SHORT REPORT

A C G publications

Rec. Nat. Prod. X:X (202X) XX-XX

records of natural products

Furan Derivatives and Amides from *Elaeocarpus apiculatus*

Shen Yao [*1] and Xinyi Yang [2]

[1]*Department of Pharmacy, The First People's Hospital of Linping District, Hangzhou 311100, China*
[2]*Betta Pharmaceutical Co., Ltd., Hangzhou 311100, China*

(Received March 06, 2022; Revised May 13, 2022; Accepted May 17, 2022)

Abstract: The first phytochemical study of *Elaeocarpus apiculatus* led to the isolation of five compounds, including two furan derivatives (**1** and **2**) and three amides (**3**–**5**). Among them, compound **1** was a new furan derivative, and compounds **2**–**5** were discovered from the genus *Elaeocarpus* for the first time. The characterization of these compounds was achieved by HRMS, UV, IR and NMR data. Compounds **1**, **3** and **4** showed weak nitric oxide (NO) inhibitory effects. A potential biogenetic pathway for the formation of **1** was proposed.

Keywords: *Elaeocarpus apiculatus*; Elaeocarpaceae; furan derivative; amide. © 2022 ACG Publications. All rights reserved.

1. Plant Source

The leaves of *Elaeocarpus apiculatus* were collected in June 2019 from Zhejiang Province, People's Republic of China, and was identified by one of the authors (S. Yao). A voucher specimen (accession number: DY190633) was deposited in the Herbarium of Zhejiang University (HZU).

2. Previous Studies

Elaeocarpus apiculatus (Elaeocarpaceae) is a common ornamental tree mainly distributed in south China [1]. However, no phytochemical studies on this plant have been reported.

3. Present Study

In the present investigation, five compounds (Figure 1) including a new furan derivative were isolated from *Elaeocarpus apiculatus*. The air-dried leaves of *E. apiculatus* (3 kg) were percolated 95% ethanol (15 L) to give an extract (195 g), which was dissolved in water and partitioned with ethyl acetate (EtOAc). The EtOAc portion was separated *via* macroporous resin D101 column chromatography (CC) and then separated *via* silica gel CC (petroleum ether/CH_2Cl_2, 20:1 → 0:1) to give five fractions (A–E). Compounds **3** (11 mg), **4** (10 mg) and **5** (8 mg) were isolated from fraction C by HPLC, while Compounds **1** (2 mg) and **2** (6 mg) were isolated from fraction D by repeated silica gel CC.

* Corresponding author: E- Mail: yaoshen20@foxmail.com

The article was published by ACG Publications
http://www.acgpubs.org/journal/records-of-natural-products Month-Month 202X EISSN:1307-6167
DOI: http://doi.org/10.25135/rnp.331.2203.2376
Available online :May 19, 2022

Furan derivatives and amides from *Elaeocarpus apiculatus*

*Elapifuran A (**1**)*: colorless oil, $[\alpha]^{25}_{D}$ 0 (*c* 0.1, MeCN); UV (MeCN) λ_{max} (log ε) 190 (3.61), 278 (2.98) nm; IR (KBr) ν_{max} 3441, 2924, 2853, 1719, 1670, 1517, 1465, 1025, 769 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; HRESIMS *m/z* 257.0415 $[M + Na]^+$ (calcd for $C_{12}H_{10}O_5Na^+$, 257.0420).

