

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>

The sesquiterpenes from the roots of *Cacalia roborowskii*

Zhan-Xin Zhang^a; Dong-Qing Fei^a

^a School of Pharmacy, Lanzhou University, Lanzhou, China

To cite this Article Zhang, Zhan-Xin and Fei, Dong-Qing(2009) 'The sesquiterpenes from the roots of *Cacalia roborowskii*', Journal of Asian Natural Products Research, 11: 11, 958 – 961

To link to this Article: DOI: 10.1080/10286020903264093

URL: <http://dx.doi.org/10.1080/10286020903264093>

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.

The sesquiterpenes from the roots of *Cacalia roborowskii*

Zhan-Xin Zhang and Dong-Qing Fei*

School of Pharmacy, Lanzhou University, Lanzhou 730000, China

(Received 2 June 2009; final version received 17 August 2009)

A new sesquiterpene cacaroborin (**1**) was isolated from the roots of *Cacalia roborowskii*, together with three known ones, cinalbicol (**2**), isopetasin (**3**), and 3 α -angeloyloxylactone (**4**). The structure of compound **1** was elucidated as 1 β ,10 α -dihydroxy-8 α -methoxyeremophil-7(11)-en-8 β ,12-olide on the basis of spectral evidence (1D, 2D NMR, IR, EI-MS, and HR-ESI-MS) and X-ray diffraction analysis.

Keywords: *Cacalia roborowskii*; Compositae; sesquiterpene; X-ray

1. Introduction

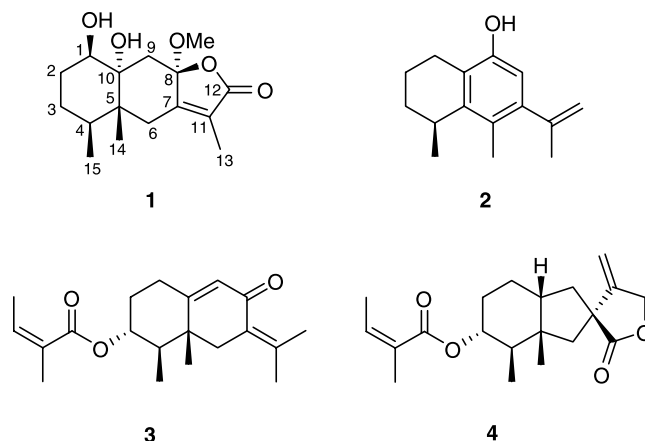
The genus *Cacalia* (Compositae) consists of about 60 species grown in northwest and southwest of China [1], and one half of them have been used as Chinese traditional folk herbs to treat many kinds of diseases [2]. Several species of the genus *Cacalia* have been investigated due to their anti-oxidant, antiradical, and anti-histamine activities [3]. *Cacalia roborowskii* (Maxim) Ling is a perennial herb, and some eremophilane sesquiterpenes have been isolated previously [4–6]. Continuing our search for bioactive constituents from the Compositae plants, we have investigated the constituents of *C. roborowskii*, which led to the isolation and structural elucidation of one new and three known sesquiterpenes (Figure 1).

2. Results and discussion

Compound **1**, isolated as colorless needles, possessed the molecular formula C₁₆H₂₄O₅ on the basis of the positive HR-ESI-MS at m/z 297.1694 [M+H]⁺. Its IR spectrum showed absorption bands for

γ -lactone (1761 cm⁻¹) and hydroxyl (3536 cm⁻¹) groups. The EI-MS indicated the fragment ions formed due to the loss of H₂O at m/z 278 [M–H₂O]⁺ and 260 [M–2H₂O]⁺, which confirmed the presence of the hydroxyl groups. Meanwhile, in the EI-MS, the fragment ion formed due to the loss of CH₃OH at m/z 264 [M–CH₃OH]⁺ displayed the presence of an OMe group, which was in accordance with the NMR spectral data [δ_{H} 3.16 (3H, s) and δ_{C} 50.1 (q)] (Table 1). Apart from the OMe group, in the ¹H NMR spectrum, the presence of three methyls at δ_{H} 1.89 (3H, s, CH₃-13), 0.87 (3H, s, CH₃-14), and 0.86 (3H, d, J = 6.8 Hz, CH₃-15), an oxygenated methine at δ_{H} 3.66 (1H, brs, H-1), and a hydroxy group at δ_{H} 4.05 (1H, s) was observed. The ¹³C NMR spectrum (Table 1) indicated the presence of 15 carbon signals including three methyls, four methylenes, two methines (one oxygenated), and six quaternary carbons (one ester carbonyl, one acetal, one oxygenated, and two olefinic carbons). These information suggested that compound **1** was a sesquiterpene with an OMe group.

