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Feroniellides A and B, apotirucallane triterpenes with novel cyclic acetals from *Feroniella lucida*

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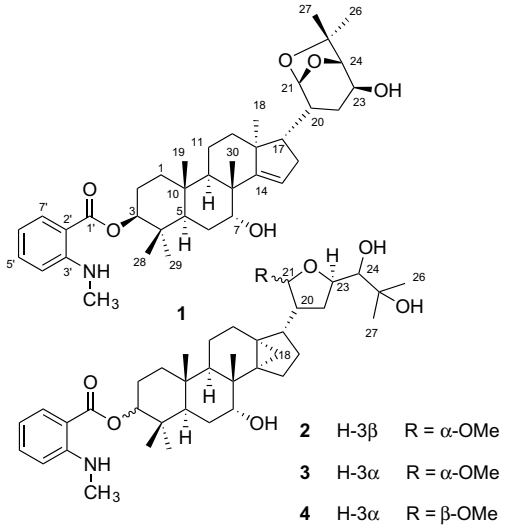
Abstract—The isolation and structure elucidation of two new triterpenes named feroniellides A (**1**) and B (**2**) from *Feroniella lucida* are described. Feroniellide A has a novel dioxabicyclic [3.2.1]octane moiety, and feroniellide B is the C-3 epimer of the known triterpenoid **3**. Their overall structures and relative configurations were established by combined spectral data analysis. The cytotoxicity of **1** and **2** was also evaluated against human KB and HeLa carcinoma cells.

Apotirucallane triterpenes have been found in several Meliaceae species and also in several of the Simaroubaceae and Rutaceae. These compounds can be categorized into two groups: 14,18-cycloapotirucallane and Δ^{14}-18-methylapotirucallane. Apotirucallane triterpenes have demonstrated several intriguing bioactivities, for example, dysobinin, a CNS depressant from *Dysoxylum alliaceum*[1] and meliavokin, a potent cytotoxin from *Melia volkensii*, which showed equivalent potency to adriamycin against the human breast tumor cell line.[2] In our search for biologically active metabolites from *Feroniella lucida* roots,[3] we recently reported the isolation of three new cytotoxic furanocoumarins, feroniellins A–C, bearing highly oxygenated side chains.

We also noticed the presence of other cytotoxic metabolites in the less polar fractions of the CH_2Cl_2 extract. An attempt to identify these active components led to the isolation of two new apotirucallane triterpenes named feroniellides A (**1**) and B (**2**).

F. lucida roots (3.8 kg), collected in Nakornpanom, in June 2005, were extracted as previously described.[3] The combined CH_2Cl_2 extracts were dissolved in MeOH and subsequently filtered to afford a residue. The residue (52 g) was chromatographed on silica gel eluting with CH_2Cl_2–*n*-hexane (1:1, 3:2, 4:1, and 1:0) and MeOH–CH_2Cl_2 (1:99→1:9) to yield eight fractions. The combined fractions 2 and 3 (530 mg) were further purified on Sephadex LH-20 [*n*-hexane–CH_2Cl_2–MeOH (6:3:1)] to yield feroniellide A (**1**, 20 mg). Fraction 4 (380 mg) was subsequently purified on Sephadex LH-20 [*n*-hexane–CH_2Cl_2–MeOH (5:4:1)] followed by ODS HPLC (85% MeOH–H_2O) to afford feroniellide B (**2**, 6 mg) and two known triterpenoids (**3** and **4**).[5]



