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Mini review

# Three new arylbenzofurans from *Lavandula angustifolia* and their bioactivities

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ABSTRACT

Three new arylbenzofurans, 2-(7-methoxy-2-(4-methoxyphenyl)-3-methylbenzofuran-5-yl)ethanol (**1**), 4-(5-(2-hydroxyethyl)-7-methoxy-3-methylbenzofuran-2-yl)phenol (**2**), and 2-(6-methoxy-2-(4-methoxyphenyl)-3-methylbenzofuran-5-yl)ethanol (**3**), together with three known ones (**4**–**6**) were isolated from the whole plant of *Lavandula angustifolia*. Their structures were determined by means of HRESIMS and extensive 1D and 2D NMR spectroscopic studies. Compounds **1**–**3** and **5** were tested for their anti-tobacoo mosaic virus (TMV) activities, and Compounds **1**–6 were tested for their cytotoxicity activities. In our assay, Compounds **1**–**3** showed high anti-TMV activity with inhibition rate of 38.2, 35.2, and 34.0%, which superior to positive control Ningnanmycin. Compounds **1**–**6** also showed weak inhibitory activities against some tested human tumor cell lines with IC50 values in the range of 2.2–8.2 μM.



**Contents**



## 1. Introduction

*Lavandula angustifolia* (*L. angustifolia*) *Mill.* is a perennial shrub of the family Lamiaceae. It originated in the southern Europe and the Mediterranean area, and is commercially cultivated in many countries *L. angustifolia* is also a very popular aromatic plant and commonly used for perfumes, cosmetics and medicines (Cavanagh and Wilkinson, 2002). In previous work, a number of bioactive compounds, such as flavonoids (Bajalan et al., 2016; Panuccio et al., 2016; Farhoudi and Lee, 2014), lactone (Lesage-Meessen et al., 2015), coumarins (Bourgaud et al., 2006; Haig et al., 2009; Areias et al., 2000), terpenes (Jullien et al., 2014; Demissie et al., 2011),

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fatty acids (Topcun et al., 2007), and the like, were isolated from the genus of this plants. Some of these compounds have showed various bioactivities, such as antimicrobial, antioxidant, fungistatic, antiviral and cytotoxicity. In this study, three new arylbenzofurans (**1**–**3**) and three known ones (**4**–**6**) arylbenzofurans were isolated from the whole plant of *L. angustifolia*. Their structures were identified by spectroscopic methods, including HRMS and $^{1}$D and $^{2}$D NMR. In addition, the anti-tobacco mosaic virus (anti-TMV) activity and cytotoxicity activities of these compounds were also evaluated.

## 2. Results and discussion

A 70% aq. acetone extract prepared from the whole plant of *Lavandula angustifolia* was subjected repeatedly to column chromatography and preparative HPLC to afford three new arylbenzofurans, 2-(7-methoxy-2-(4-methoxyphenyl)-3-methylbenzofuran-5-yl) ethanol (**1**), 4-(5-(2-hydroxyethyl)- 7-methoxy-3-methylbenzofuran-2-yl) phenol (**2**), and 2-(6-methoxy-2-(4-methoxyphenyl)-3-methylbenzofuran-5-yl) ethanol (**3**), and three known arylbenzofurans (**4**-**6**). The structures of the compounds **1–6** were as shown in Fig. 1, and the $^{1}$H and $^{13}$C NMR data of **1–3** were listed in Table 1. The known compounds, compared with literature, were identified as 2-(2′-methoxy-4′-hydroxy)-aryl-3- methy-6-hydroxy-benzofuran (**4**) (Wang et al., 2013), ebenfuran IV (**5**), and iteafuranal B (**6**) (Luo et al., 2014).

Compound **1** was obtained as yellow gum. Its molecular formula was determined as $C_{19}H_{20}O_4$ by HRESIMS (*m/z* 335.1252 $[M+Na]^+$; calcd $C_{19}H_{20}NaO_4$ for 335.1259), indicating the presence of 10° of unsaturation in the molecule. The UV spectrum showed absorption maxima at 210, 272 and 312 nm, and the IR spectrum showed absorption bands at 3440, 1625, 1510, 1462 $cm^{-1}$, indicating the presence of hydroxy and aromatic ring. The structure of **1** was further elucidated by interpretation of NMR data, including DEPT, HMBC and HSQC data (Table 1). The $^{1}$H and $^{13}$C NMR spectra of **1** (Table 1) along with analysis of the DEPT spectra displayed 19 carbon signals and 20 proton signals, respectively, corresponding to a 1,2,3,5-tetrasubstituted phenyl ring (C-1–C-6, H-4 and H-6), a 1,4-substituted phenyl ring (C-1'–C-6', $H_2$-2',6', and $H_2$-3',5'), a 2-hydroxyethyl group (C-7 and C-8; $H_2$-7 and $H_2$-8), a methyl group (C-9' and $H_3$-9'), a pair of double bond (C-7' and C-8'), and two methoxy groups ($\delta_C$ 56.4 and 55.9 q; $\delta_H$ 3.85 and 3.80 s). Its $^{1}$H and $^{13}$C NMR spectroscopic data (two phenyl rings, C-7′–C-9′) were similar to those of known compound, 7-methoxy-2-(4-methoxyphenyl)-3-methyl-5-(3-prenyl)-benzofuran (Du et al., 2016)