*Corresponding author. Email: feidq@lzu.edu.cn

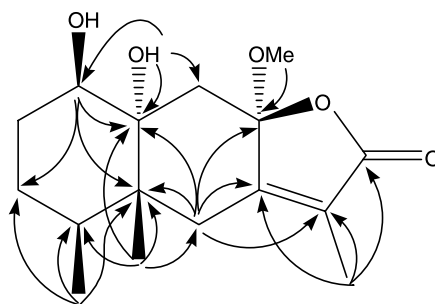
Figure 1. Structures of compounds **1**–**4**.

In the HMBC spectrum (Figure 2), the cross-peaks for three characteristic methyls with correlative carbons [CH₃-13 (δ_{H} 1.89, s) with C-7 (δ_{C} 156.8, s), C-11 (δ_{C} 126.5, s), C-12 (δ_{C} 171.2, s); CH₃-14 (δ_{H} 0.87, s) with C-4 (δ_{C} 34.5, d), C-5 (δ_{C} 44.9, s), C-6 (δ_{C} 33.8, t), C-10 (δ_{C} 73.8, s);

and CH₃-15 (δ_{H} 0.86, d, J = 6.8 Hz) with C-3 (δ_{C} 25.4, t), C-4 (δ_{C} 34.5, d), C-5 (δ_{C} 44.9, s)] indicated that compound **1** was an eremophilane-type sesquiterpene lactone, which is in accordance with the structure segment eremophil-7(11)-en-8,12-olide [7]. The oxygenated methine signal at δ_{H} 3.66 (1H, brs) showed HMBC correlations with C-3 (δ_{C} 25.4, t), C-5 (δ_{C} 44.9, s), and C-10 (δ_{C} 73.8, s), suggesting the presence of a hydroxyl at C-1. The singlet at δ_{H} 4.05 (1H, s) showed HMBC correlations with C-1 (δ_{C} 75.1, d), C-9 (δ_{C} 41.8, t), and C-10 (δ_{C} 73.8, s), indicating another hydroxyl at C-10. The OMe signal at δ_{H} 3.16 (3H, s) correlated with C-8 (δ_{C} 106.1, s), so the OMe group should be at

Table 1. ¹H (400 MHz) and ¹³C (100 MHz) NMR spectral data of compound **1** [in CDCl₃, J in Hz, δ in ppm, TMS as the internal standard].

No.	δ_{H}	δ_{C} (DEPT)
1	3.66 (1H, brs)	75.1 (d)
2a	2.19 (1H, m)	29.0 (t)
2b	1.54 (1H, m)	
3a	1.54 (1H, m)	25.4 (t)
3b	1.33 (1H, m)	
4	2.16 (1H, m)	34.5 (d)
5		44.9 (s)
6a	2.42 (1H, d, J = 12.8)	33.8 (t)
6b	2.28 (1H, d, J = 12.8)	
7		156.8 (s)
8		106.1 (s)
9a	2.46 (1H, d, J = 14.4)	41.8 (t)
9b	2.11 (1H, d, J = 14.4)	
10		73.8 (s)
11		126.5 (s)
12		171.2 (s)
13	1.89 (3H, s)	8.3 (q)
14	0.87 (3H, s)	14.5 (q)
15	0.86 (3H, d, J = 6.8)	15.3 (q)
8-OMe	3.16 (3H, s)	50.1 (q)
10-OH	4.05 (1H, s)	

Figure 2. Selected correlations in the HMBC spectrum of compound **1**.

