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THREE TETRANORTRITERPENOIDS FROM FRUITS OF *SOYMIDA FEBRIFUGA*

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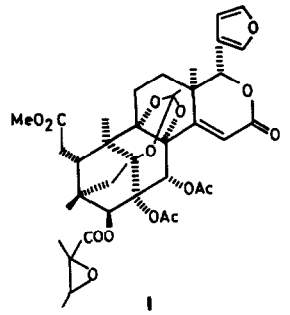
Key Word Index—*Soymida febrifuga*; Meliaceae; tetranortriterpenoids; epoxyfebrinin B; 14,15-dihydroepoxyfebrinin B; febrinolide.

Abstract—Three new tetranortriterpenoids, epoxyfebrinin B, 14,15-dihydroepoxyfebrinin B and febrinolide, have been isolated from the fruits of *Soymida febrifuga* and their structures assigned on the basis of their spectroscopic properties.

INTRODUCTION

Soymida febrifuga is a large deciduous tree found in Indian forests and is commonly known as the Indian red-wood. The heartwood is dark brown in colour and is hard and durable. The bark has a bitter taste and is used as a febrifuge in diarrhoea, dysentery and fevers and as a bitter tonic in general debility [1]. Previous investigations of the various parts of the plant led to the isolation of methyl angolensate, deoxyandirobin and two tetranortriterpenoids with a modified furan ring from the bark [2–5], obtusifoliol and the flavonoids syringetin and dihydrosyringetin from the root heartwood [6], quercetin 3-*O*-rhamnoside and quercetin 3-*O*-rutinoside from the leaves [7], and the tetranortriterpenoids febrifugin [8] and febrinins A and B [9] together with the flavonoids naringenin, quercetin, myricetin and dihydromyricetin from the heartwood [10]. The present paper deals with the isolation of three new tetranortriterpenoids, epoxyfebrinin B (**1**), 14,15-dihydroepoxyfebrinin B (**2**) and febrinolide (**3**), together with deoxyandirobin, 17β-hydroxy-6α-acetoxyazadiradione [11], methyl angolensate and sitosterol from the fruits of *S. febrifuga*.



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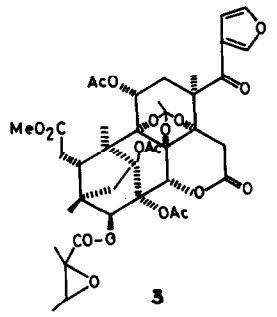
2 14,15 - Dihydro



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RESULTS AND DISCUSSION

Extraction of the powdered fruits with cold methanol and treatment of the concentrated extract with ether afforded a gummy mass, which was separated into neutral and acidic fractions. Column chromatography of the neutral fraction, followed by preparative TLC afforded the known compounds mentioned above together with two new tetranortriterpenoid fractions, SF-5 and SF-6. The latter was eventually shown to be a mixture of two compounds (see below).

The first new tetranortriterpenoid, SF-5, $C_{38}H_{44}O_{15}$, mp 255–261°, *m/z* 740, was identified as epoxyfebrinin B (**1**). It has three tertiary methyls (δ_H 0.91, 1.12 and 1.15), an orthoacetate (δ_H 1.62; δ_C 119.7), two acetates (δ_H 1.94 and 2.12), an epoxytiglate [δ_H 1.27 (3H, *d*, J = 6 Hz), 1.61 (3H, *s*), 3.2 (1H, *q*, J = 6 Hz)] and a carbomethoxyl group (δ_H 3.68). Comparison of the ^{13}C resonances (Table 1) with the published data for phragmalin derivatives [12] suggested that SF-5 has a phragmalin nucleus with an unsaturated ring D lactone [δ_C 161 (*s*), 119.5 (*d*) and 163.5 (*s*)]. The presence of singlets at δ_H 5.18 and 5.30 (H-3 and H-17) and 5.91 and 6.06 (H-30 and H-15) is consistent with this suggestion and leads to structure **1** for SF-5. The corresponding tiglate, febrinin B, has been isolated from the heartwood of *S. febrifuga* [9] and thus SF-5 is epoxyfebrinin B. The epoxytiglate moiety is placed at C-3 by analogy with entandrophragmin [13].

