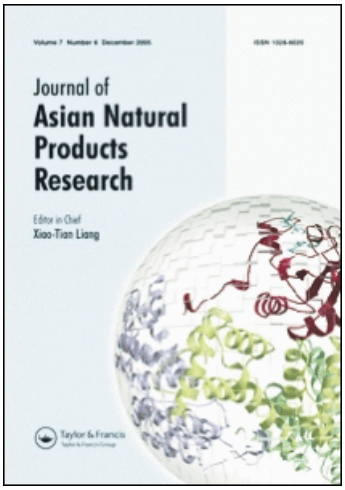

Journal of Asian Natural Products Research

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Resorcinol derivatives from *Ardisia maculosa*

Ying Zheng[a]; Feng-E Wu[b]
[a] Chengdu Library of Chinese Academy of Sciences, Chengdu, China [b] Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, China

To cite this Article Zheng, Ying and Wu, Feng-E(2007) 'Resorcinol derivatives from *Ardisia maculosa*', Journal of Asian Natural Products Research, 9: 6, 545 — 549
To link to this Article: DOI: 10.1080/10286020600882692
URL: http://dx.doi.org/10.1080/10286020600882692

Journal of Asian Natural Products Research, Vol. 9, No. 6, September 2007, 545–549

Resorcinol derivatives from *Ardisia maculosa*

YING ZHENG‡ and FENG-E WU†*

‡Chengdu Library of Chinese Academy of Sciences, Chengdu 610041, China
†Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, China

(Received 20 January 2006; revised 26 April 2006; in final form 30 April 2006)

Besides a series of known sterols and triterpenoids, a new resorcinol (**1**) and a known resorcinol (**2**) have been isolated from ethanol extract of *Ardisia maculosa* for the first time. The structures of these resorcinol derivatives were elucidated as 2-methyl-5-(*Z*-heptadec-8-enyl) resorcinol and 5-*Z*-heptadec-8-enyl) resorcinol by HRESI-MS, NMR (^{1}H, ^{13}C, HSQC, HMBC) experiments. In our *in vitro* assay, compounds **1** and **2** showed no antimicrobial activities, however, compound **2** exhibited cytotoxity activity against human cancer cell line with GI_{50} value of 2.14×10^{-4} mmol/ml.

Keywords: Antimicrobial activity; *Ardisia maculosa*; Cytotoxity; Resorcinol

1. Introduction

Ardisia maculosa Mez (Myrsinaceae) is an endemic herbaceous plant distributed in the southwest region of China, and has not been phytochemically investigated till now. This plant is used against diphtheria, gastric ulcer and enteritis [1]. The medicinal uses of *A. maculosa* prompted us to investigate polar components in its EtOH extract. Two resorcinols were isolated and their structures elucidated as 2-methyl-5- (*Z*-heptadec-8-enyl) resorcinol (**1**) and 5-(*Z*-heptadec-8-enyl) resorcinol (**2**), together with four other known compounds, α-amyrin [2], β-amyrin [2], ergosta-7, 22-dien-3β-ol [3], and ethyl caffeoate [4]. The known compounds were identified on the basis of spectral comparison with published data from the literature.

2. Results and discussion

The molecular formula of compound **1** was derived by high-resolution mass spectrometry to be $C_{24}H_{40}O_2$. The IR spectrum showed characteristic bands at 3421, 1590 and 1630 cm^{-1} attributable to a hydroxyl group, benzene ring and an olefinic bond, respectively. Compound **1** showed only one signal for aromatic protons (δ 6.25, 2H) in agreement with the assigned

*Corresponding author. Email: fewu@cib.ac.cn

Journal of Asian Natural Products Research
ISSN 1028-6020 print/ISSN 1477-2213 online © 2007 Taylor & Francis
http://www.tandf.co.uk/journals
DOI: 10.1080/10286020600882692