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Feroniellide A (**1**)[4] was obtained as a colorless powder. The molecular formula $C_{38}H_{55}NO_6$ was determined by HRESIMS [*m*/*z* 622.4105 $[M+H]^+$, Δ −0.2 mmu]. The ^1H NMR spectrum displayed signals in three notable regions: 1,2-substituted benzene (δ 6.8–8.0), oxygenated and olefinic protons (δ 3.6–5.6), and methylene and methyl signals (δ 0.6–2.2). The UV (MeOH) absorbance at 255 and 354 together with the resonances in the downfield region [δ 7.84 (1H, dd, $J = 1.2$ and 8.0 Hz), 7.31 (1H, ddd, $J = 1.2$, 8.0, 8.2 Hz), 6.62 (1H, d, $J = 8.4$ Hz), and 6.53 (1H, t, $J = 7.6$ Hz)] and the singlet methyl [δ 2.80 (3H, s)] indicated the existence of an *N*-methyl anthranilate residue (Table 1).[5]

The ^{13}C NMR spectrum revealed 38 carbon signals, 30 of which were accounted for by a triterpenoid skeleton. In the upfield region, the ^1H NMR spectrum showed seven singlet methyls at δ 1.30, 1.23, 1.00, 0.98, 0.94, and 0.86 (6H), in addition to overlapped resonances of the methine and methylene protons (δ 1.4–2.2). These data suggested that the structure of **1** possessed an apotirucallane skeleton.

The *N*-methyl anthranilic acid unit was connected to C-3 as evident from the slightly downfield shifts[5] of 80.5 (C-3) and 4.64 (H-3) along with an HMBC cross peak between H-3 and C-1′ (δ_C 168.2). The location of the double bond at C-14 was determined from HMBC correlation of δ 5.38 (H-15) to δ 46.6 (C-13), 161.9 (C-14), 33.4 (C-16), and 55.2 (C-17).

The COSY spectrum (Fig. 1) demonstrated the contiguous spin system from H-24 to H-20, which was in turn coupled to H-21 and H-17. The occurrence of a cyclic

Table 1. ^1H and ^{13}C NMR data[a] for feroniellin A (**1**) in $CDCl_3$

No.	δ_C		δ_H (mult, *J* in Hz)	HMBC (H→C)
1	33.4	α	1.20 m	
		β	1.35 m	
2	23.6	α	1.71 m	
		β	1.85 m	
3	80.5		4.64 dd (4.8, 11.6)	C-1, 4, 5, 1′
4	37.6			
5	46.7		1.68 m	
6	27.6		1.58 m (2H)	
7	72.3		3.85 br s	C-5, 8
8	44.2			
9	41.8		1.98 m	
10	37.5			
11	16.9	α	1.52 m	
		β	1.70 m	
12	34.0	α	1.50 m	
		β	1.77 m	
13	46.6			
14	161.9			
15	119.7		5.38 br d (2.0)	C-13, 14, 16, 17
16	33.4	α	2.08 m	
		β	1.93 m	
17	55.2		1.58 m	
18	19.7		1.00 s	C-12, 13, 14, 17
19	15.5		0.86 s	C-1, 5, 9, 10
20	37.4		2.05 m	
21	102.9		5.47 br s	C-20, 22, 24, 25
22	31.1	α	1.66 m	C-21
		β	1.73 m	C-21
23	65.4		3.69 br s	C-20
24	83.3		3.77 br s	C-22, 23, 25, 26
25	79.2			
26	29.0		1.23 s	C-24, 25, 27
27	20.0		1.30 s	C-24, 25, 26
28	16.4		0.94 s	C-3, 4, 5, 29
29	27.6		0.86 s	C-3, 4, 5, 28
30	27.8		0.98 s	C-7, 8, 9, 14
1′	168.2			
2′	110.8			
3′	151.8			
4′	110.0		6.62 d (8.4)	C-2′, 6′
5′	134.4		7.31 ddd (1.2, 8.0, 8.2)	C-3′, 7′
6′	114.5		6.53 t (7.6)	C-2′, 4′
7′	131.4		7.84 dd (1.2, 8.0)	C-1′, 3′, 5′
NH*Me*	29.7		2.80 s	C-3′

[a] Measured at 400 MHz (^1H) and 100 MHz (^{13}C).