

This article was downloaded by:

On: 22 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Journal of Asian Natural Products Research

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713454007>

Three new flavanols from *Daphne giraldii*

Juan Su^a; Zhi-Jun Wu^b; Yun-Heng Shen^a; Chuan Zhang^a; Hui-Liang Li^a; Rui-Hui Liu^a; Wei-Dong Zhang^a

^a Department of Phytochemistry, School of Pharmacy, Second Military Medical University, Shanghai, China ^b Department of Research and Development, Shanghai Center of Research and Development of New Drugs, Shanghai, China

To cite this Article Su, Juan , Wu, Zhi-Jun , Shen, Yun-Heng , Zhang, Chuan , Li, Hui-Liang , Liu, Rui-Hui and Zhang, Wei-Dong(2008) 'Three new flavanols from *Daphne giraldii*', *Journal of Asian Natural Products Research*, 10: 6, 547 – 550

To link to this Article: DOI: 10.1080/10286020801966641

URL: <http://dx.doi.org/10.1080/10286020801966641>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Three new flavanols from *Daphne giraldii*

Juan Su^a, Zhi-Jun Wu^b, Yun-Heng Shen^a, Chuan Zhang^a, Hui-Liang Li^a, Rui-Hui Liu^a and Wei-Dong Zhang^{a,c,*}

^aDepartment of Phytochemistry, School of Pharmacy, Second Military Medical University, Shanghai 200433, China; ^bDepartment of Research and Development, Shanghai Center of Research and Development of New Drugs, Shanghai 201203, China; ^cSchool of Pharmacy, Shanghai Jiao Tong University, Shanghai 200030, China

(Received 6 March 2007; final version received 4 July 2007)

Three new flavanols, 5-*p*-hydroxybenzoxy-7-hydroxyl-8-ethoxycarbonyl(-)-afzelechin (**1**), 5-*p*-hydroxybenzoxy-7-(2, 3, 5-trihydroxybenzoxy)-8-ethoxycarbonyl(-)-afzelechin (**2**), and 5-*p*-hydroxybenzoxy-7-(2, 3, 5-trihydroxybenzoxy)-8-methoxycarbonyl(-)-afzelechin (**3**), were isolated from *Daphne giraldii* Nitsche and their structures were elucidated by spectroscopic methods, especially by 2D-NMR and MS analyses.

Keywords: *Daphne giraldii*; Thymelaeaceae; flavanol; afzelechin

1. Introduction

Daphne giraldii Nitsche is mainly distributed in central and western China. The stems and roots of this plant (Chinese name 'Zu Shima') have been used in Chinese folk medicines to treat ache and rheumatism, especially for toothache, waistache, rheumatoid arthritis and quadriplegia.¹ Earlier chemical research on this plant was focused on diterpenoids,^{2,3} coumarins,^{4,5} and biflavonoids.⁶ In our search for natural products with biological activities, three new flavanols were isolated from *D. giraldii*. In the present study, we report the isolation and characterization of three new flavan-3-ols.

2. Results and discussion

Compound **1** was isolated as yellow powder. The HRESIMS indicated its molecular formula C₂₅H₂₂O₉ at *m/z* 489.1159 [M + Na]⁺. The UV spectrum showed the absorption maxima at 216 and 260 nm. The

characteristic carbon resonances at δ_C 80.9, 65.2 and 27.2 together with the corresponding protons at δ_H 4.80, 3.99 and 2.47 suggested that compound **1** was a derivative of flavan-3-ol. The ¹H NMR spectrum exhibited an aromatic proton singlet at δ_H 6.28, together with three aromatic quaternary carbons at δ_C 157.3, 147.7 and 106.8 in ¹³C NMR spectrum, which implied the trisubstituted ring A. In the ¹H NMR spectrum of compound **1**, a pair of two-proton doublet signals at δ_H 7.21 (2H, d, *J* = 8.0 Hz, H-2', 6') and 6.71 (2H, d, *J* = 8.0 Hz, H-3', 5') revealed 4'-OH substitution of the ring B. A *p*-hydroxybenzoxy group was assigned by the characteristic signals at δ_C 163.7 (C-1''), 119.2 (C-2''), 132.0 (C-3'', 7''), 115.5 (C-4'', 6''), and 162.6 (C-5'') in the ¹³C NMR spectrum, as well as their corresponding proton resonances at δ_H 7.90 (2H, d, *J* = 8.0 Hz, H-3'', 7'') and 6.85 (2H, d, *J* = 9.0 Hz, H-4'', 6'') in ¹H NMR spectrum, and the *p*-hydroxybenzoxy group was attached to C-5 by the HMBC correlations