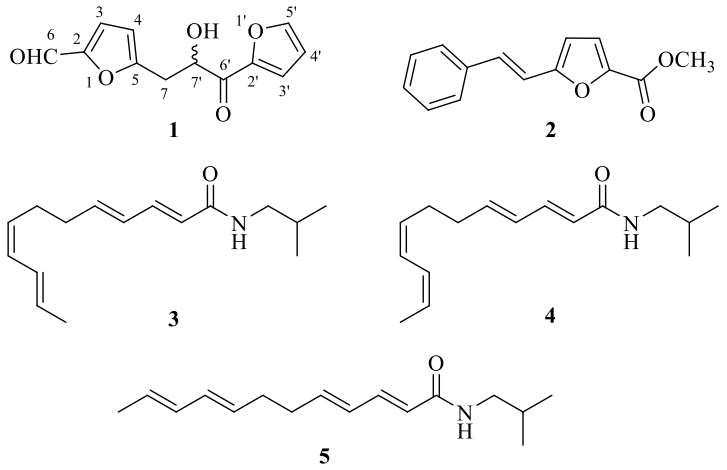

Figure 1. Structures of compounds **1**–**5** isolated from *E. apiculatus*

Elapifuran A (**1**) was obtained as colorless oil. The molecular formula was determined as $C_{12}H_{10}O_5$ by HR-ESI-MS ion at *m/z* 257.0415 $[M + Na]^+$ (calcd for $C_{12}H_{10}O_5Na^+$, 257.0420). In the IR spectrum, absorption bands at 3441 cm^{-1} (OH group) and 1719 cm^{-1} (carbonyl group) were observed. The ^{1}H NMR data of **1** (Table 1) showed an aldehyde group [δ_H 9.54 (1H, s)], five aromatic proton signals [δ_H 7.68 (1H, brs), 7.40 (1H, d, *J* = 3.6 Hz), 7.17 (1H, d, *J* = 3.5 Hz), 6.64 (1H, dd, *J* = 3.6, 1.5 Hz) and 6.41 (1H, d, *J* = 3.5 Hz)], an oxygenated methine [δ_H 5.17 (1H, m)] and a free hydroxyl group [δ_H 3.69 (1H, d, *J* = 6.6 Hz)]. Total twelve carbon resonances were resolved in the ^{13}C NMR spectrum and were further classified by HSQC as one conjugated aldehyde (δ_C 177.1), one conjugated ketocarbonyl (δ_C 188.2), eight aromatic carbons (δ_C 158.1, 152.2, 149.9, 147.7, 123.1, 119.8, 113.0 and 111.3), oxygenated methine (δ_C 71.5) and sp^3 methylene (δ_C 34.6). The above evidences indicated that compound **1** should be a furan derivative [2,3].

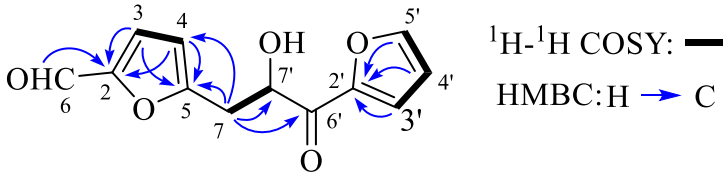

Figure 2. Key ^{1}H–^{1}H COSY and HMBC correlations of compound **1**

In the ^{1}H–^{1}H COSY spectrum, the correlations established coupling relationships of H-3/H-4, H_2-7/H-7′ and H-3′/H-4′/H-5′. The linkages of these subunits and other functionalities were deduced by the HMBC signals. The HMBC correlations of H-3 and H-4/C-2 and C-5; H-6/C-2; H_2-7/C-4 and C-5 established a 2,5-disubstituted furan ring with an aldehyde group (C-6) at C-2 and a sp^3 methylene (C-7) at C-5. The HMBC correlations from H-3′, H-4′ and H-5′ to C-2′, together with the severely up-field shifted ketocarbonyl carbon signal (δ_C 188.2, C-6′) indicated the existence of a monosubstituted furan ring with a ketocarbonyl group at C-2′. Finally, the HMBC correlations from H_2-7 to C-6′ and C-7′ generated the whole planar structure of **1**.

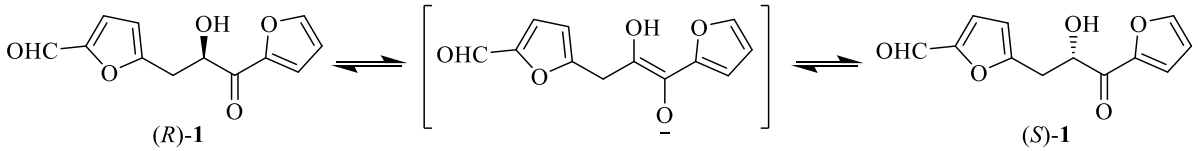

Figure 3. The tautomerism of (*R*)-**1** and (*S*)-**1**

Compound **1** was determined to be a racemate on the basis of its optical rotation being almost zero and no Cotton effects in its ECD spectrum. However, chiral-phase separation of **1** using various conditions failed, probably due to the tautomerism of (*R*)-**1** and (*S*)-**1** (Figure 3).

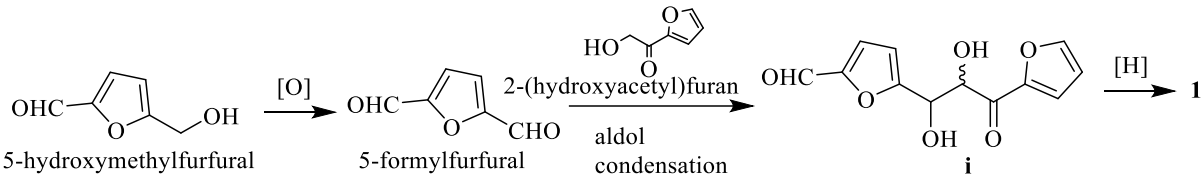

Figure 4. Proposed biosynthetic pathway of compound **1**

A potential biosynthetic pathway of was proposed for **1** (Figure 4). Briefly, **1** might be originated from 5-hydroxymethylfurfural [4], which could be converted to 5-formylfurfural via oxidation. Then, aldol condensation between 5-formylfurfural and 2-(hydroxyacetyl)furan could afford intermediate **i**. Finally, this intermediate would undergo reduction to yield compound **1**.

