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Ent-abietanes from the Godavari mangrove, *Ceriops decandra*: Absolute configuration and NF-κB inhibitory activity

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ABSTRACT

Nine new *ent*-abietanes, named decandrols A–I (**1**–**9**), which could be categorized into three groups (**1**, **2**–**6**, **7**–**9**), were isolated from the roots of an Indian mangrove, *Ceriops decandra*, collected in the swamp of Godavari estuary, Andhra Pradesh, together with six previously reported abietanes (**10**–**15**), of which the absolute configurations were first determined. The relative and absolute configurations of these compounds were unambiguously established by HR-ESIMS, extensive 1D and 2D NMR investigations, single-crystal X-ray diffraction analysis with Cu Kα radiation, and quantum-chemical electronic circular dichroism (ECD) calculations. Decandrol A (**1**) is a rare C_9-spirofused 7,8-*seco*-*ent*-abietane, whereas **2**–**15** are typically tricyclic *ent*-abietanes. Decandrols C (**3**) and E (**5**) exhibited significant NF-κB inhibitory activity at the concentration of 100 μM.

1. Introduction

Ceriops decandra, belonging to the family Rhizophoraceae, is a true mangrove plant. It is mainly distributed along the sea coasts of Africa, Madagascar, South Asia, Southeast Asia, Australia, and South Pacific islands. Globally, the mangrove genus *Ceriops* consists of at least five species, *viz. C. australis*, *C. decandra*, *C. pseudodecandra*, *C. tagal*, and *C. zippeliana* [1–4], among which *C. decandra* has long been used in India as a folk medicine for the treatment of amoebiasis, diarrhea, hemorrhage, and malignant ulcer of stomach [5]. Previously, chemical investigation of *C. decandra* afforded sixteen lupane-type triterpenes and thirty-seven diterpenes, including types of abietane, beyerane, dolabrane, kaurane, labdane, pimarane, and podocarpane [6–13]. During the course of our search for novel and bioactive terpenoid natural products from mangrove plants, chemical investigation of the roots of the Indian mangrove, *C. decandra*, yielded fifteen *ent*-abietanes, including nine new ones (**1**–**9**) and six previously reported ones (**10**–**15**, Fig. 1) [11,13]. Herein, we report the structure elucidation, absolute configuration establishment, and NF-κB inhibitory activities of these *ent*-abietanes, particularly the first determination of the absolute configurations of **10**–**15**.

2. Experimental

2.1. General experimental procedures

Optical rotations were measured on an MCP 200 modular circular polarimeter (Anton Paar GmbH). UV spectra were obtained on a GENESYS 10S UV–Vis spectrophotometer (Thermo Scientific, Shanghai, China) and NMR spectra were recorded on a Bruker AV-400 NMR spectrometer (Bruker Scientific Technology Co. Ltd., Karlsruhe, Germany) with TMS as the internal standard. Single-crystal X-ray diffraction analysis was made on an Agilent Xcalibur Atlas Gemini Ultra-diffractometer with mirror monochromated Cu Kα radiation (λ = 1.54184 Å) at 100.0 K. HR-ESIMS were measured on an LC-ESIMS system (Bruker Daltonics, Bremen, Germany), or on a ESI-QTOF mass spectrometer (SYNAPTTM G2 HDMS, Waters, Manchester, U.K.). ECD spectra were recorded on a Jasco 810 spectropolarimeter (JASCO Corporation, Tokyo, Japan) in the solvent of acetonitrile. Semi-preparative HPLC was performed on a Waters 2535 pump equipped with a 2998 photodiode array detector (Waters Corporation, Milford, MA, USA) and YMC C_{18} reversed-phase columns (250 × 10 mm i.d., 5 μm). For column chromatography, silica gel (100–200 mesh, Qingdao Marine Chemical Industrial Co. Ltd., Qingdao, China) and C_{18} reversed-phase silica gel (ODS-A-HG 12 nm, 50 μm, YMC Co. Ltd., Kyoto, Japan) were employed.