C-8. Thus, the planar structure of compound **1** was determined as 1,10-dihydroxy-8-methoxyeremophil-7(11)-en-8,12-olide.

The relative stereochemistry of compound **1** was unambiguously determined by single-crystal X-ray diffraction analysis, as shown in Figure 3. Thus, compound **1** was assigned as 1 β ,10 α -dihydroxy-8 α -methoxyeremophil-7(11)-en-8 β ,12-olide, named as cacaroborin.

Three known compounds **2–4** were isolated by repeated column chromatography of the methanol extract of the roots of *C. roborowskii* and deduced by spectral data as cinalbicol (**2**) [8], isopetasin (**3**) [9], and 3 α -angeloyloxy lactone (**4**) [10].

3. Experimental

3.1 General experimental procedures

Melting points were determined on an X-4 digital display micromelting point apparatus, and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. IR spectra were taken on a Nicolet NEXUS 670 FT-IR spectrometer. NMR spectra were recorded on a Varian Mercury plus-400 NMR spectrometer with TMS as the internal standard. HR-ESI-MS data were recorded on a Bruker Daltonics

APEX II 47e spectrometer. EI-MS data were recorded on an HP5988A GC/MS spectrometer. Silica gel (200–300 mesh) used for column chromatography and silica gel GF₂₅₄ (10–40 μ M) used for TLC were supplied by the Qingdao Marine Chemical Factory, Qingdao, China. Spots were detected on TLC under UV light or by heating after spraying with 5% H₂SO₄ in C₂H₅OH (v/v).

3.2 Plant material

The roots of *C. roborowskii* were collected in Zhang County, Gansu Province, China, in August 2005, and identified by Prof. Guo-Liang Zhang, School of Life Sciences, Lanzhou University. A voucher specimen (No. Co-200508) has been deposited at the College of Chemistry and Chemical Engineering, Lanzhou University.

3.3 Extraction and isolation

The powdered air-dried roots (560 g) of *C. roborowskii* were extracted with hot methanol twice to give a residue (76 g) after evaporation. The residue was separated on column chromatography over 1000 g silica gel using petroleum ether (60–90°C) mixed with gradually increasing

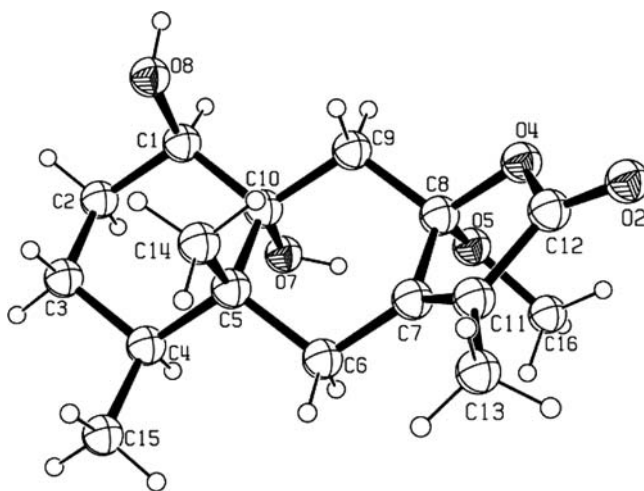


Figure 3. The X-ray crystal structure of compound **1**.

amounts of acetone (30:1, 20:1, 10:1, 5:1, 2:1, and 0:1) as the eluent. Six crude fractions (A–F) were obtained by TLC analysis. Fraction B (petroleum ether–acetone 20:1, 5.6 g) was subjected to silica gel column chromatography eluting with CHCl_3 –acetone (50:1 and 40:1) to give compounds **4** (36 mg) and **3** (40 mg). Fraction D (petroleum ether–acetone 5:1, 6.8 g) was subjected to silica gel column chromatography eluting with CHCl_3 –methanol (30:1, 20:1, and 10:1) to give four subfractions (D-1 to D-4). Fraction D-1 (1.2 g) was separated repeatedly with petroleum ether–EtOAc to afford compound **2** (5 mg). Fraction D-2 (0.8 g) was subjected to silica gel column chromatography with petroleum ether–acetone (6:1 and 3:1) to give compound **1** (7 mg).