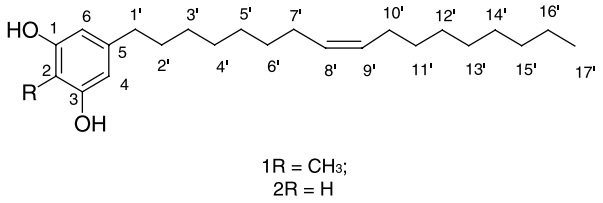

Figure 1. Structures of compounds **1** and **2**.

structure (figure 1). The position of the methyl group on the aromatic ring was verified by HMBC. The proton signal of the methyl group at δ 2.10 gave cross peaks with the carbon signal of C-2 at δ 107.3 and the carbon signals of C-1 and C-3 at δ 154.5. The ^{1}H NMR and ^{13}C NMR spectra indicated unbranched side chains (one aliphatic methyl group, no methane carbon). And the chain linked to benzene ring at 5, as confirmed by a long-range correlation of H-4 and 6/C-1′, H-1′/C-4, C-5 and C-6.

The base peaks *m/z* 138 ($C_8H_{10}O_2$), were formed by benzyl cleavage with hydrogen transfer from the γ-carbon of the side chain (figure 2) [5]. The position of the side chain double bond is indicated by ions at *m/z* 219 and 205 in the EI-MS spectra resulting from the cleavage α and β to the double bond. This is supported by the mass spectral behaviour of the nonanoic acid prepared by reaction of **1** with ozonolysis. And for the stereochemistry on the double bond, the lack of the IR absorption around 960 cm^{-1}, which was characteristic for *trans* double bond, suggested the double bond to be *cis* [6]. In order to confirm this point, the heteronuclear (^{13}C–^{1}H) chemical shift correlation spectrum (HSQC) was obtained. According to the HSQC contour plot, the signals at δ 27.2 in the long side chain were clearly assigned to the allylic carbons of C-7′ and C-10′. Comparison of the allylic (δ 27.2) and olefinic (δ 130.0, 129.8) carbon signals with a model compound 3-(8-*Z*-heptadecenyl)-1,2-dimethoxybenzene (allylic carbons *cis* carbons: δ 27.18, olefinic carbons: δ 129.82 and 129.87) and its 8-*E* isomer (allylic carbons: δ 32.58, olefinic carbons: δ 130.28 and 130.34), permitted us to determine that the stereochemistry of double bond in compound **1** is *cis* [7]. Thus, the structure of compound **1** was established as 2-methyl-5-(*Z*-heptadec-8-enyl) resorcinol.

The structure of compound **2** was identified as 5-(*Z*-heptadec-8-enyl) resorcinol by comparison its spectral data with values reported in the literature [8].

The resorcinols were evaluated for their cytotoxic activity against a panel of human cancer cell lines. Compound **2** showed cytotoxic activity against MDA-MB-231 cell line with GI_{50} value 2.14 × 10^{-4} mmol/ml. However, in our *in vitro* antimicrobial experiment, the two compounds did not show obvious antimicrobial activities.

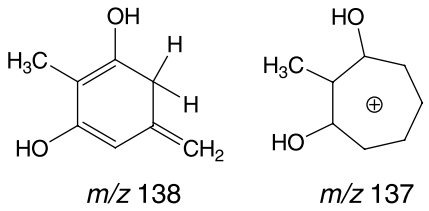

Figure 2. EI-MS fragments of compound **1**.

3. Experimental

3.1 General experimental procedures

Melting points were determined on a XRC-1 apparatus and are uncorrected. UV spectra were recorded on Perkin Elmer Lambda 35 UV/Vis spectrometer. IR spectra were measured on a Perkin Elmer Spectrum One FT-IR spectrometer. 1D- and 2D-NMR spectra were performed on a Bruker Avance 600 instrument. Chemical shift values are in ppm (δ) with TMS as internal standard. Column chromatography was carried out on silica gel (200–300 mesh, Qingdao Marine Chemical Inc., China). MS were detected on Bruker Dalonics Apex II mass spectrometer (HRESI-MS), Finnigan LCQDECA (ESI) and VG7070E (EI).

