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Three new diarylheptanoids and their antioxidant property

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Abstract

Three new diarylheptanoids, i.e., sodium(5*S*,2*E*)-1,7-bis(4-hydroxyphenyl)-1-hydroxy-2-hepten-5-sulfonate (**1**), sodium(5*R*,2*E*)-1,7-bis(4-hydroxyphenyl)-1-hydroxy-2-hepten-5-sulfonate (**2**) and 3,5-diacetoxy-1-(3-methoxy-4,5-dihydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane (**3**) were isolated from the rhizomes of *Zingiber officinale*. The structures of the new compounds were elucidated on the basis of spectroscopic methods. The antioxidant activities of **3** were assayed by *in vitro* models involving DPPH free radicals and superoxide anion radicals.

Keywords: Diarylheptanoid; *Zingiber officinale*; Antioxidant

The rhizomes of *Zingiber officinale* Roscoe (Zingiberaceae), with the common name of ginger, have a long history of medical application in China for its tonic effects. It is quite frequently listed in the prescriptions of traditional Chinese medicine for the treatment of rheumatism, vomiting, duodenum and gastric ulcer [1]. A number of active principles from this species have been reported [2–9], among them diarylheptanoids exhibited rather important bioactivities such as inhibitory effects on the biosyntheses of prostaglandid and leukotriene [10], activities of anti-fungal and anti-oxidation [6,11], and cancer chemopreventive activity [12]. In our efforts to exploring the association of diarylheptanoids and antioxidation, three new diarylheptanoids were identified from the methanol extract of *Z. officinale* collected in Yunnan province of southwestern China. According to the bioassays, these new diarylheptanoids were found to possess potent activities on scavenging DPPH free radicals as well as remarkable inhibitory effects on the formation of superoxide anion free radicals. The structure determination of these three new compounds was also reported herein.

Compounds **1** and **2** were obtained as a mixture in yellow amorphous powder and could not be 426.0849 ($[M + Na]^+$) of **1** and **2** revealed the molecular formula of $C_{19}H_{21}O_6SNa$. The ^1H and ^{13}C further separated even by HPLC. The ESI-MS at *m/z* 377 ($[M–Na]^-$) and the HR-ESI-MS at *m/z* NMR spectra (Table 1) of the mixture showed

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two sets of closely similar signals for two hexahydrocurcumin derivatives with almost the same intensity. Furthermore, the ^{1}H and ^{13}C NMR spectra of **1** and **2** showed signals due to a *trans*-olefin pair [δ 6.08 (dd, 1H, J = 15.2, 8.8 Hz, 2-H), 5.73 (m, 1H, 3-H)], two *para*-substituted aromatic rings [δ 6.69, 6.99 (d, 4H, J = 8.4 Hz, 2′, 6′-H; 3′, 5′-H), 6.77, 7.31 (d, 4H, J = 8.8 Hz, 2″, 6″-H; 3″, 5″-H)], as well as two methines [δ 4.52 (d, 1H, J = 8.8 Hz,), 3.62 (m, 1H)] bearing an oxygen function and a sulfonyl functionality, respectively. This deduction is in agreement with the molecular formula. Furthermore, the pair of sodium sulfonyl diarylheptanoids isomers (**1** and **2**) showed their structural characteristics partially similar with those of shogasulfonic acids [13] as well as partially similar with those of (1*S*,5*R*,2E)-1,7-diphenylhept-2-ene-1,5-diol [14]. 2D-NMR experiments were performed to gather more information for structure elucidation. The ^{1}H–^{1}H COSY data of **1** and **2** indicated the presence of partial structures marked by bold lines in Fig. 1. Meanwhile, in the HMBC experiment, long-range correlations were observed between the proton and carbon pairs of **1** and **2**, e.g., H-2 and C-4/C-1′, H-1 and C-2′/C-3, H-5 and C-3/C-7, H-7 and C-2″, illustrated with warped arrows in Fig. 1. All of the spectral data including the chemical shifts of C-2 and C-3 evidenced this pair of isomers containing an allyl alcohol and a non-conjugated sulfonyl group. Taking the fact of sulfonyl functionality usually appearing at C-5 for diarylheptanoids (e.g. shogasulfonic acids) into account, it would be rather rationale to assume that the attachment of the sulfonyl group of **1** and **2** should be at C-5, which appeared at δ 71.3 and 71.4, respectively (Table 1). The hypothetic biogenetic pathway of this pair of enantiomers is illustrated in Fig. 2. The pair of diarylheptanoid enantiomers was therefore revealed as sodium(5*S*,2*E*)-1,7-bis(4-hydroxyphenyl)-1-hydroxy-2-hepten-5-sulfonate (**1**) and sodium(5*R*,2*E*)-1,7-bis(4-hydroxyphenyl)-1-hydroxy-2-hepten-5-sulfonate (**2**).