The second crystalline fraction, mp 229–232°, proved to be a mixture of two compounds separable by preparative TLC. The less polar component (**2**), $C_{38}H_{46}O_{15}$, *m/z* 742, has the same functionality as **1** (see Experimental) with the exception of the double bond in ring D and is therefore the

Table 1. ^{13}C NMR spectral data of compounds 1, 2 and 3

Carbon	Epoxyfebrinin B (1)	Dihydroepoxy-febrinin B (2)*	Febrinolide (3)
1	84.8	86.8	84.7
2	80.5	82.4	72.4
3	84.2	82.4	82.6
4	47.7†	46.1	53.4
5	36.2	36.1	33.4
6	34.0	33.6	39.1†
7	172.8	172.8	172.3
8	82.3‡	85.3	89.8
9	82.2‡	85.3	83.1
10	46.2†	46.0	44.9
11	25.2	25.4	66.4
12	29.7	29.3	29.6
13	37.9	34.3	52.5
14	161.1	43.2	81.9
15	119.5	26.4	37.4†
16	163.5	—	167.4
17	76.8	79.0	199.0
20	120.5	121.2	124.6
21	141.6	140.6	147.7
22	109.9	109.7	110.4
23	143.1	143.2	143.2
29	40.1	40.2	39.8
30	68.9	69.3	66.4
O⟍ O–C– O⟋	119.7	119.0	119.0
OMe	52.1	51.9	52.0
	170.4	170.6	170.0
C=O	170.1	170.3 (2)	169.8
	169.4	168.3	169.4
			168.9
Epoxytiglate	58.0	59.3	5.81 (*d*)
	58.0	58.5	57.7 (s)
C–$\underline{C}H_3$	21.8	21.7	21.7
	21.0	21.2 (2)	21.4
	20.8		21.2 (2)
	19.0	19.6	16.1 (2)
	16.8	16.9	15.3
	14.7	14.6	13.5
	13.4	13.5	
	13.1	13.2	13.2

*Spectrum obtained only in a mixture with 3.
†,‡Resonances may be interchanged.
Assignments of the oxygenated carbons are tentative.

corresponding dihydro derivative, 14,15-dihydroepoxy-febrinin B (2).

The more polar component of the mixture is the entandrophragmin derivative, febrinolide (3), $C_{40}H_{46}O_{18}$, *m/z* 814. Its ^1H NMR spectrum indicates the presence of three tertiary methyl groups (δ_H 0.78, 1.10 and 1.48), an orthoacetate (δ_H 1.78; δ_C 119.0), three acetates (δ_C 1.96, 2.08 and 2.10), an epoxytiglate [δ_H 1.36 (3H, *d*, J = 6 Hz), 1.55 (3H, *s*), 3.41 (1H, *q*, J = 6 Hz)] and a carbomethoxyl group (δ_H 3.57). The presence of an acetate at C-11 is indicated by the proton resonance at δ4.95 (*dd*, J = 5, 11 Hz). Singlet resonances for H-3 (δ_H 5.43) and H-30 (δ_H 6.06) are also present but the usual H-17 resonance is absent. The ^1H chemical shifts of the β-substituted furan (δ_H 6.80, 7.45 and 8.13) clearly reveal the presence of a ketonic carbonyl at C-17. This is confirmed by a major fragment in the mass spectrum at *m/z* 95 and by a ^{13}C resonance at δ_C 199.0. Support for the entandrophragmin skeleton of febrinolide (3) comes from comparison of its ^{13}C chemical shifts (Table 1) with published data [13] and from the fact that the C-15 methylene group resonates as an AB quartet (J = 18 Hz) at 2.59 and 3.03 showing that C-14 is fully substituted. The C-16 carbonyl group which results from the opening of the normal ring D lactone must form a lactone with the C-30 hydroxyl group. We favour structure 3 for febrinolide, which represents a new modification of the entandrophragmin nucleus; however, an alternative arrangement of the orthoacetate cannot be excluded. 17-Oxotetranortriterpenoids are relatively rare, pseudrelone B [14] and oriciopsin [15] being the previously reported examples.

EXPERIMENTAL

Mps are uncorr. IR spectra were recorded in $CHCl_3$ solns. ^1H NMR spectra were run in $CDCl_3$ using TMS as internal standard and the chemical shifts are expressed in δ ppm. ^{13}C NMR spectra were run at 25.16 MHz in $CDCl_3$. All CC separations were carried out on neutral alumina (Grade I). Silica gel G (Centron) was used for TLC and prep. TLC. All CC separations were monitored by TLC. The known compounds isolated were identified by direct comparison (mmp, IR and co-TLC) with authentic samples.

Plant material. Fruits of *Soymida febrifuga* A. Juss were collected from the forest near Kothagudem in Andhra Pradesh, India. A herbarium specimen has been deposited at the Central Institute of Medicinal and Aromatic Plants Regional Centre, Bangalore.

Extraction and isolation procedure. The fruits of *S. febrifuga* were powdered in a Wiley type disintegrator and the powder (7.5 kg) was extracted with MeOH (4 × 20 l.) by cold percolation. The combined extract was concd to *ca* 3.5 l. by distillation under red. pres., whereby a thick syrupy mass was obtained. The syrup was repeatedly treated with *n*-hexane (4 × 3 l.) and then with Et_2O (6 × 3 l.). The hexane extract on concn gave a waxy material (520 g) which was not investigated. The Et_2O extract was further separated by treatment with 2% NaOH soln into acid (18 g) and neutral (16 g) fractions. The neutral fraction (16.0 g) was chromatographed over neutral alumina (600 g) eluting with a mixture of C_6H_6–EtOAc.