3.2 Plant material

Ardisia maculosa was collected from Xishuangbanna, Yunnan province, China, in April 2001, and identified by Professor Jing-yun Cui. A voucher specimen (No. 20010402) is deposited in the herbarium of Chengdu Institute of Biology, Chinese Academy of Sciences.

3.3 Extraction and isolation

Dried and powdered *A. maculosa* (4.5 kg) was extracted with 95% EtOH at room temperature to give an extract (356 g), which was suspended in MeOH (90%)–H_2O (10%) and extracted with petroleum ether. Then the MeOH fraction was evaporated under reduced pressure. The residue suspended in H_2O was extracted with EtOAc, and n-BuOH successively. The Petroleum ether extract (85 g) was separated by column chromatography (silica gel, petroleum ether/EtOAc 20:1, 10:1, 5:1, 1:1) to yield four fractions. Fraction 3 (23 g) was subjected to column chromatography (silica gel, petroleum ether/EtOAc10:1–5:1) to yield three fractions (Fr. 3A, Fr. 3B, Fr. 3C), then the Fraction 3A (7.2 g) was purified on MCI chromatography (MeOH/H_2O 6:1–8:1) to give compound **1** (46 mg). After preparation on column chromatography (silica gel, petroleum ether/Me_2CO 10:1) Fraction 3B (2.5 g) gave compound **2** (86 mg).

3.4 Bioassay

The *in vitro* disk diffusion assay to test antimicrobial activity was conducted as previously described [9]. Six microorganism species (*Escherichia coli, Staphylococcus aureus, Bacillus subtilis, Mycobacterium smegatis, Candida albicans, Aspergillus niger*) were evaluated for growth inhibition by compounds **1** and **2**. Each microorganism was grown on an agar medium. Plates were inoculated by spreading the spore or cell suspension evenly over the surface of the agar medium to obtain confluent growth. The zone of inhibition at each disk was measured at 24 and 48 h.

Cell lines were grown in RPMI 1640 culture medium containing 5% fetal bovine serum and 5 mM L-glutamine. The cells were harvested from exponential-phase maintenance culture and dispensed on 96-well plates in 100 µl volumes. All cell lines were cultured at 37°C in an atmosphere of 5% CO_2 in air (100% humidity). At a log phase of their growth cycle, the cells were treated in triplicate with testing samples and comparing compound

Table 1. NMR data of compound **1** in $CDCl_3$.

Position	δ_C	δ_H	*HMBC*
1 and 3	154.5		
2	107.3		
4 and 6	107.8	6.25 (2H, s)	C-1 and C-3, C-2, C-5, C-1′
5	142.0		
1′	35.5	2.45 (2H, t, 7.6)	C-2′, C-3′, C-5, C-4 and C-6
2′	31.2	1.55 (2H, m)	C-1′, C-3′, C-4′, C-5
3′–6′ and 11′–14′	27.3–29.7	1.26–1.29 (20H, brs)	C-16′, C-3′–6′, C-11′–14′, C-17′
15′	31.8		
16′	22.7		
7′ and 10′	27.2	2.01 (4H, m)	C-11′–14′, C-8′, C-9′
8′	130.0	5.35 (2H, m)	C-9′, C-10′ and C-7′, C-8′
9′	129.8		
17′-Me	14.1	0.88 (3H, t, 7.0)	C-16′, C-15′
2-Me	7.7	2.10 (3H, s)	C-1, C-2, C-3
1,3-OH		4.71 (2H, s)	C-1 and C-3, C-2, C-4 and C-6

taxol, then the cells were incubated for 48 h at 37°C in a humidified atmosphere of 5% CO_2. The growth inhibitory effects of **1**, **2** and taxol on the corresponding cells were evaluated with SRB assay [10].