*Corresponding author. Email: wdzhangy@hotmail.com

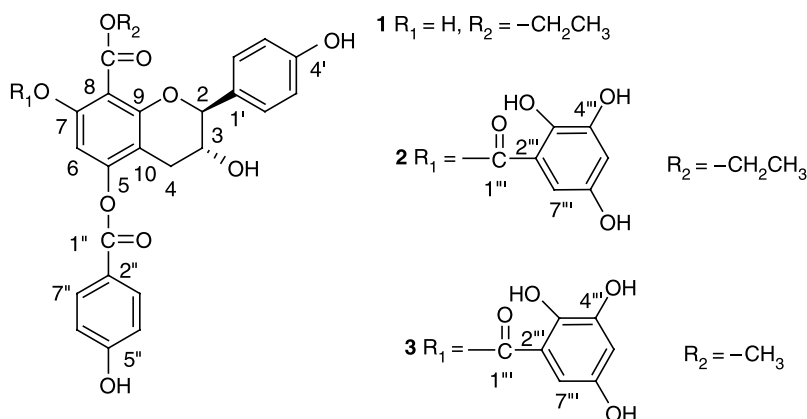


Figure 1. Structures of compounds **1–3**.

of H-6 with C-1''' and C-10. Also, an ethoxycarbonyl group substituted at C-8 was determined by the carbon signals at δ_{C} 164.0 (C=O), 60.2 (OCH₂), and 13.6 (Me) and the corresponding proton signals at δ_{H} 3.94 (2H, m, OCH₂) and 0.90 (3H, t, Me). A hydroxyl was assigned to C-7 by the HMBC correlation of H-6 with C-7. On the basis of the above evidences, compound **1** was determined as 5-*p*-hydroxybenzoyl-7-hydroxyl-8-ethoxycarbonyl-(–)-afzelechin.

Compound **2**, a yellow powder, possesses the molecular formula C₃₂H₂₆O₁₃ due to its HRESIMS at m/z 641.1269 [M + Na]⁺. The ¹H NMR spectrum showed characteristic resonances for flavanol-3-ol at δ_{H} 4.92 (1H, d, $J = 6.0$ Hz), 4.02 (1H, m) and 2.57 (2H, m), and the ¹³C NMR spectrum exhibited the corresponding carbon resonances at δ_{C} 81.0, 65.1, and 27.2. As deduced in compound **1**, a *p*-hydroxybenzoyl and an ethoxycarbonyl were determined by the interpretation of the NMR spectral data of compound **2** and were attached to C-5 and C-8, respectively. Moreover, two aromatic proton resonances at δ_{H} 6.14 (1H, d, $J = 2.0$ Hz) and 5.71 (1H, d, $J = 2.0$ Hz), as well as seven carbon resonances at δ_{C} 100.4, 101.7, 102.8, 151.6, 161.6, 161.8, and 162.0 in the ¹³C NMR spectrum, revealed the presence of a 2, 3, 5-trihydroxybenzoyl. The H-6 was observed as an HMBC correlation to C-1''', hinting the linkage of 2,

3, 5-trihydroxybenzoyl at C-7. Therefore, the structure of compound **2** was elucidated as 5-*p*-hydroxybenzoyl-7-(2,3,5-trihydroxybenzoyl)-8-ethoxycarbonyl-(–)-afzelechin.

Compound **3** was isolated as yellow powder. The HRESIMS of compound **3** showed a quasimolecular ion at m/z 627.1114 [M + Na]⁺, resulting in a molecular formula C₃₂H₂₆O₁₃. Its molecular weight was 14, less than that of compound **2**. The ¹H and ¹³C NMR spectra of compound **3** were quite similar to those of compound **2** except for one methoxy group in **3** instead of the ethoxy group in **2**. The proton resonance at δ_{H} 3.57 (MeO) showed the HMBC correlations with C=O (δ_{C} 167.69) and C-8, suggesting that methoxycarbonyl being attached to C-8. Thus, compound **3** was determined as 5-*p*-hydroxybenzoyl-7-(2,3,5-trihydroxybenzoyl)-8-methoxycarbonyl-(–)-afzelechin (Figure 1).

