



Azaphilone and isocoumarin derivatives from the sponge-derived fungus *Eupenicillium* sp. 6A-9



Bin-Bin Gu¹, Ying wu¹, Jie Tang, Wei-hua Jiao, Lei Li, Fan Sun, Shu-Ping Wang, Fan Yang, Hou-Wen Lin*

Research Center for Marine Drugs, State Key Laboratory of Oncogenes and Related Genes, Department of Pharmacy, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200127, China

ARTICLE INFO

Article history:

Received 18 May 2018

Revised 21 June 2018

Accepted 25 June 2018

Available online 25 June 2018

Keywords:

Azaphilone

Isocoumarin

Sponge

Eupenicillium sp.

Theoretical calculation

Cytotoxicity

ABSTRACT

Three new azaphilones, eupenicilazaphilones A–C (**1–3**), and one new isocoumarin, eupenicillin A (**4**), as well as five known azaphilones were isolated from the sponge-derived fungus *Eupenicillium* sp. 6A-9. Their structures were elucidated by detailed spectroscopic analysis, comparison with literature data, and ¹³C NMR chemical shifts and TDDFT/ECD calculations. The antibacterial activity against *Staphylococcus aureus* ATCC25923, methicillin-resistant *Staphylococcus aureus* ATCC4330, and *Acinetobacter baumannii* ATCC19606 as well as the cytotoxic activity towards human cancer lines MCF-7 and A549 were examined.

© 2018 Published by Elsevier Ltd.

Introduction

In recent years, marine-derived fungi have gained ever-increasing attention as a promising reservoir for biologically and pharmaceutically active marine natural products (MNPs) and have become the third-largest MNP-source [1–5]. Sponge-derived fungi, as fungi with unique habitat, have also received increasing attention for novel bioactive MNPs [1,6,2–4]. As part of our efforts for bioactive fungal metabolites, chemical investigations of fungi isolated from several marine sponges collected from Yongxing Island were initiated [7–10]. Prior investigation of the fungus *Eupenicillium* sp. 6A-9 (KM582643) isolated from the marine sponge *Plakortis simplex* in our group has resulted in the isolation of several immuno-alleviating meroterpenoids [10]. Continuing investigation of the remaining subfractions of its EtOAc extract yielded four new compounds, eupenicilazaphilones A–C (**1–3**) and eupenicillin A (**4**), together with five known azaphilones, geumsanol F (**5**) [11], hypocrellone A (**6**) [11], WB (**7**) [12], geumsanol G (**8**) [11], isochromophilone VI (**9**) [13] (Fig. 1). The structures and absolute configurations of these compounds were resolved by virtue of detailed spectroscopic analysis, comparison with literature data, and ¹³C NMR chemical shifts and TDDFT/ECD calculations. Herein, we reported the isolation, structure elucidation, and biological activities of these compounds.

Results and discussion

Eupenicilazaphilone A (**1**) has a molecular formula of C₁₉H₂₇O₆Cl with 6 degrees of unsaturation, based on its [M+H]⁺ molecular ion at *m/z* 387.1566 in its HR-ESI-MS (calcd. for C₁₉H₂₈O₆Cl, 387.1574). Positive ESI-MS spectrum revealed pseudomolecular ion peaks at *m/z* 387 and 389 [M+H]⁺ with a ratio of 3:1, indicating the presence of one chlorine atom in **1**. Its UV spectrum exhibited a maximum absorption at 363 nm, suggesting an extended conjugated chromophore. Analysis of ¹H and HSQC NMR spectroscopic data of **1** (Table S1) revealed the presence of four methyls (δ_{H} 1.33, 1.33, 0.89, 0.89), two *trans*-coupled olefinic protons (δ_{H} 6.31, 6.63, *J* = 15.5 Hz), five methines (δ_{H} 6.10, 4.04, 3.41, 3.20, 1.56), and two methylenes (δ_{H} 4.15, 4.55; 1.27, 1.43). Its ¹³C and DEPT spectra (Table S1) exhibited a total of 19 carbon resonances divided into 7 sp² carbons [1 carbonyl carbon (δ_{C} 195.4) and 6 olefinic carbons (δ_{C} 163.0, 146.3, 144.3, 122.9, 118.1, 102.9)] and 12 sp³ carbons [2 oxygenated quaternary carbons (δ_{C} 79.2, 77.0), 4 methine (δ_{C} 79.8, 75.9, 38.7, 37.7), 2 methylene (δ_{C} 69.7, 30.1), and 4 methyl (δ_{C} 26.1, 23.6, 14.2, 12.2) carbon atoms]. As one carbonyl and six olefinic carbons require 4 degrees of unsaturation, **1** was further evidenced to be a bicyclic compound.

