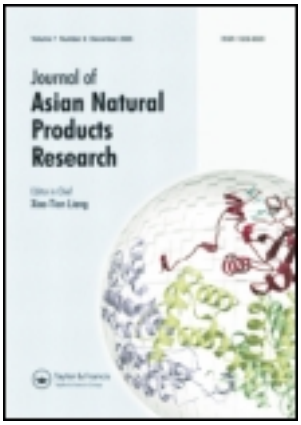

Journal of Asian Natural Products Research

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/ganp20

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Feng Wang [a b], Zhan-Lin Li [b], Hong-Hua Cui [a], Hui-Ming Hua [b], Yong-Kui Jing [c] & Sheng-Wang Liang [a]

[a] College of Traditional Chinese Materia Medica, Guangdong Pharmaceutical University, Guangzhou, 510006, China

[b] Department of Natural Products Chemistry, Shenyang Pharmaceutical University, Shenyang, 110016, China

[c] Mount Sinai School of Medicine, New York, NY, 10029, USA

Available online: 15 Mar 2011

To cite this article: Feng Wang, Zhan-Lin Li, Hong-Hua Cui, Hui-Ming Hua, Yong-Kui Jing & Sheng-Wang Liang (2011): Two new triterpenoids from the resin of *Boswellia carterii*, Journal of Asian Natural Products Research, 13:03, 193-197

To link to this article: http://dx.doi.org/10.1080/10286020.2010.548808

Journal of Asian Natural Products Research
Vol. 13, No. 3, March 2011, 193–197

Two new triterpenoids from the resin of *Boswellia carterii*

Feng Wang[ab]*, Zhan-Lin Li[b], Hong-Hua Cui[a], Hui-Ming Hua[b], Yong-Kui Jing[c] and Sheng-Wang Liang[a]

[a]*College of Traditional Chinese Materia Medica, Guangdong Pharmaceutical University, Guangzhou 510006, China;* [b]*Department of Natural Products Chemistry, Shenyang Pharmaceutical University, Shenyang 110016, China;* [c]*Mount Sinai School of Medicine, New York, NY 10029, USA*

(*Received 5 November 2010; final version received 14 December 2010*)

Two new triterpenoids, 3-oxotirucalla-7,9(11),24-trien-21-oic acid (**1**) and 18Hα,3β,20β-ursanediol (**2**), along with 15 known triterpenes, α-amyrin, α-boswellic acid, β-boswellic acid, acetyl α-boswellic acid, acetyl β-boswellic acid, 9,11-dehydro-β-boswellic acid, 9,11-dehydro-α-boswellic acid, acetyl 11α-methoxy-β-boswellic acid, 11-keto-β-boswellic acid, acetyl 11-keto-β-boswellic acid, acetyl α-elemolic acid, 3β-hydroxytirucalla-8,24-dien-21-oic acid, elemonic acid, 3α-hydroxytirucalla-7,24-dien-21-oic acid, and 3α-hydroxytirucall-24-en-21-oic acid, were isolated from the resin of *Boswellia carterii* Birdw.

Keywords: triterpenoids; *Boswellia carterii* Birdw (Burseraceae); 3-oxotirucalla-7,9(11),24-trien-21-oic acid; 18Hα,3β,20β-ursanediol

1. Introduction

Boswellia carterii Birdw is an arbor distributed in Somalia and Ethiopia. Its resin was used to treat coronary heart disease, angina pectoris, and ulcer in China [1]. Previous research for the resin showed the presence of a number of triterpenes including oleanane-, ursane-, and tirucallane-type [2,3]. Boswellic acid-type triterpenes have been reported to inhibit the activity of 5-lipoxygenase and topoisomerases [4–6] and to induce apoptosis in several types of tumor cells including colon, prostate, and malignant glioma [7–10]. As our continuing work on searching bioactive triterpenes from natural medicines, chemical investigation of the resin of *B. carterii* led to the isolation of two new triterpenes (**1** and **2**) and 15 known triterpenes (Figure 1). The known triterpenes were identified as α-amyrin [11], α-boswellic acid [2], β-boswellic acid [2], acetyl α-boswellic acid [2], acetyl β-boswellic acid [2], 9,11-dehydro-β-boswellic acid [3], 9,11-dehydro-α-boswellic acid, acetyl 11α-methoxy-β-boswellic acid [12], 11-keto-β-boswellic acid [13], acetyl 11-keto-β-boswellic acid [2], acetyl α-elemolic acid [13], 3β-hydroxy-tirucalla-8,24-dien-21-oic acid [13], elemonic acid [13], 3α-hydroxy-tirucalla-7,24-dien-21-oic acid [3], and 3α-hydroxytirucall-24-en-21-oic acid [3] by comparison of their spectroscopic data with those of published values. Details of the isolation, structure elucidation of compounds **1** and **2**, and their antileukemia activities are presented here.