3. Experimental

3.1 General experimental procedures

Optical rotations were measured on a Perkin–Elmer 341 polarimeter; UV spectra were performed on a Shimadzu UV210A, λ_{max} (log ϵ) in nm; IR spectra were obtained on a Perkin–Elmer 577 spectrometer, in cm^{–1}; ¹H and ¹³C NMR, HSQC, HMBC and NOESY spectra were recorded on a Bruker

Table 1. ^1H NMR and ^{13}C NMR spectral data for compounds 1–3 in DMSO- d_6 (ppm).

Position	1		2		3	
	δ_c	δ_H (mult., J)	δ_c	δ_H (mult., J)	δ_c	δ_H (multi., J)
2	80.9	4.80 (d, 7.0)	81.0	4.92 (d, 6.0)	80.9	4.91 (d, 7.0)
3	65.2	3.99 (m)	65.1	4.02 (m)	65.0	4.05 (m)
4	27.2	2.47 (m)	27.2	2.57 (m)	27.0	2.57 (m) 2.76 (1H, m)
5	157.3		158.8		158.5	
6	101.5	6.28 (s)	102.2	6.33 (s)	101.9	6.33 (s)
7	147.7		149.5		148.9	
8	106.8		104.5		104.7	
9	153.1		154.9		154.4	
10	106.2		106.5		106.4	
1'	129.2		129.1		129.0	
2'	127.8	7.21 (d, 8.0)	127.7	7.18 (d, 9.0)	127.6	7.19 (d, 9.0)
3'	114.8	6.71 (d, 8.0)	114.8	6.71 (d, 9.0)	114.8	6.71 (d, 9.0)
4'	156.9		156.9		156.8	
5'	114.8	6.71 (d, 8.0)	114.8	6.71 (d, 9.0)	114.8	6.71 (d, 9.0)
6'	127.8	7.21 (d, 8.0)	127.7	7.18 (d, 9.0)	127.6	7.19 (d, 9.0)
1''	163.7		164.1		163.9	
2''	119.2		119.3		119.1	
3''	132.0	7.90 (d, 8.0)	132.2	7.90 (d, 8.0)	132.1	7.91 (d, 9.0)
4''	115.5	6.85 (d, 9.0)	115.5	6.85 (d, 9.0)	115.4	6.86 (d, 9.0)
5''	162.6		162.5		162.5	
6''	115.5	6.85 (d, 9.0)	115.5	6.85 (d, 9.0)	115.4	6.86 (d, 9.0)
7''	132.0	7.90 (d, 8.0)	132.2	7.91 (d, 8.0)	132.1	7.91 (d, 9.0)
1'''			161.6		161.5	
2'''			101.7		101.4	
3'''			161.8		161.9	
4'''			151.6		151.6	
5'''			102.8	5.71 (d, 2.0)	102.7	5.71 (d, 2.0)
6'''			162.0		162.1	
7'''			100.4	6.14 (d, 2.0)	100.4	6.14 (d, 2.0)
C = O	164.0		167.4		167.7	
OCH ₂	60.2	3.94 (m)	60.9	4.04 (m)		
CH ₃	13.6	0.90 (t, 7.0)	13.6	1.05 (t, 7.0)		
OCH ₃					51.9	3.57 (s)

AVANCE^{II} 600 NMR; HRESI-MS were performed on a JMS-HX 110 instrument.

3.2 Plant material

The stem barks of *Daphne giraldii* Nitsche (Thymelaeaceae) were collected in May 2005 from Shanxi Province, China and were authenticated by Professor CeMing Tan. A voucher specimen (No. 2005051509) has been deposited in the School of Pharmacy, Second Military Medical University.

