Derivatives of Vibralactone from Cultures of the Basidiomycete

Boreostereum vibrans

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China is extraordinarily rich in higher fungi. To date about 10000 species of fungi have been reported from the vast territory of China. Among them, nearly 6000 species, belonging to about 1200 genera, are higher fungi (excluding lichens). Higher fungi in bio-resources belong to the very productive biologically sources which produce a large and diverse variety of secondary metabolites. We have been interested in the biologically active substances present in untapped and diverse source of higher fungi from China.1)

The fungus Boreostereum vibrans (BERK. & M. A. CURTIS) DAVYDeka & BONDARTEVA (synonym: Stereum vibrans BERK. & M. A. CURTIS) belonged to the family of Boreostereumae.2) Vibralactone (5), a lipase inhibitor with an unusual fused β-lactone, was obtained from the culture broth of B. vibrans in our previous report.3) Interestingly, a structurally closely related metabolite, percyquinnin, of undetermined relative and absolute configuration has been isolated from cultures of Stereum complicatum.5) Previous chemical investigations on the genus Stereum led to the isolation of various sesquiterpenoids,6—15) acetylenic compounds,16) glycerolipids,17) steroids,18) alkaloids19) benzaldehydes and benzo-furans,20,21) phenolic compounds, chromene and aromatic aldehyde derivatives.22,23) To find more compounds with the unique skeleton of vibralactone, the further study was undertaken to investigate the minor constituents of this fungus.

Four derivatives of vibralactone: 1,5-secovibralactone (1), vibralactone B (2), vibralactone C (3) and acetylated vibralactone (4), together with known compound vibralactone (5), had been isolated from cultures of the basidiomycete Boreostereum vibrans. The structures of 1—4 were elucidated on the basis of spectroscopic methods. The absolute configuration of 1 was suggested to be S by computational methods.

Key words vibralactone; Boreostereum vibrans; basidiomycete

Four new natural products possessing vibralactone skeleton, 1,5-secovibralactone (1), vibralactone B (2), vibralactone C (3) and acetylated vibralactone (4), together with known compound vibralactone (5), had been isolated from cultures of the basidiomycete Boreostereum vibrans. The structures of 1—4 were elucidated on the basis of spectroscopic methods. The absolute configuration of 1 was suggested to be S by computational methods.

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Its IR spectrum showed the presence of a carbonyl (1811 cm\(^{-1}\)) and a double bond (1631 cm\(^{-1}\)), respectively. The 1H- and 13C-NMR spectral data of 2 (Tables 1, 2) were similar to those of 5, which suggested that 2 possessed the same vi-bralactone skeleton. The characteristic differences were that \(\delta\)C for carbons 2 and 3 in 2 (\(\delta\)C 61.3, 77.1, respectively) were shifted upfield compared to those of 5 (\(\delta\)C 122.2, 146.7, respectively). The differences were caused by the double bond in 5 being displaced by an epoxy ring in 2. In the HMBC spectrum of 2 the expected significant correlations: from H-2 to C-4, C-5, C-7, C-8 and C-13 were observed. The relative configurations of 2 were established by rotating frame Over-hauser enhancement spectroscopy (ROESY) experiment. The correlations between H-2 and H-13 reflected that the epoxide ring was \(\beta\)-oriented. From the above data, compound 2 was identified as (1S,2R*,3R*,5S*)-2,3-epoxyvibralactone and named vibralactone B.

Compound 3 was obtained as a colorless oil. The molecular formula of C\(_{12}\)H\(_{14}\)O\(_{3}\) was established by HR-ESI-MS (m/z 229.0840 [M\(+\)Na], Calcd for C\(_{12}\)H\(_{14}\)O\(_{3}\) Na: 229.0840). The IR spectrum showed a \(\beta\)-lactone and a conjugated carbonyl group absorption bands at 1822 and 1686 cm\(^{-1}\), respectively. The 1H- and 13C-NMR spectral data (Tables 1, 2) of 3 were very similar to that of 5.22) The main difference was the hydroxymethyl group in 5 replaced by aldehyde (\(\delta\)C 188.9, \(\delta\)H 9.83) in 3. Based on the NMR data and the reference, 24) the structure of 3 was suggested as shown in Fig. 1 and named vibralactone C.

The molecular formula of 4 was deduced as C\(_{14}\)H\(_{18}\)O\(_{4}\) from its HR-ESI-MS. Comparison of the 1H- and 13C-NMR spectra data of 4 with 5 revealed that 4 had one more acetyl group (\(\delta\)C: 170.5, 20.8, \(\delta\)H 21.1) than 5, which caused down-field chemical shift of H-13 (\(\delta\)H 4.66). Thus, the structure of compound 4 was established as shown in Fig. 1 and named acetylated vibralactone.
Experimental

General Experimental Procedures  Melting point was measured on an XRC-1 apparatus (Sichuan University, Sichuan, People's Republic of China). Optical rotations were obtained in Horiba SEPA-300 digital polarimeter. UV spectra were measured in Shimadzu UV-2401 PC spectrophotometer. IR spectra were recorded on Bruker Tensor-27 spectrometer. NMR spectra were performed on Bruker AM-400 and DRX-500 instruments in CDCl₃, with TMS as internal standard. Mass spectra were recorded on VG Autospec-3000 mass spectrometer and API QSTAR pulsar 1 spectrometer. Chromatography (CC) and TLC were carried out on Silica gel (200—300 mesh) and precoated silica gel GF254 plates (Qingdao Marine Chemical Inc., China).

Mushroom Material and Culture  B. vibrans was provided and fermented by Prof. Da-Gan Ji, Kunming Institute of Botany. The voucher specimen was deposited at the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences. Culture medium: potato (peeled) 200.0 g, glucose 20.0 g, KH₂PO₄ 3.0 g, MgSO₄ 1.5 g, citric acid 0.1 g, and thiamin hydrochloride 10 mg in 1 l of deionized water (pH 6.5 before autoclaving). The fungus was grown in Erlenmeyer flasks (size: 500 ml; media: 300 ml). Fermentation was carried out on a rotary shaker at 22 °C and 150 rpm for 14 d.

Extraction and Isolation  The mycelium from 21 l was filtered, and the filtrate was extracted three times with EtOAc (20 l). The organic layer was subjected to column chromatography over silica gel (40 cm, 200—300 mesh, 9 g) eluting with petroleum ether/EtOAc (30 : 1, v/v, 0.4 l) to yield 13 mg mixture, which was further purified on silica gel column eluting with petroleum ether to afford 3 (14 mg) and 4 (7 mg). Fraction F (135 mg) was further purified by repeated chromatographies on silica gel column (2×30 cm, 200—300 mesh, 9 g) eluting with petroleum ether/EtOAc (7 : 1; 0.4 l) to afford 2B (14 mg). Positive HR-ESI-MS of [M]+: 247.0953 (Calcd for C₁₂H₁₆O₄Na: 247.0946).

Acetylated Vibralactone C (4): Colorless oil; [α]D²⁴ : −89.2° (c=0.19, CHCl₃). IR (KBr) cm⁻¹: 2967, 2920, 2857, 1822, 1747, 1443, 1378, 1241, 1111, 1008, 833. NMR data, see Tables 1 and 2. Positive HR-ESI-MS m/z: 273.1104 [M+Na]+ (Calcd for C₁₅H₁₈O₄Na: 273.1102).

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References and Notes