A consecutive ¹H–¹H COSY correlation, H₂-1/H-8a/H-8, along with HMBC correlations from H-1 α (δ_{H} 4.55) to C-3 (δ_{C} 163.0), C-4a (δ_{C} 146.3) and C-8a (δ_{C} 38.7), from H-8a (δ_{H} 3.20) to C-4a, and from H-4 (δ_{H} 6.10) to C-3 and C-8a were sufficient to generate the 3,4-dihydro-2*H*-pyran ring and its exocyclic oxygenated

* Corresponding author.

E-mail address: hwlin@sjtu.edu.cn (H.-W. Lin).

¹ Contribute equally to this work.

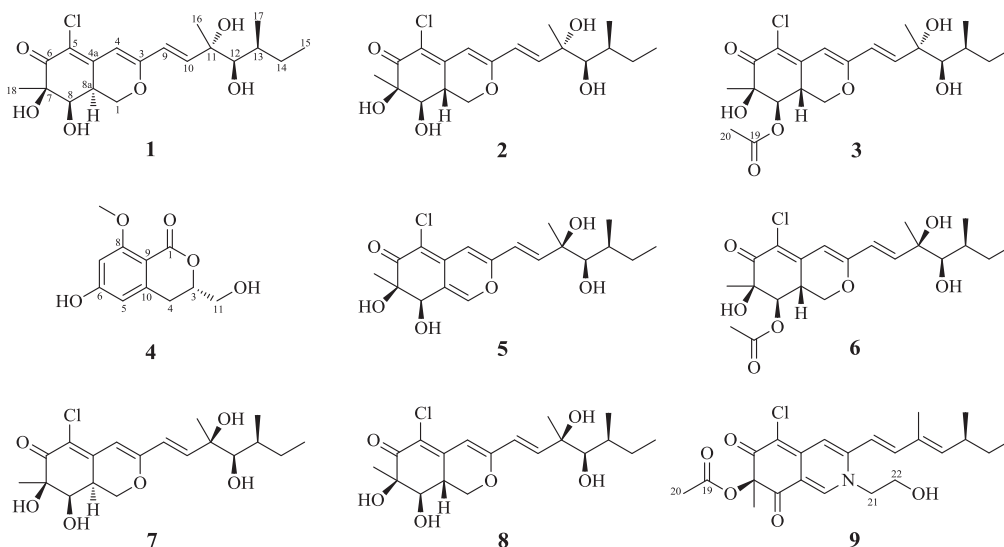


Fig. 1. Structures of compounds 1–9.

methine carbon C-8 (δ_C 75.9) (Fig. 2). Besides, H-4 and H-8a showed three-bond connectivities to C-5 (δ_C 118.1). H-8 (δ_H 4.04) showed two-bond correlation to C-7 (δ_C 79.2) and three-bond cor-

relations to C-4a and C-6 (δ_C 195.4). Me-18 (δ_H 1.33) exhibited three-bond couplings to C-6 and C-8 and two-bond coupling to C-7. These data together could establish a bicyclic core moiety, indicating the presence of an azaphilone skeleton [11,14]. The ^1H – ^1H COSY cross-peaks [H-12/H-13(Me-17)/H₂-14/Me-15 and H-9/H-10] and HMBC correlations [Me-16 (δ_H 1.33)/C-10 (δ_C 144.3), C-11 (δ_C 77.0), and C-12 (δ_C 79.8)] established the 3,5-dimethylhept-1-ene-3,4-diol side chain. This chain was connected to C-3 by HMBC connectivities of H-9 (δ_H 6.31) and H-10 (δ_H 6.63) to C-3, thereby completing the structure of eupenicilazaphilone A (1) as shown, which has the same planar structure as that of the previously reported azaphilones, WB (7) [12] and geumsanol G (8) [11]. All these assignments were supported by the other NMR spectroscopic data shown (Fig. 2).