3.3.1 $1\beta,10\alpha$ -Dihydroxy- 8α -methoxyerye mophil-7(11)-en- $8\beta,12$ -olide (**1**)

Colorless needles, mp 157–160°C; $[\alpha]_{\text{D}}^{26}$ –118 ($c = 0.7$, CHCl_3); IR (KBr) ν_{max} (cm^{-1}): 3536, 2940, 1761, 1695, 1452, 1378, 1311, 1168, 939; ^1H NMR (400 MHz, CDCl_3) and ^{13}C NMR (100 MHz, CDCl_3) spectral data are listed in Table 1; EI-MS m/z (%): 296 $[\text{M}]^+(1)$, 278 $[\text{M} - \text{H}_2\text{O}]^+(1)$, 264 $[\text{M} - \text{CH}_3\text{OH}]^+(22)$, 260 $[\text{M} - 2\text{H}_2\text{O}]^+(1)$, 246 $[\text{M} - \text{H}_2\text{O} - \text{CH}_3\text{OH}]^+(3)$, 141 (16), 124 (100), 43 (90); HR-ESI-MS m/z : 297.1694 $[\text{M} + \text{H}]^+$ (calcd for $\text{C}_{16}\text{H}_{25}\text{O}_5$, 297.1697).

3.4 X-ray crystallography of compound **1**

Crystal data: $\text{C}_{16}\text{H}_{24}\text{O}_5$ (fw = 296.35), crystal dimensions $0.26 \times 0.20 \times 0.18$ mm, monoclinic, space group $P2_1$, $a = 14.338$ (2) Å, $b = 6.9212$ (12) Å, $c = 15.891$ (3) Å, $\beta = 98.294$ (3)°, $V = 1560.5$ (4) Å³, $Z = 4$, $D_{\text{C}} = 1.261$ mg/m³, $F(000) = 640$, $\text{MoK}\alpha = 0.71073$ Å. The reflection data

were collected on a Bruker Smart Apex CCD diffractometer, using graphite-monochromated $\text{MoK}\alpha$ radiation. A total of 5677 reflections were collected in the range $2.07^\circ \leq \theta \leq 25.50^\circ$, of which 3838 unique reflections with $I > 2\sigma(I)$ were collected for the analysis. The structure was solved by direct methods using Bruker SHELXL-97 and refined by full-matrix least squares on F^2 using Bruker SHELXL-97. The final R and R_{w} factors were 0.0628 and 0.1522, respectively. Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre under the reference number CCDC 734461.

Acknowledgements

We thank Prof. Zhong-Jian Jia of the College of Chemistry and Chemical Engineering, Lanzhou University for supporting our work.

References

- [1] Institute of Botany, *Iconographia Cormopfytorum Sinicorum* (Science Press, Beijing, 1973).
- [2] The China Medicinal Materials Co., *Zhongguo Zhongyao Ziyuan Zhiyao* (Science Press, Beijing, 1994).
- [3] N.P. Krasovskaya, N.I. Kulesh, and V.A. Denisnko, *Chem. Nat. Comp.* **25**, 545 (1989).
- [4] S.M. Zhang, G.L. Zhao, R. Li, and G.Q. Lin, *Chin. Chem. Lett.* **9**, 61 (1998).
- [5] S.M. Zhang, G.L. Zhao, and G.Q. Lin, *Chin. Chem. Lett.* **9**, 65 (1998).
- [6] S.M. Zhang, G.L. Zhao, R. Li, and G.Q. Lin, *Phytochemistry* **48**, 519 (1998).
- [7] D.Q. Fei, S.G. Li, C.M. Liu, G. Wu, and K. Gao, *J. Nat. Prod.* **70**, 241 (2007).
- [8] F. Bohlmann and W.R. Abraham, *Phytochemistry* **17**, 1629 (1978).
- [9] Y. Zhao, H.R. Peng, and Z.J. Jia, *J. Nat. Prod.* **57**, 1626 (1994).
- [10] J. Jakupovic, M. Grenz, and F. Bohlmann, *Planta Med.* **55**, 571 (1989).