2. Results and discussion

Compound **1** was obtained as colorless needles, and its molecular formula was

*Corresponding author. Email: wfeng1230@163.com

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020.2010.548808
http://www.informaworld.com

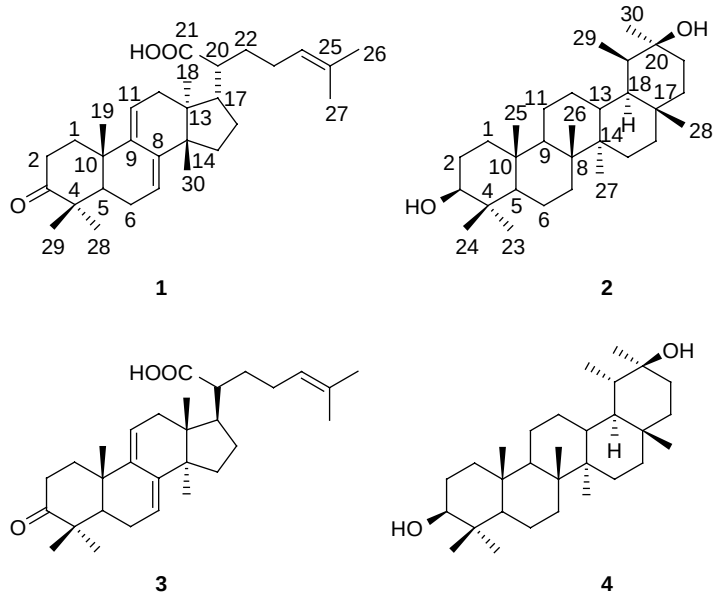

Figure 1. The structures of compounds **1**–**4**.

determined as $C_{30}H_{44}O_3$ on the basis of its HREIMS spectrum (*m/z* 451.32041 $[M - H]^+$). The ^1H NMR spectrum showed seven methyl singlets and the ^{13}C NMR spectrum revealed 30 carbon signals, which were sorted by DEPT experiment as seven methyls, eight methylenes, six methines, and nine quaternary carbons, of which six sp^2 carbons and two carbonyl groups were suggested based on the chemical shifts (see Table 1). Due to tirucallane-type as only a tetracyclic triterpenoid isolated from the resin in previous studies, compound **1** was presumed as a tirucallane-type triterpene in view of biogenetic source. The ^{13}C NMR spectrum indicated the presence of two carbonyl groups, resonating at δ 214.9 (C-3) and 178.5 (C-21), two conjugated double bonds at δ 119.0 (C-7), 141.6 (C-8), 144.2 (C-9), and 116.6 (C-11), and a single double bond at δ 124.8 (C-24) and 131.8 (C-25). The gross structure of compound **1** was deduced from its HMBC spectrum. The conjugated double bond positions at C-7(8) and C-9(11) were determined by the long-range correlations between the methyl group at δ 1.07 and carbons at δ 50.4 (C-5) and 144.2 (C-9) and between the methyl group at δ 0.96 and carbons at δ 141.6 (C-8), 49.7 (C-14), 31.2 (C-15), and 44.5 (C-13). The HMBC correlations of H-26 (δ 1.64) and H-27 (δ 1.60) with C-24 (δ 124.8) and C-25 (δ 131.8) indicated a double bond located at C-24. The tirucallane-type triterpene had the same tetracyclic skeleton as a lanostane-type triterpene, but the orientation of the methyl group at C-13 and the side chain at C-17 was different from that in lanostane-type triterpene, i.e. the tirucallane-type triterpene had the α-orientation for both the methyl group and the side chain, while the lanostane-type had β-orientation for both of them. The ^{13}C NMR spectral data of compound **1** are extremely in analog with (20ξ)-3-oxolanosta-7,9(11),24-trien-21-oic acid (dehydrotrametenonic acid, **3**) [14], which easily lead to mistake compound **1** as the above lanostane-type one (**3**). The relative stereochemistry was determined based on the NOESY experiment. The NOESY correlations of H-30/H-19, H-19/H-28, H-

Table 1. ^{1}H NMR and ^{13}C NMR spectral data of compounds **1** and **2** in $CDCl_3$.