3.4.1 Ardisin E (1). White wax ($CHCl_3$); mp 38–39°C; UV (MeOH) λ_{max} 272, 205 nm; IR (KBr) ν_{max} 3421, 3005, 2925, 2854, 1630, 1590, 1521, 1456, 1427, 1328, 1284, 1072, 720, 659 cm^{-1}; ^1H NMR and ^{13}C NMR data, see table 1; EI-MS *m/z* 360 (13) [M] + , 264 (2), 219 (2), 205(2), 191(1), 180(3), 178 (1), 163 (2), 153(2), 151 (12), 150 (3), 107 (11), 139 (10), 138 (100), 125 (2), 123 (3), 69 (6), 55 (10), 41(11); ESI-MS *m/z* 359 $[M - H]^-$, 394 $[M + Cl]^-$; HRESI-MS *m/z* 359.2940 $[M - H]^-$ (calcd for $C_{24}H_{39}O_2$, 359.2945).

3.4.2 5-(*Z*-heptadec-8-enyl) resorcinol (2). White needles ($CHCl_3$); mp 37–38°C; IR (KBr) ν_{max} 3414, 3005, 2925, 2854, 1626, 1599, 1465, 1155, 998, 695; ^1H NMR($CDCl_3$, 600 MHz) δ 6.25 (2H, d, $J = 2.1$ Hz, H-4 and H-6), 6.18 (1H, t, $J = 2.1$ Hz, H-2), 5.36 (2H, m, H-8′ and H-9′), 4.69 (2H, s, OH), 2.48 (2H, t, $J = 7.4$, H-1′), 2.02 (4H, m, H-7′ and 10′), 1.57 (2H, m, H-2′), 1.26–1.29 (20H, brs, 3′–6′, 11′–14′, 15′ and 16′), 0.89 (3H, t, $J = 0.70$ Hz, H-17′); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 156.6 (C-1 and C-3), 146.1 (C-5), 130.0 and 129.9 (C-8′ and C-9′), 108.0 (C-4 and C-6), 100.1 (C-2), 35.8 (C-1′), 31.9 (C-15′), 31.0 (C-2′), 29.8, 29.6, 29.4, 29.3, 29.2, 27.3 (C-3′—C-6′ and C-11′—C-14′), 27.2 (C-7′ and C-10′) 22.6 (C-16′), 14.1 (C-17′); EI-MS *m/z* [M] 346 (12), 205 (2), 191 (2), 166 (3), 163 (4), 137 (14), 136 (3), 125 (11), 124 (100), 123 (29), 69 (7), 123 (3), 67 (5), 57 (7), 55 (17), 43(14), 29(9); ESI-MS *m/z* 345 $[M - H]^-$.

References

[1] Z.Y. Wu, T.Y. Zhou, P.G. Xiao. Xinghua Bencao Gangyao (in Chinese). *List of Chinese Medicine Herb*, Vol. **1**, p. 385, Shanghai Scientific and Technological Press, Shanghai (1988).
[2] K.Y. Sim, M.M.-J Toubiana, B.C. Das. *Phytochemistry*, **10**, 2803 (1971).
[3] R.J. Abraham, J.R. Monasterios. *J. Chem. Soc. Perkin 2*, 662 (1974).
[4] J. Orijala, C.A.J. Erdelmeier, A.D. Wright, R. Topul, S. Otto. *Phytochemistry*, **34**, 813 (1993).
[5] N.H. Anh, H. Ripperger, J. Schmidt, A. Porzel, T.V. Sung, G. Adam. *Planta Med.*, **62**, 479 (1996).

[6] I. Kubo, T. Kamikawa, I. Miura. *Tetrahedron Lett.*, **24**, 3825 (1983).
[7] M. Sumino, T. Sekine, N. Ruangrungi, K. Igarashi, F. Igarashi. *Chem. Pharm. Bull.*, **50**, 1484 (2002).
[8] K. Seki, K. Haga, R. Kaneko. *Phytochemistry*, **38**, 965 (1995).
[9] Y. Zheng, Y. Deng, F.E. Wu. *J. Nat. Prod.*, **67**, 1617 (2004).
[10] P. Skehan, R. Storeng, D. Scudiero, A. Monks, J. McMahon, D. Vistica, J.T. Warren, H. Bokesch, S. Kenney, M.R. Boyd. *J. Natl. Cancer Inst.*, **82**, 1107 (1990).