Table 1. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR data for compound **1** (δ in ppm, J in Hz) in CD_3Cl_3

No	δ_H	δ_C	no.	δ_H	δ_C
2		152.2	2′		149.9
3	7.17, d (3.5)	123.1	3′	7.40, d (3.6)	119.8
4	6.41, d (3.5)	111.3	4′	6.64, dd (3.6, 1.5)	113.0
5		158.1	5′	7.68, brs	147.7
6	9.54, s	177.1	6′		188.2
7a	3.39, dd (15.3, 4.0)	34.6	7′	5.17, m	71.5
7b	3.11, dd (15.3, 7.9)		7′-OH	3.69, d (6.6)	

The known compounds were identified as 5-styrylfuran-2-carboxylic acid methyl ester (**2**) [5], (2*E*,4*E*,8*Z*,10*E*)-*N*-isobutyldodeca-2,4,8,10-tetraenamide (**3**) [6], (2*E*,4*E*,8*Z*,10*Z*)-*N*-isobutyldodeca-2,4,8,10-tetraenamide (**4**) [7] and (2*E*,4*E*,8*E*,10*E*)-*N*-isobutyldodeca-2,4,8,10-tetraenamide (**5**) [6], by comparison with the published data.

The inhibitory effects of compounds **1**–**5** on nitric oxide production induced by lipopolysaccharide were evaluated using a Griess assay [8], and quercetin (IC_{50} = 16.6 ± 1.2 μM) was used as a positive control. Compounds **1**, **3** and **4** showed weak inhibitory activity with IC_{50} values of 54.6 ± 8.9, 38.6 ± 4.4 and 44.6 ± 5.6 μM, respectively, without cytotoxicity. Other two compounds showed no obvious inhibitory effects.

The *Elaeocarpus* is characterized by alkaloids, glycosides, flavonoids, triterpenes, tannins and fatty acids, etc [9]. This is the first phytochemical study of *Elaeocarpus apiculatus*, from which two furan derivatives (**1** and **2**) and three amides (**3**–**5**) were isolated. All compounds were isolated from this genus for the first time. The current study could enrich the structural diversity of *Elaeocarpus* metabolites.

Acknowledgments

This work was partially supported by the Hangzhou Medical and Health Science Foundation of China (No. B20210235).

Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products

ORCID
Shen Yao: 0000-0002-6847-2691
Xinyi Yang: 0000-0001-8565-4238

References

[1] Editor Committee for Flora of China of Chinese Academy of Science (1989). Science Publishing House, Beijing. PP. 10.
[2] Y. S. Li, Z. J. Chen and D. Y. Zhu (2005). A novel bis-furan derivative, two new natural furan derivatives from *Rehmannia glutinosa* and their bioactivity, *Nat. Prod. Res.* **19**, 165-170.
[3] L. L. Chen, P. Wang, H. Q. Chen, Z. K. Guo, H. Wang, H. F. Dai and W. L. Mei (2017). New furan derivatives from a mangrove-derived endophytic fungus *Coriolopsis* sp. J5, *Molecules* **22**, 261.
[4] S. Fotso, R. P. Maskey, D. Schröder, A. S. Ferrer, I. Grün-Wollny and H. Laatsch (2008). Furan oligomers and *β*-carbolines from terrestrial Streptomycetes, *J. Nat. Prod.* **71**, 1630-1633.
[5] J. Q. Gu, E. J. Park, J. S. Vigo, J. G. Graham, H. H. S. Fong, J. M. Pezzuto and A. D. Kinghorn (2002). Activity-guided isolation of constituents of *Renealmia nicolaioides* with the potential to induce the phase II enzyme quinone reductase, *J. Nat. Prod.* **65**, 1616-1620.
[6] I. Yasuda, K. Takeya and H. Itokawa (1981). Structures of amides from *Asiasarum heterotropoides* Maek. var. *mandshuricum* Maek, *Chem. Pharm. Bull.* **29**, 564-566.
[7] N. J. Matovic, P. Y. Hayes, K. Penman, R. P. Lehmann and J. J. De Voss (2011). Polyunsaturated alkyl amides from *Echinacea*: synthesis of diynes, enynes, and dienes, *J. Org. Chem.* **76**, 4467-4481.
[8] J. Li, K. W. Zeng, S. P. Shi, Y. Jiang and P. F. Tu (2012). Anti-neuroinflammatory constituents from *Polygala tricornis* Gagnep, *Fitoterapia* **83**, 896-900.
[9] A. Dadhich, A. Rishi, G. Sharma and S. Chandra (2013). Phytochemicals of *Elaeocarpus* with their therapeutic value: a review, *Int. J. Pharma Bio Sci.* **4**, 591-598.

A C G
publications
© 2022 ACG Publications