Compound **3** was obtained as colorless oil, $[\alpha]_{D}^{20}$ + 5.0 (*c* 0.52, chloroform). The molecular formula of **3** was established as $C_{25}H_{32}O_9$ on the basis of its EI-MS, elemental analysis, and ^{13}C NMR data. Its ^{1}H, ^{13}C NMR and IR

Table 1
NMR spectral data of compounds **1–3** [^{1}H, 400 MHz and ^{13}C, 100 MHz in CD_3OD, δ ppm]

Position	**1**	**2**	**1**, **2**	**3**	
	δ_C	δ_C	δ_H (mult, J in Hz)	δ_C	δ_H (mult, J in Hz)
1	70.6	70.6	4.52 (d, J = 8.8)	31.4	2.52 (dt, J = 15.6, 7.8), 2.54 (dt, J = 15.9, 7.8)
2	132.5	132.5	6.08 (dd, J = 15.2, 8.8)	36.6	1.84 (q, J = 7.2)
3	129.8	129.8	5.73 (m)	69.8	4.97 (m)
4	42.0	41.6	2.29 (m)	38.5	1.76 (dt, J = 11.7, 5.7), 1.92 (dt, J = 14.0, 6.9)
5	71.3	71.4	1.73 (m)	69.8	4.97 (m)
6	39.9	39.9	1.64 (m)	36.5	1.84 (q, J = 7.2)
7	31.9	32.0	2.55 (m), 2.66 (m)	31.2	2.52 (dt, J = 15.6, 7.8), 2.54 (dt, J = 15.9, 7.8)
1′	134.4	134.4		133.1	
2′	130.3	130.3	6.99 (d, J = 8.4)	108.4	6.36 (br s)
3′	115.9	115.9	6.69 (d, J = 8.4)	146.8	
4′	156.2	156.2		130.5	
5′	115.9	115.9	6.69 (d, J = 8.4)	143.8	
6′	130.3	130.3	6.99 (d, J = 8.4)	103.2	6.26 (br s)
1″	130.3	130.3		133.2	
2″	131.4	131.4	7.31 (d, J = 8.8)	110.9	6.66 (d, J = 1.6)
3″	116.0	116.0	6.77 (d, J = 8.8)	146.3	
4″	157.7	157.7		143.7	
5″	116.0	116.0	6.77 (d, J = 8.8)	114.2	6.80 (d, J = 8.0)
6″	131.4	131.4	7.31 (d, J = 8.8)	120.7	6.62 (dd, J = 8.0, 1.6)
3-OAc				170.8 21.1	2.00 (s)
5-OAc				170.8 21.1	2.00 (s)
3′-OMe				56.1	3.84 (s)
3″-OMe				55.9	3.82 (s)

Note: The δ_c assignments of **1** and **2** could be interchanged.

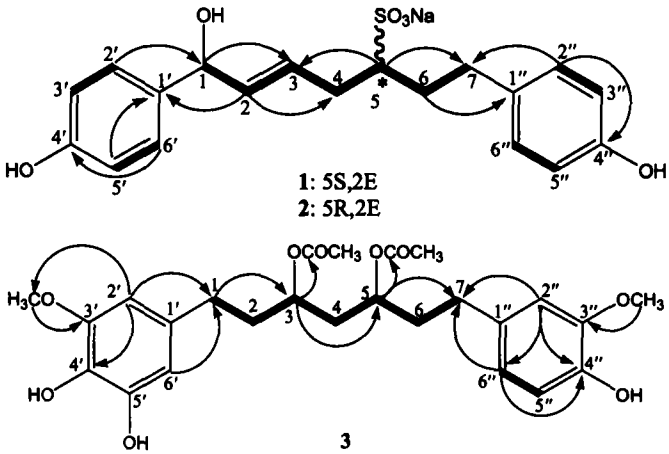

Fig. 1. Structures and key ^{1}H–^{1}H COSY (bold) and HMBC (arrow) correlations of compounds **1**, **2** and **3**.

