [(M+H)\(^+\)] Exact Mass:581.1031; found:581.1029.

**Note:** Compound 4i was isolated in lower yield because the amount of the byproduct generated from the double-Michael addition increased. The structure of the byproduct is:
Compound 4j: 87.5 mg, 72% yield, 7 h, white solid, mp = 168-170°C, according to procedure A; 
\( R_f = 0.53 \) (hexane/ethyl acetate = 5/1);

**IR (film)** \( \lambda_{\text{max}} \) 3471, 2951, 2871, 1700, 1610, 1579, 1411, 1225, 1138, 1022, 872;

**\(^1\)H NMR** (400 MHz, CDCl\(_3\)) \( \delta \) 13.31 (s, 1H), 7.09 (s, 1H), 4.44 (d, \( J = 3.5 \) Hz, 1H), 4.01 (m, 1H), 2.30 (m, 1H), 1.90 (m, 4H), 1.73 (m, 3H), 1.64 (m, 3H), 1.58 (s, 3H), 1.50 (m, 5H), 1.40 (s, 3H), 1.39 (s, 3H), 1.37 (s, 3H), 0.92 (m, 1H);

**\(^{13}\)C NMR** (100 MHz, CDCl\(_3\)) \( \delta \) 209.3, 207.9, 202.2, 201.9, 162.5, 161.7, 158.8, 107.1, 106.0, 98.5, 60.0, 56.7, 56.3, 50.7, 47.2, 41.0, 31.4, 30.3, 30.1, 27.3, 26.1, 25.0, 24.8, 24.7, 24.0, 22.5, 22.2;

**HRMS** (ESI) calcd for C\(_{28}\)H\(_{33}\)IO\(_7\) [(M+H)\(^+\)] Exact Mass: 609.1344; found:609.1345.

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Compound 4k: 86.5 mg, 68% yield, 7 h, white solid, mp = 180-182°C, according to procedure A; 
\( R_f = 0.50 \) (hexane/ethyl acetate = 5/1);

**IR (film)** \( \lambda_{\text{max}} \) 3480, 2979, 2930, 2854, 1712, 1619, 1588, 1424, 1227, 1146, 1073, 997, 946;

**\(^1\)H NMR** (400 MHz, CDCl\(_3\)) \( \delta \) 13.20 (s, 1H), 7.20 (s, 1H), 4.16 (d, \( J = 2.0 \) Hz, 1H), 4.01 (m, 1H), 1.77 (m, 8H), 1.59 (s, 3H), 1.57 (m, 2H), 1.47 (dd, \( J = 29.4, 13.6 \) Hz, 4H), 1.39 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H), 1.17 (m, 6H), 0.66 (m, 1H);
13C NMR (100 MHz, CDCl₃) δ 209.8, 207.8, 202.4, 201.6, 162.3, 161.7, 158.7, 107.0, 105.6, 98.7, 59.8, 56.6, 56.4, 49.9, 49.7, 39.7, 32.8, 29.5, 29.4, 28.2, 27.1, 26.1, 26.0, 26.0, 25.8, 24.7, 23.8, 22.6, 22.2;
HRMS (ESI) calcd for C₃₀H₇₁O₇ [(M+H)+] Exact Mass: 637.1657; found: 637.1651.

2.3 Synthesis of (±)-myrtuspirone A and (-)-myrtuspirone A

To a solution of compound 4 (1.0 g, 1.8 mmol) or (-)-4 (1.0 g, 1.8 mmol) in tetrahydrofuran (THF; 20 mL) under argon were added palladium acetate [Pd(OAc)₂; 20.2 mg, 0.09 mmol, 5 mol%], 1,1’-bis(diphenylphosphino)ferrocene (pddf; 99.8 mg, 0.18 mmol, 10 mol%) and dimethylzinc (ZnMe₂; 7.5 mL, 5 equiv., 1.2 M in toluene) at 0 °C. The resulting solution was stirred for 30 min and warmed up to room temperature. After overnight, the mixture was quenched with saturated aqueous ammonium chloride (15 mL) and extracted with ethyl acetate (3×20 mL), and the combined organic layers were dried over Na₂SO₄, filtered and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (2.5%-5% hexane/ethyl acetate) to afford (±)-myrtuspirone A (1) (519.5 mg, 65%) or (-)-myrtuspirone A (1) (519.5 mg, 65%, 90% ee) as white solid. Compound (-)-myrtuspirone A (1) was re-crystallised from n-hexane containing a few drops of CH₂Cl₂ to provide (-)-myrtuspirone A (1) (364 mg, >99% ee) as white crystals.