The fractions eluted with C_6H_6–EtOAc (9:1) afforded mainly waxes (3.2 g). Elution with C_6H_6–EtOAc (3:1) gave a mixture (1.3 g) which was shown by TLC (hexane–EtOAc 1:1) to consist of two compounds. This mixture was rechromatographed over neutral alumina to give compounds SF-1 (sitosterol), mp 133–135° and SF-2 (30 mg) (deoxyandirobin), mp 172–175° (MeOH).

Fractions eluted with C_6H_6–EtOAc (3:2) gave a product (1.7 g) consisting of two compounds and polar material (TLC). It was rechromatographed over neutral alumina, eluting with a mixture of hexane–EtOAc of increasing polarity. The initial fractions afforded a mixture (100 mg) which was separated by multiple prep. TLC (C_6H_6–EtOAc, 7:3). The less polar compound, SF-3 (40 mg), mp 289–291° (MeOH–Et_2O), was identified as 17β-hydroxy-6α-acetoxyazadiradione, lit. [11] 288–292°. The more polar compound, SF-4 (30 mg), mp 199–201° (MeOH), was identified as methyl angolensate. The later fractions of the hexane–EtOAc (1:1) eluate gave mainly methyl angolensate (300 mg).

Elution with C_6H_6–EtOAc (1:1) and C_6H_6–EtOAc (2:1) gave fractions which showed similar spots on TLC and they were combined. The material from these fractions was subjected to repeated prep. TLC (hexane–EtOAc, 1:1) to obtain the tetranortriterpenoid fractions SF-5 (30 mg) and SF-6 (60 mg). Fraction SF-5 crystallized from MeOH as colourless needles, mp 258–261° to give epoxyfebrinin B (**1**), $C_{38}H_{44}O_{15}$. MS: *m/z* 740 (Found: C, 61.30; H, 5.65. $C_{38}H_{44}O_{15}$ requires: C, 61.62; H, 5.95%). IR ν_{max} cm^{-1}: 3120, 2900, 2850, 1745, 1725, 1650, 1455, 1370, 1295, 1050; ^1H NMR: δ0.91, 1.12, 1.15 (3*s*, 3H each, 3 × Me), 1.27 (*d*, *J* = 7.5 Hz, 3H, Me of epoxytiglate), 1.61 (*s*, 3H, O–MeC(–O)–O), 1.62 (*s*, 3H, Me of epoxytiglate), 1.94, 2.12 (2*s*, 3H each, 2 × OAc), 3.68 (*s*, 3H, COOMe), 5.18 and 5.30 (each 1H *s*, H-3 and H-17), 5.91 and 6.06 (each 1H *s*, H-30 and H-15), 6.45, 7.41 and 7.53 (*br s*, 1H each, furan Hs).

Fraction SF-6, mp 229–232°, was found to be a mixture of two compounds. Separation by prep. TLC yielded two bands. The first band yielded the less polar component, 14,15-dihydroepoxyfebrinin B (**2**), $C_{38}H_{46}O_{15}$; MS: *m/z* 742 $[M]^+$; ^1H NMR: δ0.92, 1.04, 1.15 (3*s*, 3H each, 3 × Me), 1.36 (*d*, *J* = 6 Hz, 3H, Me of epoxytiglate), 1.63 (*s*, 3H, Me of epoxytiglate), 1.75 (*s*, 3H, O–MeC(–O)–O), 1.90, 2.10 (2*s*, 3H each, 2 × OAc), 3.70 (*s*, 3H, COOMe), 5.18, 5.56 and 6.23 (each 1H *s*, H-3, H-17 and H-30), 6.48, 7.40, 7.52 (3*s*, furan Hs). The second band gave febrinolide (**3**), $C_{40}H_{46}O_{18}$; MS: *m/z* 814 $[M]^+$; ^1H NMR: δ0.78, 1.10, 1.48 (3*s*, 3H each, 3 × Me), 1.36 (*d*, *J* = 6 Hz, 3H, Me of epoxytiglate), 1.55 (*s*, 3H, Me of epoxytiglate), 1.78 (*s*, 3H, O–MeC(–O)–O), 1.96, 2.08, 2.10 (3*s*, 3H each, 3 × OAc), 3.57 (*s*, 3H, COOMe), 2.59, 3.08 (AB*q*, *J* = 18 Hz, H-15), 4.95 (*dd*, *J* = 5, 11 Hz, H-11), 5.43 (*s*, 1H, H-3), 6.06 (*s*, 1H, H-30), 6.80, 7.45, 8.13 (*br s*, 1H each, furan Hs).

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