spectra were similar to those of a known compound **4**, (3*R*,5*S*)-3,5-diacetoxy-1-(4′-hydroxy-3′,5′-dimethoxyphenyl)-7-(4″-hydroxy-3″-methoxyphenyl)heptane which was also obtained from the ethanol extract of the rhizomes of *Zingiber officinale* [9]. However, the 5′-methoxy signal of **4** was absent in the ^{1}H and ^{13}C NMR spectra of **3** (Table 1), instead, the presence of a phenolic hydroxyl group was suggested by the characteristic base peak at *m/z* 153 ($[CH_2C_6H_2(OH)_2(OCH_3)]^+$) in its EI-MS spectrum and the molecular ion peak of **3** (14 mass units lower than that of **4**). Furthermore, NOESY experiment of **3** revealed the correlation between the broadened singlet at δ 6.36 (H-2′) and the methyl singlet at δ 3.84. Taking together with the NOE correlation between the doublet at δ 6.66 (H-2″) and methyl singlet at δ 3.82 indicated the methoxy groups located at C-3′ and C-3″ position, respectively. Therefore, **3** should be assigned as 3,5-diacetoxy-1-(3′-methoxy-4′,5′-dihydroxyphenyl)-7-(4″-hydroxy-3″-methoxyphenyl)heptane. The structure was further confirmed by the HMBC and ^{1}H–^{1}H COSY correlations as shown in Fig. 1.

The *in vitro* antioxidant assay displayed that compound **3** was capable of scavenging DPPH free radicals and inhibiting the formation of superoxide anion radicals [15]. The IC_{50} of **3** on DPPH scavenging is 24.4 ± 1.2 μg/mL, while the positive control, curcumin, demonstrated its IC_{50} value at 11.6 ± 1.8 μg/mL in the same experiment. Furthermore, the inhibitory efficacy of **3** on superoxide anion radicals was 48.6% at the concentration of 50 μg/mL, which was similar to that of the positive control, curcumin (61.3 ± 4.7%) at the same test concentration [16].

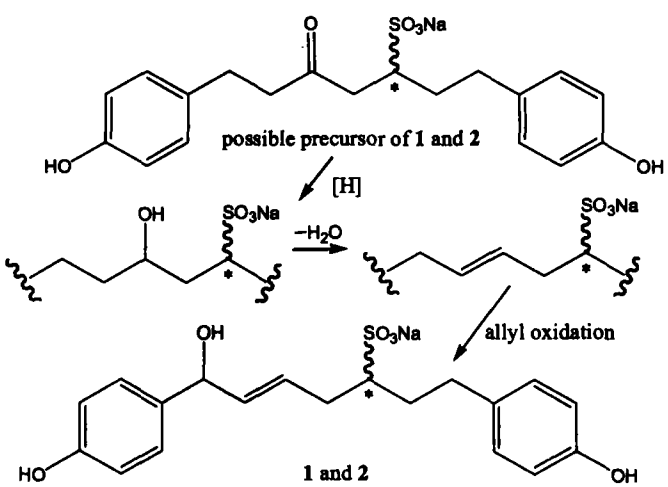

Fig. 2. Possible biopath of compounds **1** and **2**.

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References

[1] H.Q. Meng, Zhongxiyi Jiehe Zazhi 10 (1990) 638 (in Chinese).
[2] T.S. Wu, Y.C. Wu, P.L. Wu, et al. Phytochemistry 48 (1998) 889.
[3] S.I. Uehara, I. Yasuda, K. Akiyama, et al. Chem. Pharm. Bull. 35 (1987) 3298.
[4] H. Kikuzaki, M. Kobayashi, N. Nakatani, Phytochemistry 30 (1991) 3647.
[5] H. Kikuzaki, J. Usuguchi, N. Nakatani, Chem. Pharm. Bull. 38 (1991) 120.
[6] K. Endo, E. Kanno, Y. Oshima, Phytochemistry 29 (1990) 797.
[7] H. Kikuzaki, S.M. Tsai, N. Nakatani, Phytochemistry 31 (1992) 1783.
[8] J.P. Ma, X.L. Jin, L. Yang, et al. Phytochemistry 65 (2004) 1137.
[9] W.S. He, X.Y. Wei, L. Li, et al. Zhiwu Xuebao 43 (2001) 757.
[10] F. Kiuchi, S. Iwakami, M. Shibuya, et al. Chem. Pharm. Bull. 40 (1992) 387.
[11] A. Jitoe, T. Masuda, T.J. Mabry, Tetrahedron Lett. 35 (1994) 981.
[12] M.T. Huang, R.C. Smart, C.Q. Wong, et al. Cancer Res. 48 (1988) 5941.
[13] Y. Hori, T. Miura, Y. Hirai, et al. Phytochemistry 62 (2003) 613.
[14] E.M. Flamme, W.R. Roush, J. Am. Chem. Soc. 124 (2002) 13644.
[15] J. Robak, R.J. Gryglewski, Biochem. Pharmcol. 37 (1998) 837.
[16] A. Tapia, J. Rodriguez, C. Theoduloz, et al. J. Ethnopharmacol. 95 (2004) 155.