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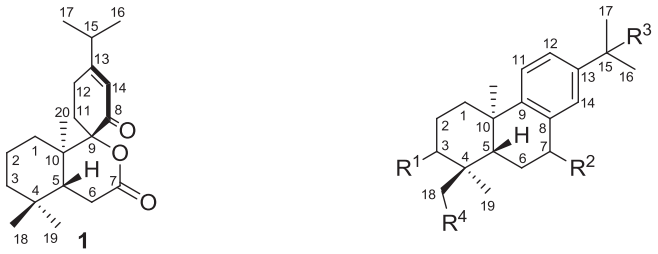
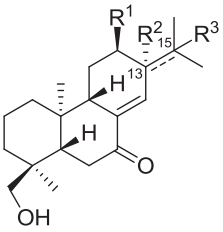


1

2 R^1 = O R^2 = α-OH R^3 = H R^4 = H
3 R^1 = α-OH R^2 = H R^3 = H R^4 = H
4 R^1 = O R^2 = α-OH R^3 = OH R^4 = H
5 R^1 = H R^2 = O R^3 = OH R^4 = H
6 R^1 = α-OH R^2 = O R^3 = H R^4 = OH
10 R^1 = α-OH R^2 = O R^3 = H R^4 = H
11 R^1 = α-OH R^2 = O R^3 = OH R^4 = H
12 R^1 = H R^2 = O R^3 = OH R^4 = OH
13 R^1 = H R^2 = O R^3 = H R^4 = OH
14 R^1 = O R^2 = O R^3 = H R^4 = H
15 R^1 = O R^2 = O R^3 = OH R^4 = H



7 R^1 = OH R^2 = R^3 = H $\Delta^{13(15)}$
8 R^1 = H R^2 = R^3 = H $\Delta^{13(15)}$
9 R^1 = H R^2 = OH R^3 = OH

Fig. 1. Structures of compounds **1–15**.

2.2. Plant material

The roots of *Ceriops decandra* were collected in October 2009 at the Godavari estuary, Andhra Pradesh, India. The identification of the mangrove plant was performed by Mr. Tirumani Satyanandamurty (Government Degree College at Amadala valasa, Srikakulam District, Andhra Pradesh, India). A voucher sample (CD-002) is maintained at the Marine Drugs Research Center, College of Pharmacy, Jinan University.

2.3. Extraction and isolation

The air-dried and powdered roots (13.0 kg) of *Ceriops decandra* were extracted with 95% (*v*/v) EtOH (5 × 40.0 L) at room temperature. The EtOH extract (1.2 kg) was then partitioned between EtOAc and water (3:1, v/v) to afford the EtOAc portion (170.0 g), which was subjected to silica gel column chromatography (150 × 14 cm i.d.), eluted with a gradient mixture of chloroform/methanol (from 100:0 to 5:1), to yield 240 fractions. Fractions 10 to 44 (5.6 g) were combined and separated by C_{18} reversed-phase silica gel column chromatography (50 × 5 cm i.d), eluted with a gradient mixture of acetone/water (from 50:50 to 100:0) to give 70 subfractions. The subfraction 13 (10.0 mg) was purified by semi-preparative HPLC (MeCN/H_2O, 70:30, 3.0 mL/min) to yield compound **14** (8.0 mg, t_R = 18.0 min). The subfraction 27 (15.0 mg) was purified by semi-preparative HPLC (MeCN/H_2O, 68:32, 3.0 mL/min) to give compound **3** (1.8 mg, t_R = 44.0 min).

Fractions 45 to 113 (7.8 g) were combined and subjected to C_{18} reversed-phase silica gel column chromatography (50 × 5 cm i.d), eluted with a gradient mixture of acetone/water (from 30:70 to 100:0) to give 58 subfractions. The subfraction 17 (25.0 mg) was purified by semi-preparative HPLC (MeCN/H_2O, 55:45, 3.0 mL/min) to afford compound **1** (1.8 mg, t_R = 24.0 min).

