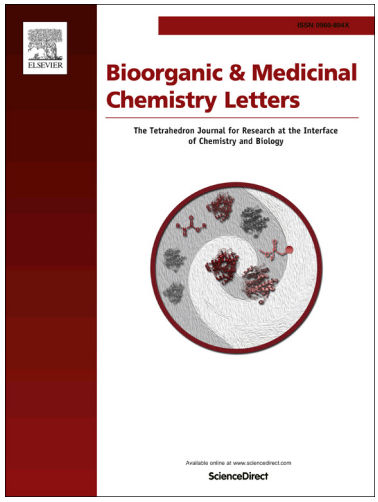

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An antibacterial *ortho*-quinone diterpenoid and its derivatives from *Caryopteris mongolica*

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ABSTRACT

To identify antibacterial components in traditional Mongolian medicinal plant *Caryopteris mongolica*, an *ortho*-quinone abietane caryopteron A (**1**) and three its derivatives caryopteron B-D (**2–4**) were isolated from the roots of the plant together with three known abietanes demethylcryptojaponol (**5**), 6α-hydroxydemethyl cryptojaponol (**6**), and 14-deoxycoleon U (**7**). The chemical structures of these abietane derivatives were elucidated on the basis of spectroscopic data. Compounds **1–4** had C-13 methylcyclopropane substructures, and **2–4** had a hexanedioic anhydride ring C instead of *ortho*-quinone in **1**. The stereochemistry of these compound was assumed from NOE spectra and ECD Cotton effects. Compounds **1** and **5–7** showed antibacterial activities against the Gram-positive bacteria *Staphylococcus aureus*, *S. epidermidis*, *Enterococcus faecalis*, and *Micrococcus luteus*, being **1** the more potent.

Caryopteris mongolica Bunge. (Lamiaceae) is a traditional herbal medicine from Mongolia, and the aerial parts of this plant are used for the treatment of aches, edema, and rheumatism.[1] The presence of iridoid glycosides, alkaloids, diterpenoid glycoside, and flavone glycosides in the aerial parts of *C. mongolica* was reported.[2-4] We examined the crude extract from the roots of *C. mongolica* for antibacterial activities using *Staphylococcus aureus*, *Enterococcus faecalis*, and *Micrococcus luteus*, which are Gram-positive bacteria, it showed activities (diameter of inhibition zone: *S. aureus*, 24.4 mm; *E. faecalis*, 26.3 mm; *M. luteus*, 25.0 mm; each sample was tested at 500 μg/disc). To identify antibacterial components in *C. mongolica*, the chemical constituents of the roots were investigated. Four diterpenoids (**1–4**) with three membered rings – spiro (methylcyclopropane) substructures – were obtained together with three known abietane diterpenoids (**5–7**). Similar diterpenoids with spiro-substructures have been isolated from Lamiaceae plants, such as from *Coleus garckeanus*,[5] *Plectranthus lanuginosus*,[6] and *Anisochilus harmandii*.[7] In addition, their antibacterial and antiplasmodial activities were discussed and reported recently.[7,8]

Roots of *C. mongolica*[9] (285 g) were extracted with acetone-H_2O (4:1), and a crude extract (24.6 g) was obtained. The extract was washed using H_2O and the water insoluble residue (4.0 g) was dissolved in MeOH-H2O (1:1), passed through Diaion HP-20 porous polymer gel (60 × 230 mm, Mitsubishi), and eluted with MeOH-H_2O (1:1) (1.55 g), MeOH-H_2O (4:1) (290 mg), and MeOH (1.66 g). The MeOH fraction was chromatographed on an ODS packed column (Ultra Pack ODS-SM-50C-M, 37 × 100 mm, Yamazen) and subjected to preparative HPLC [TSK-gel ODS-120T, 21.5 × 300 mm, mobile phases: acetonitrile-H_2O (3:2) and (7:3), Tosoh; Develosil C30-UG-5, 20 × 250 mm, mobile phases: acetonitrile-H_2O (3:2) and (7:3), Nomura Chemical] yielding **1** (13.4 mg), **2** (13.0 mg), **3** (5.5 mg), **4** (4.8 mg), **5** (24.6 mg), **6** (18.4 mg), and **7** (16.1 mg). Known abietane diterpenoids were identified based on spectroscopic data as demethylcryptojaponol (**5**),[10] 6α-hydroxydemethyl cryptojaponol (**6**),[10] and 14-deoxycoleon U (**7**).[11] Compounds **1–4** were obtained as amorphous powders, and their molecular formulae, estimated from mass spectra, suggested that they were diterpenoids. The ^{1}H- and ^{13}C-NMR spectra (Table 1) of **2–4** were recorded, and they showed very similar resonances. Compound **1** also had a moiety similar to **2–4**; however, only **1** had two keto groups in the ^{13}C-NMR spectrum.

Caryopteron A (**1**)[12] was determined to have the molecular formula $C_{20}H_{24}O_4$ by HRFABMS (*m/z* 329.1754, calcd for $C_{20}H_{25}O_4$, 329.1754). In the ^{1}H NMR spectrum, a singlet methyl proton resonance at δ_H 1.36 (3H, H-20), two broad singlet proton resonances at δ_H 1.61 (3H, H-18) and 1.66 (3H, H-19), and

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