Rₛ= 0.5 (hexane/ethyl acetate = 7/1);
[α]d²⁵ = -83.3 (c = 0.1 in MeOH);

1H NMR (400 MHz, DMSO) δ 13.06 (s, 1H), 11.13 (s, 1H), 4.23 (d, J = 2.5 Hz, 1H), 3.93 (m, 1H), 2.12 (m, 1H), 1.89 (s, 3H), 1.47 (s, 3H), 1.35 (s, 3H), 1.31 (s, 3H), 1.24 (s, 4H), 1.11 (s, 3H), 1.10 (s, 3H), 1.01 (d, J = 7.0 Hz, 3H), 0.53 (d, J = 6.6 Hz, 3H);

13C NMR (100 MHz, DMSO) δ 210.7, 208.1, 202.8, 202.2, 163.0, 161.1, 155.1, 106.1, 103.7, 98.7, 98.5, 59.0, 55.7, 47.9, 38.8, 29.3, 24.1, 23.9, 22.6, 22.4, 21.8, 19.4, 19.1, 17.3, 8.0;

HRMS (ESI) calcd for C₂₅H₃₁O₇ [(M-H)-] Exact Mass: 443.2075; found: 443.2075.
Table S5 Compared NMR data [CDCl₃] between synthetic (-)-myrtuspirone A and the isolated natural product.

| position | Isolated (500M) | Synthesized (400M) | Error (iso.-syn.) | Isolated (125M) | Synthesized (100M) | Error (iso.-syn.) |
|----------|-----------------|--------------------|-------------------|----------------|--------------------|-------------------|
| 1        | -               | -                  | -                 | -              | -                  | -                 |
| 2        | -               | -                  | -                 | -              | -                  | -                 |
| 3        | 4.22 (d, J = 2.5 Hz, 1H) | 4.23 (d, J = 2.5 Hz, 1H) | -0.01             | 98.7           | 98.7               | 0                 |
| 3a       | -               | -                  | -                 | 47.9           | 47.9               | 0                 |
| 4        | -               | -                  | -                 | 103.8          | 103.8              | 0                 |
| 5        | -               | -                  | -                 | 155.1          | 155.1              | 0                 |
| 6        | -               | -                  | -                 | 160.1          | 160.1              | 0                 |
| 7        | -               | -                  | -                 | 163.0          | 163.0              | 0                 |
| 7a       | -               | -                  | -                 | 98.5           | 98.5               | 0                 |
| 8        | 2.12 (m, 1H)    | 2.12 (m, 1H)       | 0                 | 161.1          | 161.1              | 0                 |
| 9        | 0.53 (d, J = 6.6 Hz, 3H) | 0.53 (d, J = 6.6 Hz, 3H) | 0                 | 29.3           | 29.3               | 0                 |
| 9        | 1.00 (d, J = 7.0 Hz, 3H) | 1.01 (d, J = 7.0 Hz, 3H) | -0.01             | 17.3           | 17.3               | 0                 |
| 10       | -               | -                  | -                 | 21.8           | 21.8               | 0                 |
| 11       | -               | -                  | -                 | 210.7          | 210.7              | 0                 |
| 12       | 3.92 (m, 1H)    | 3.93 (m, 1H)       | -0.01             | 38.7           | 38.7               | 0                 |
| 13       | 1.10 (d, J = 6.7 Hz, 3H) | 1.11 (s, 3H)       | -0.01             | 19.4           | 19.4               | 0                 |
| 14       | 1.10 (d, J = 6.7 Hz, 3H) | 1.10 (s, 3H)       | 0                 | 19.1           | 19.1               | 0                 |
| 15       | 1.89 (s, 3H)    | 1.89 (s, 3H)       | 0                 | 8.0            | 8.0                | 0                 |
| 2'       | -               | -                  | -                 | 208.1          | 208.1              | 0                 |
| 3'       | -               | -                  | -                 | 59.0           | 59.0               | 0                 |
| 4'       | -               | -                  | -                 | 202.8          | 202.8              | 0                 |
| 5'       | -               | -                  | -                 | 55.7           | 55.7               | 0                 |
| 6'       | -               | -                  | -                 | 202.2          | 202.2              | 0                 |
| 7'       | 1.35 (s, 3H)    | 1.35 (s, 3H)       | 0                 | 22.6           | 22.6               | 0                 |
| 8'       | 1.46 (s, 3H)    | 1.47 (s, 3H)       | -0.01             | 22.4           | 22.4               | 0                 |
| 9'       | 1.31 (s, 3H)    | 1.31 (s, 3H)       | 0                 | 23.9           | 23.9               | 0                 |
| 10'      | 1.23 (s, 3H)    | 1.24 (s, 3H)       | -0.01             | 24.1           | 24.1               | 0                 |
| 4-OH     | 11.13 (s, 1H)   | 11.13 (s, 1H)      | 0                 | -              | -                  | -                 |
| 6-OH     | 13.02 (s, 1H)   | 13.06 (s, 1H)      | -0.04             | -              | -                  | -                 |
3. Synthetic $^1$H and $^{13}$C NMR spectra