Detailed comparison of its NMR data with those of 7 and 8 (Tables S1 and S9–S11) indicated that the western azaphilone core moieties of compounds 1 and 7 are completely identical (with same relative configurations at C-7, C-8, and C-8a), which can be verified from its NOESY spectrum (Fig. 3), whereas the relative

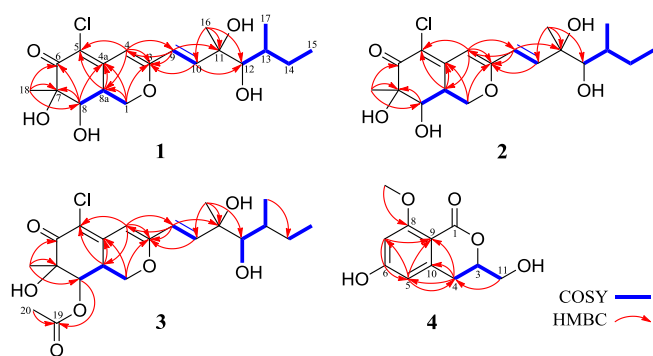


Fig. 2. Key COSY and HMBC correlations of 1–4.

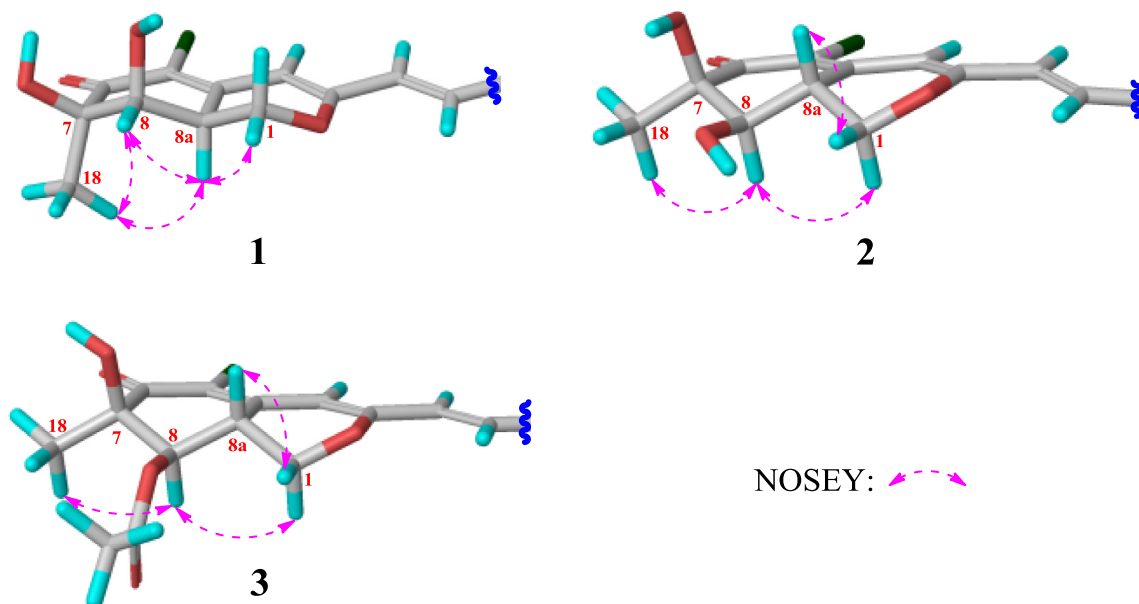


Fig. 3. Key NOESY correlations of 1–3.

Download English Version:

<https://daneshyari.com/en/article/8943016>

Download Persian Version:

<https://daneshyari.com/article/8943016>

[Daneshyari.com](https://daneshyari.com)