**Table 1**
$^{1}$H and $^{13}$C NMR data for compounds **1–3** (Date obtained in $C_5D_5N$).

| No. | 1 | | 2 | | 3 | |
|---|---|---|---|---|---|---|
| | $d_C$ | $d_H$ (m, *J*, Hz) | $d_C$ | $d_H$ (m, *J*, Hz) | $d_C$ | $d_H$ (m, *J*, Hz) |
| 1 | 126.5 s | | 126.4 s | | 121.1 s | |
| 2 | 143.6 s | | 143.4 s | | 149.0 s | |
| 3 | 148.6 s | | 148.9 s | | 98.1 d | 6.99 s |
| 4 | 109.3 d | 7.38 d (2.2) | 109.5 d | 7.41 d (2.2) | 153.3 s | |
| 5 | 133.6 s | | 133.8 s | | 125.3 s | |
| 6 | 114.3 d | 7.65 d (2.2) | 114.6 d | 7.68 d (2.2) | 120.4 d | 7.31 s |
| 7 | 41.3 t | 2.70 t (7.2) | 41.5 t | 2.68 t (7.2) | 35.9 t | 2.67 t (7.2) |
| 8 | 62.2 t | 3.71 t (7.2) | 62.5 t | 3.69 t (7.2) | 61.3 t | 3.71 t (7.2) |
| 1′ | 122.2 s | | 122.3 s | | 122.5 s | |
| 2′,6′ | 130.0 d | 7.77 d (8.8) | 130.5 d | 7.76 d (8.8) | 130.1 d | 7.77 d (8.8) |
| 3′,5′ | 115.7 d | 6.77 d (8.8) | 116.9 d | 6.73 d (8.8) | 115.5 d | 6.78 d (8.8) |
| 4′ | 160.3 s | | 157.6 s | | 160.3 s | |
| 7′ | 152.4 s | | 152.0 s | | 151.5 s | |
| 8′ | 111.3 s | | 111.6 s | | 111.3 s | |
| 9′ | 8.9 q | 2.19 s | 9.1 q | 2.16 s | 9.0 q | 2.17 s |
| 3-OMe | 56.4 q | 3.85 s | 56.5 q | 3.84 s | | |
| 4-OMe | | | | | 56.3 q | 3.88 s |
| 4′-OMe | 55.9 q | 3.80 s | | 3.80 s | 55.8 q | 3.82 s |
| Ar-OH | | | | 10.84 s | | |

which suggested that compound **1** should be a 3-methyl-2-arylbenzofuran. In addition, the 3-methyl-2-arylbenzofuran skeleton of **1** was also constructed by the HMBC correlations (Fig. 2) of $H_3$-9′ with C-1, C-7′, and C-8′; of $H_2$-2′,6′ with C-7′; and of H-6 with C-8′. The position of the 2-hydroxyethyl group at the C-5 of the arylbenzofuran was elucidated by the HMBC correlations from $H_2$-7 to C-4, C-5, and C-6; H-8 to C-5; H-4 to C-7; and H-6 to C-7. The HMBC correlations from two methoxy protons ($\delta_H$ 3.84 and 3.85) to C-3 ($\delta_C$ 148.6) and C-4′ ($\delta_C$ 160.3) supported two methoxy groups located at C-3 and C-4′, respectively. Thus, the structure of **1** was established as 2-(7-methoxy-2-(4-methoxyphenyl)-3- methylbenzofuran-5-yl) ethanol.

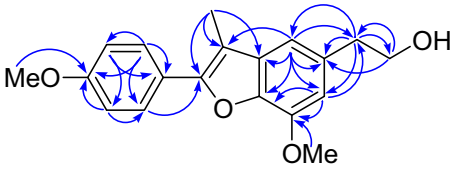


**Fig. 2.** Key HMBC correlations of **1**.

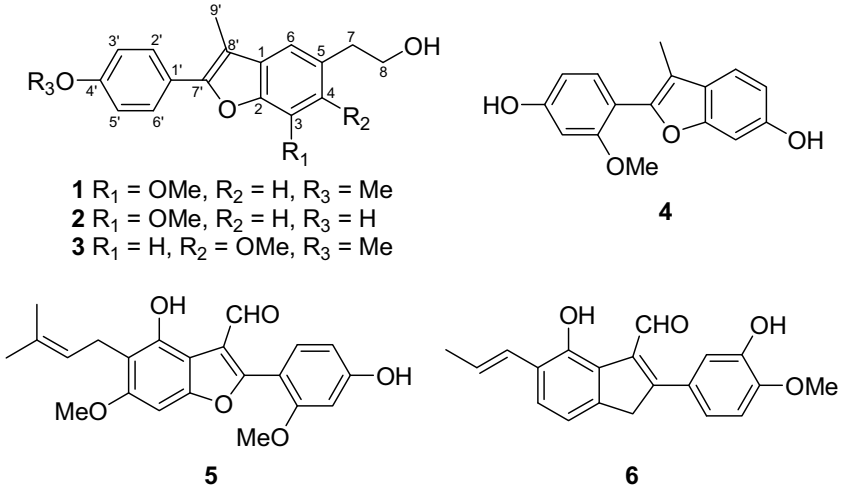


**Fig. 1.** The structures of arylbenzofurans (**1–6**) from *L. angustifolia*.