	1			**2**	
	δ_H (J, Hz) (600 MHz)	δ_C (75 MHz)	HMBC (H → C)	δ_H (J, Hz) (600 MHz)	δ_C (75 MHz)
1	1.91 m, 1.64 m	37.0	C-19	1.68 m	38.6
2	2.76 td (12.5, 5.2), 2.29 m	35.0	C-1, 3	1.64 m, 1.57 m	28.5
3		214.9		3.24 dd (10.9, 5.2)	79.0
4		47.8			38.8
5	1.67 dd (11.4, 4.8)	50.4	C-4, 10, 19, 29	0.69 m	55.0
6	2.10 m, 1.42 m	27.3	C-5, 7, 8, 10	1.51 m, 1.37 m	18.3
7	5.40 br s	119.0	C-14	1.40 m	34.3
8		141.6			41.2
9		144.2		1.20 m	49.4
10		36.4			36.9
11	5.14 br s	116.6	C-10	1.46 m, 1.52 m	21.3
12	2.42 m	36.4	C-9, 11, 13, 14	1.66 m, 1.58 m	27.4
13		44.5		1.82 td (12.0, 4.3)	38.8
14		49.7			43.0
15	1.74 m, 1.40 m	31.2	C-8, 13, 14, 30	1.33 m, 1.21 m	26.5
16	2.10 m, 2.06 m	24.4		1.34 m, 1.17 m	38.3
17	2.48 q (10.8)	48.2	C-20		35.6
18	1.00 s	16.6	C-12, 13, 14	1.05 m	47.9
19	1.07 s	19.9	C-5, 9, 10	1.53 m	41.9
20	2.62 td (11.1, 3.2)	48.8			75.0
21		178.5		1.51 m	37.8
22	1.91 m, 1.75 m	33.2		1.27 m, 1.21 m	40.2
23	2.36 m, 2.26 m	26.7	C-24, 25	0.97 s	28.0
24	5.31 t (7.0)	124.8	C-26, 27	0.77 s	15.4
25		131.8		0.84 s	16.1
26	1.64 s	25.8	C-24, 25, 27	1.04 s	16.0
27	1.60 s	17.7	C-24, 25, 26	0.94 s	14.6
28	0.96 s	24.8	C-8, 13, 14, 15	0.90 s	18.3
29	1.07 s	22.1	C-3, 4, 5, 30	1.06 d (6.0)	17.4
30	1.03 s	23.4	C-3, 4, 29	1.09 s	21.4

28/H-17, and H-18/H-20 indicated the H-17 on the β-face and the methyl group at C-13 on the α-face of the molecule, which confirmed the side chain at C-17 in α-orientation and the tirucallane-type skeleton of compound **1** (Figure 2). So, compound **1** was characterized as 3-oxotirucalla-7,9(11),24-trien-21-oic acid.

Compound **2** was obtained as colorless needles, and its molecular formula was determined as $C_{30}H_{52}O_2$ on the basis of its HREIMS spectrum at m/z 444.3961 $[M]^+$.

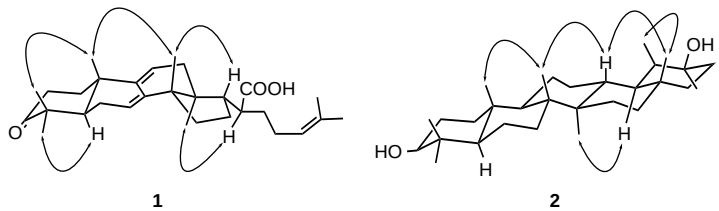

Figure 2. Key NOESY correlations of compounds **1** and **2**.

The ^{1}H NMR spectrum exhibited eight methyl signals at δ 1.09 (3H, s, H-29), 1.06 (3H, d, $J = 6.0$ Hz, H-30), 1.04 (3H, s, H-26), 0.97 (3H, s, H-23), 0.94 (3H, s, H-27), 0.90 (3H, s, H-28), 0.84 (3H, s, H-25), 0.77 (3H, s, H-24), and an oxygenated methine signal at δ 3.24 (H-3, dd, $J = 10.9$, 5.2 Hz). The ^{13}C NMR spectrum showed 30 carbon atoms, which were sorted by DEPT experiment as eight methyls, ten methylenes, six methines, and six quaternary carbons. An oxygenated quaternary carbon resonating at δ 75.0 and an oxymethine carbon at δ 79.0 were exhibited, and no olefinic carbon was observed in the ^{13}C NMR spectrum. Based on the above data, compound **2** was deduced as an ursane-type triterpene. The ^{1}H NMR and ^{13}C NMR spectra are similar to the corresponding data of 3β,20*S*-dihydroxytaraxastane (**4**) [15] except the chemical shift values at C-19, 29, 30, and suggested that the C-19 in compound **2** may be of R-configuration, which was confirmed by the analysis of coupling constants and the NOESY experiment. H-13(β) signal resonating at δ 1.82 (1H, td, $J = 12.0$, 4.3 Hz) together with the NOESY correlation between H-18 and H-27 revealed the axial α-orientation of H-18. The NOESY correlations for H-25 with H-26, H-26 with H-13, H-13 with H-28, and H-28 with H-29 indicated that they are on the β-face. So, compound **2** was assigned as 18Hα,3β,20β-ursanediol. The ^{1}H and ^{13}C NMR spectral data were assigned by the ^{1}H–^{1}H COSY, HSQC, and HMBC spectra (Table 1).