3.3 Extraction and isolation

The stem barks of *Daphne giraldii* (11 kg) were extracted three times with 95% EtOH at room temperature. After the removal of EtOH, the water suspension was partitioned with petroleum ether, CHCl₃, EtOAc and *n*-BuOH. The EtOAc extract (200 g) was submitted to column chromatography over silica gel (100–200 mesh) eluting with the gradient CHCl₃–MeOH (15:1 to 5:1) to yield fractions 1–5. The fraction 2 (30 g) was separated by column chromatography over silica gel (100–200 mesh), eluting with the

gradient CHCl₃–MeOH (12:1 to 10:1), and were repeatedly purified through ODS column chromatography, eluting with MeOH–H₂O (5:5 to 6:4), to provide compounds **1** (98 mg), **2** (30 mg), and **3** (46 mg).

3.3.1 Compound 1

Yellow powder; $[\alpha]_D^{20}$ –51.4 (*c* 0.319, MeOH); UV $[\lambda]_{\max}^{\text{MeOH}}$ nm (log ϵ): 216 (3.33) and 260 (2.05); IR (KBr) cm⁻¹: 3313, 1724, 1698, 1606, 1519, 1441, 1293, 1172, 1057, 987 and 762; ¹H NMR (600 MHz, DMSO-*d*₆) and ¹³C NMR (150 MHz, DMSO-*d*₆) spectral data (see Table 1); HRESIMS: *m/z* 489.1159 [M + Na]⁺ (calcd for C₂₅H₂₂O₉Na, 489.1162).

3.3.2 Compound 2

Yellow powder; mp 177–178°C; $[\alpha]_D^{20}$ –93 (*c* 0.3075, MeOH); UV $[\lambda]_{\max}^{\text{MeOH}}$ nm (log ϵ): 214 (0.567) and 260 (0.386); IR (KBr) cm⁻¹: 3365, 1701, 1662, 1517, 1519, 1445, 1288, 1166, 1054, 849, and 762; ¹H NMR (600 MHz, DMSO-*d*₆) and ¹³C NMR (150 MHz, DMSO-*d*₆) spectral data (see Table 1); HRESIMS: *m/z* 641.1269 [M + Na]⁺ (calcd for C₃₂H₂₆O₁₃Na, 641.1271).

3.3.3 Compound 3

Yellow powder; $[\alpha]_D^{20}$ –102 (*c* 0.1095, MeOH); UV $[\lambda]_{\max}^{\text{MeOH}}$ nm (log ϵ): 214 (1.10)

and 260 (0.724); IR (KBr) cm⁻¹: 3420, 1734, 1666, 1517, 1519, 1438, 1262, 1166, 1082, 849, and 763; ¹H NMR (600 MHz, DMSO-*d*₆) and ¹³C NMR (150 MHz, DMSO-*d*₆) spectral data (see Table 1); HRESIMS: *m/z* 627.1114 [M + Na]⁺ (calcd for C₃₁H₂₄O₁₃Na, 627.1115).

Acknowledgements

This research was partially supported by the program for Changjiang Scholars and Innovative Research Team in University (PCSIRT), the National Science Foundation of China (No. 20402024), and the Scientific Foundation of Shanghai of China (Nos 03QMH1414, 04DZ19842, 04DZ19856, 04DZ19857, 05DZ19733, 06DZ19717, and 06DZ19005). The authors are grateful to Professor CeMing Tan for collecting and identifying the plant.

References

- ¹Jiangsu New Medical College, *Dictionary of Chinese Herbal Medicine*, (Shanghai People's Publishing House, Shanghai, 1977), Vol. 2, p. 1739.
- ²C.R. Wang, B.Z. An, S.M. Li, and B.N. Zhou, *Acta Chim. Sin.* 45, 993 (1987).
- ³G.X. Zhou, Y.C. Yang, and J.G. Shi, *China J. Chin. Mater. Med.* 31, 555 (2006).
- ⁴S.G. Liao, B.L. Zhang, Y. Wu, and J.M. Yue, *Helv. Chim. Acta.* 88, 2873 (2005).
- ⁵S.H. Li, L.J. Wu, Y.H. Gao, Y.H. Chen, and Y. Li, *J. Asian Nat. Prod. Res.* 7, 839 (2005).
- ⁶G.X. Zhou, Y.C. Yang, J.G. Shi, and W.Y. Hu, *Chin. Trad. Herb. Drugs.* 33, 1061 (2002).