(-)-4
4c

1H NMR spectrum showing chemical shifts for 4c.

13C NMR spectrum showing chemical shifts for 4c.
4g

Ω (ppm)

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(-)-myrtuspirone A (1)
4. HPLC chromatogram of (-)-myrtuspirone A

(-)-1: HPLC analysis: Daicel Chiralpak OD-H column; hexane/i-propanol = 70:30, 0.8 mL/min, λ = 280 nm; $t_R[(+)-1] = 7.8$ min, $t_R[(-)-1] = 4.1$ min. 90% ee; re-crystallised: $>99\%$ ee.
5. Antibacterial activity assay

5.1. Microorganisms

*Staphylococcus aureus* ATCC 33591 [methicillin-resistant *S. aureus* (MRSA)], *Staphylococcus aureus* ATCC 700699 [vancomycin-intermediate *S. aureus* (VISA)], *Enterococcus faecium* ATCC 700221 [vancomycin-resistant *E. faecium* (VRE)], *Staphylococcus aureus* ATCC 29213 [methicillin-susceptible *S. aureus* (MSSA)], *Enterococcus faecalis* ATCC 29212, *Staphylococcus epidermidis* ATCC 12228 were standard isolates from ATCC (Manassas, VA, USA).

5.2 Antibiotics and reagents

Vancomycin was purchased from the National Institute for the Control of Pharmaceutical and Biological Products, People’s Republic of China. Mueller-Hinton (MH) agar and MH broth were purchased from Difco. Cation-adjusted MH broth (CAMHB) was prepared according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI) [4]. All other reagents were purchased from Sigma Chemical Co.

5.3 MIC determination

MICs were determined by the agar dilution method recommended by the CLSI [4]. Drug-containing plates were inoculated using a multipoint inoculator (Denley Instruments, Bolney, Sussex, United Kingdom) with inocula of about $10^4$ CFU/spot and incubated at 35°C for 18 h. The MIC was determined as the lowest concentration of the antibiotic that inhibited the growth of the bacteria on the plate. The quality control strains recommended by the CLSI were included as internal controls throughout the study.

5.4 In vitro antibacterial activities of myrtuspirone A (1)

The antibacterial activities of (±)-myrtuspirone A, (+)-myrtuspirone A, and (-)-myrtuspirone A were evaluated against six Gram-positive and five Gram-negative bacteria (Table S6). These compounds exhibited moderate antibacterial activity against all Gram-positive bacteria including three multiresistant strains (MRSA, VISA and VRE) with MIC values ranging from 16 to 32 μg/mL.
| compounds | S. aureus ATCC 33591 (MRSA) | S. aureus ATCC 700699 (VISA) | E. faecium ATCC 700221 (VRE) | S. aureus ATCC 29213 | E. faecalis ATCC 29212 | S. epidermidis ATCC 12228 | Klebsiella subsp. pneumoniae ATCC 700603 | Klebsiella pneumoniae ATCC BAA-2146 | Pseudomonas aeruginosa ATCC 27853 | Acinetobacter baumannii ATCC 19606 | Escherichia coli ATCC 25922 |
|-----------|-----------------------------|-----------------------------|-----------------------------|-----------------------|-------------------------|--------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| (+)-1     | 16                          | 16                          | 16                          | 16                    | 32                      | 32                       | >128                            | >128                            | >128                            | >128                            | >128                            |
| (-)-1     | 16                          | 32                          | 16                          | 32                    | 32                      | 32                       | >128                            | >128                            | >128                            | >128                            | >128                            |
| Vancomycin| 1                           | 8                           | >128                        | 1                     | 2                       | 1                        | >128                            | >128                            | >128                            | >128                            | >128                            |
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