3. Experimental

3.1 General experimental procedures

Melting points (uncorrected) were measured on a Yanaco MP-S3 micro-melting point apparatus. Optical rotations were measured with a Perkin-Elmer 241MC polarimeter. IR was conducted on a Perkin IFS-55 spectrometer. NMR spectra were recorded on a Bruker ARX 300 NMR spectrometer and a Bruker ARX 600 NMR spectrometer. The chemical shifts were quoted relative to TMS, and the coupling constants were in Hz. DEPT, HMBC, HSQC, COSY, and NOESY were measured on a Bruker ARX 600 NMR spectrometer. EIMS (70 eV) was conducted on a Shimadzu GCMS-QP5050A spectrometer. HREIMS were recorded on an Autospec-UltimaETOF instrument. The chromatographic silica gel (200–300 mesh) was produced by Qingdao Ocean Chemical Factory (Qingdao, China), and Sephadex LH-20 was bought from GE Healthcare (London, England).

3.2 Plant material

The resin of *B. carterii* was bought from Liaoning Medicinal Material Corporation, Shenyang, China and identified by Prof. Qishi Sun of Shenyang Pharmaceutical University. A voucher specimen (20070918) has been deposited in the Department of Natural Products Chemistry, Shenyang Pharmaceutical University, Shenyang, China.

3.3 Extraction and isolation

The resin of *B. carterii* (1000 g) was extracted with $CHCl_3$. After removing the solvent, the extract (678 g) was chromatographed on a column of silica gel with gradient elution using petroleum ether with increasing proportions of EtOAc to give four fractions (Parts 1–4). Part 3 (150 g) was separated by column chromatography on silica gel, eluted with EtOAc/petroleum ether (8:2–7:3) to produce 59 fractions. Subfractions 8–19 were combined and separated by silica gel H column chromatography and eluted with acetone/petroleum ether (100:10, 100-15) to give compound **2** (4 mg). Part 4 (87 g) was separated by column chromatography on silica gel, eluted with EtOAc/petroleum ether (7:1–2:1) to produce 113 fractions. Subfractions 1–35 were combined and

chromatographed on a column of Sephadex LH-20 eluted with MeOH followed by open ODS column to give compound **1** (6 mg).

3.3.1 3-Oxotirucalla-7,9(11),24-trien-21-oic acid (*1*)

Colorless needles (acetone), mp 267–269°C, $[\alpha]_D^{20}$ −40.0 ($c = 0.4$, $CHCl_3$). IR (KBr) ν_{max} 3440 (OH), 1703 (COOH), 1695 (CO), 1652 (C=C) cm^{-1}. ^1H and ^{13}C NMR spectral data (see Table 1). HREIMS: *m/z* 451.3204 $[M - H]^+$ (calcd for $C_{30}H_{43}O_3$, 451.3212).

3.3.2 18Hα,3β,20β-Ursanediol (*2*)

Colorless needles (acetone), mp 293–295°C, $[\alpha]_D^{20}$ −33.0 ($c = 0.3$, $CHCl_3$). IR (KBr) ν_{max} 3558 (OH), 2921 and 2855 (CH), 1463 (CH) cm^{-1}. ^1H and ^{13}C NMR spectral data (see Table 1). EIMS: *m/z* (rel. int) 444 $[M]^+$ (2.7), 374 (52), 207 (35), 189 (51). HREIMS: *m/z* 444.3961 $[M]^+$ (calcd for $C_{30}H_{52}O_2$, 444.3967).

Acknowledgements

The authors wish to thank Mrs Wen Li and Mr Yi Sha (Shenyang Pharmaceutical University, Shenyang 110016, China) for the NMR experiment.

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