Fractions 114 to 145 (5.0 g) were combined and subjected to C_{18} reversed-phase silica gel column chromatography (50 × 5 cm i.d), eluted with a gradient mixture of acetone/water (from 30:70 to 100:0) to give 40 subfractions. The subfraction 13 (50.0 mg) was purified by semi-preparative HPLC (MeOH/H_2O, 60:40, 3.0 mL/min) to afford compound **15** (3.6 mg, t_R = 13.2 min), whereas the subfraction 23 (180.0 mg) was purified by semi-preparative HPLC (MeOH/H_2O, 72:28, 3.0 mL/min) to give compounds **2** (19.0 mg, t_R = 14.0 min) and **10** (37.0 mg, t_R = 17.0 min). The subfraction 25 (50.0 mg) was purified by semi-preparative HPLC (MeOH/H_2O, 75:25, 3.0 mL/min) to yield compounds **5** (6.9 mg, t_R = 32.7 min) and **13** (12.0 mg, t_R = 34.5 min).

Fractions 146 to 190 (6.0 g) were combined and subjected to C_{18} reversed-phase silica gel column chromatography (50 × 5 cm i.d), eluted with a gradient mixture of acetone/water (25:75 to 100:0) to give 38 subfractions. The subfraction 8 (95.0 mg) was purified by semi-preparative HPLC (MeCN/H_2O, 35:65, 3.0 mL/min) to afford compounds **8** (2.3 mg, t_R = 34.0 min) and **9** (4.7 mg, t_R = 13.2 min). The subfractions 9 to 19 (985.0 mg) were combined and purified by semi-preparative HPLC (MeCN/H_2O, 40:60, 3.0 mL/min) to give compounds **4** (17.0 mg, t_R = 16.5 min), **6** (7.5 mg, t_R = 38.0 min), **11** (12.0 mg, t_R = 14.0 min), and **12** (32.0 mg, t_R = 28.5 min), whereas the subfraction 26 (40.0 mg) was purified by semi-preparative HPLC (MeCN/H_2O, 55:45, 3.0 mL/min) to afford compound **7** (1.8 mg, t_R = 26.3 min).

2.3.1. Decandrol A (1)

White amorphous power; $[\alpha]_D^{25}$ = +232.3 (*c* = 0.13, acetone); UV (MeCN) λ_{max} (log ε) 203 (3.46), 235 (3.38) nm; ECD (0.19 mM, MeCN) λ_{max} ($\Delta\varepsilon$) 226.2 (+1.3), 243.2 (+15.1), 317.4 (+1.8) nm; ^{1}H NMR data see Table 1 and ^{13}C NMR data see Table 3; HR-ESIMS *m/z* 341.2093 $[M + Na]^+$ (calcd for $C_{20}H_{30}NaO_3$, 341.2087).

2.3.2. Decandrol B (2)

Colorless oil; $[\alpha]_D^{25}$ = −67.1 (*c* = 0.14, acetone); UV (MeCN) λ_{max} (log ε) 205 (3.60), 253 (4.57) nm; ECD (0.33 mM, MeCN) λ_{max} ($\Delta\varepsilon$) 219.0 (−3.5), 224.4 (−4.0) nm; ^{1}H NMR data see Table 1 and ^{13}C NMR data see Table 3; HR-ESIMS *m/z* 301.2173 $[M + H]^+$ (calcd for $C_{20}H_{29}O_2$, 301.2168).

2.3.3. Decandrol C (3)

White amorphous power; $[\alpha]_D^{25}$ = −34.0 (*c* = 0.1, acetone); UV (MeCN) λ_{max} (log ε) 204 (3.77) nm; ECD (0.46 mM, MeCN) λ_{max} ($\Delta\varepsilon$) 207.0 (−4.6), 222.4 (−5.7) nm; ^{1}H NMR data see Table 1 and ^{13}C NMR data see Table 3; HR-ESIMS *m/z* 269.2275 $[M + H - H_2O]^+$ (calcd for $C_{20}H_{29}$, 269.2269).

2.3.4. Decandrol D (4)

Colorless oil; $[\alpha]_D^{25}$ = −38.3 (*c* = 0.35, acetone); UV (MeCN) λ_{max} (log ε) 204 (3.67) nm; ECD (0.47 mM, MeCN) λ_{max} ($\Delta\varepsilon$) 222.0 (−2.0), 294.6 (−0.1) nm; ^{1}H NMR data see Table 1 and ^{13}C NMR data see Table 3; HR-ESIMS *m/z* 351.1736 $[M + Cl]^-$ (calcd for $C_{20}H_{28}ClO_3$,