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Furanoterpenoids from *Siphonochilus aethiopicus*

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Abstract

Two new furanoterpenoid derivatives, namely 4aαH-3,5α,8aβ-trimethyl-4,4a,9-tetrahydro-naphtho[2,3-*b*]-furan-8-one and 2-hydroxy-4aαH-3,5α,8aβ-trimethyl-4,4a,9-tetrahydronaphtho[2,3-*b*]-furan-8-one, were isolated from *Siphonochilus aethiopicus*, a member of the family Zingiberaceae. Their structures were elucidated using high field NMR techniques.

Keywords: *Siphonochilus aethiopicus*; Zingiberaceae; Wild ginger; Sesquiterpenes; Furanoterpenoid; Eudesmane

1. Introduction

Siphonochilus aethiopicus, commonly known as wild ginger, is a member of the family Zingiberaceae and is restricted to southern Africa, including South Africa, Zimbabwe, Malawi and Zambia. The rhizomes and roots are much used for colds, coughs and influenza, but also for hysteria, pain and several other traditional and cultural practises (Hutchings, 1962; Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 1997). Pressure on wild populations has led to local extinctions, notably KwaZulu-Natal (Cunningham, 1988).

We now report the first results from a chemotaxonomical investigation which resulted in the isolation of two new compounds (**1**, **2**).

2. Results and discussion

A chemotaxonomic survey of plants and plant parts from various provenances invariably yielded substantial quantities of an essential oil, with a low content of monoterpenenoids, but with substantial amounts (up to 0.2% wet weight) of an unknown major constituent, (**1**) accompanied by a minor compound (**2**). The purification of **1** and **2** was effected by flash chromatography over silica gel deactivated with 2% triethylamine in toluene. The new furanoterpenoid **1** was assigned the composition, $C_{15}H_{18}O_2$, on the basis of mass spectrometry and accurate mass determination of a molecular ion at *m*/*z* at 230. The NMR data (see Tables 1 and 2), especially the correlations observed in the COSY and HMBC experiments, gave unambiguous proof of the structure. The fifteen signals in the ^{13}C NMR spectrum, one a carbonyl carbon resonating at δ 204.0 as well as five other low field signals suggested that 1 is an oxygenated sesquiterpene. The ^{1}H NMR spectrum exhibited, amongst others, a furan proton signal at δ 7.02, two sets of doublets at δ 5.91 and 6.66, respectively, one AB system and three methyl signals, of which one is secondary. Irradiation of the methyl signal at δ 1.21 allowed the assignment of H-5 at δ 2.40. This proton represents the X part of an ABX system. The proton-proton coupling constants associated with that system allows the assignment of the relative stereochemistry of **1**. Thus, proton H-4a, exhibiting a threefold doublet at δ 1.81 with two 10 Hz proton-proton couplings indicated that H-4a is *trans* to H-5 and that the structure is fairly rigid. Confirmation that the methyl substitution occurred on position 3 and not C-2 is given by the observed directly bonded (C,H) coupling of 198.9 Hz measured for C-2 which complies with reported data (Pretsch et al., 1989; Ojida et al.,1994;).

A strong peak at *m*/*z* 247, equivalent to protonated **2** and little fragmentation, was evident in the FAB–mass

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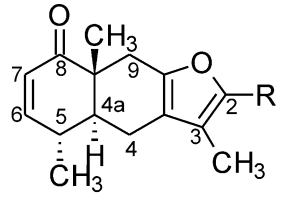
Table 1
^{1}H (500.13 MHz) NMR spectral data for **1** and **3** and ^{1}H (300.060 MHz) NMR spectral data for **2** in $CDCl_3$ compounds

H	**1**		**2**		**3**	
	δ_H	*J* (Hz)	δ_H	*J* (Hz)	δ_H	*J* (Hz)
2	7.02 *br m*	–	–	–	–	–
4A	2.68 *ddd*	15.7; 5.4: 1.6	2.80 *dd*	13.5; 3.6	2.87 *dd*	13.7; 3.7
4B	2.12 *dddd*	15.7; 10.8; 3.0; 1.4	2.42 *ddq*	13.2; 13.2; 1.5	2.21 *ddq*	13.7; 12.7; 1.4
4a	1.81 *ddd*	10.8; 10.2; 5.4	1.55 *ddd*	13.2; 9.9; 3.6	1.57 *ddd*	12.7; 9.8; 3.7
5	2.40 *dqdd*	10.2; 7.1; 2.7; 2.1	2.47 *dqdd*	10.2; 7.2; 2.4; 2.4	2.44 *dqdd*	9.8; 7.2; 2.8; 2.0
6	6.66 *dd*	10.1; 2.1	6.63 *dd*	10.2; 2.1	6.62 *ddd*	10.1; 2.0; 0.4
7	5.91 *dd*	10.1; 2.7	5.84 *dd*	10.2; 3.0	5.84 *dd*	10.1; 2.8
9A	2.73 *dd*	16.7; 1.4	1.63 *d*	14.4	3.04 *d*	14.9
9B	2.64 *br d*	16.7	2.64 *d*	14.4	1.53 *d*	14.9
2-OH	–	–	4.51 *br s*	–	–	–
2-$OCOCH_3$	–	–	–	–	2.01 *s*	–
3-Me	1.90 *d*	1.3 (H-2)	1.78 *d*	1.5 (H-4B)	1.83 *d*	1.4 (H-4B)
5-Me	1.21 *d*	7.1	1.21 *d*	7.2	1.22 *d*	7.2
8a-Me	1.02 *s*	–	1.33 *s*	–	1.24 *s*	–

Table 2
^{13}C (125.76 MHz) NMR data for **1** and **3** and ^{13}C (75.459 MHz) NMR data for **2** in $CDCl_3$

C	**1**	**2**	**3**
	δ_c	δ_c	δ_c
2	137.5 Dq	172.2	167.9 Sm
3	119.0 Sm	103.5	103.7 Sm
3a	114.6 Sm	122.3	124.1 Sm
4	22.5 T	24.1	24.1 Tm
4a	45.0 Dm	49.9	49.7 Dm
5	34.2 Dm	33.8	33.7 Dm
6	154.2 Dqn	153.7	153.1 Dm
7	126.6 Dd	126.1	126 Dd
8	204.0 Sm	203.0	201.6 Sm
8a	44.9 Sm	44.8	44.5 Sm
9	31.9 Tm	43.6	42.8 DDm
9a	149.3 Sm	158.5	155.6 Sm
3-Me	8.1 Q	8.3	8.3 Q
5-Me	18.7 Qm	18.0	18.0 Qm
8a-Me	16.6 Qm	16.6	16.3 Qm
$OCOCH_3$	–	–	170.8 Sm
$OCOCH_3$	–	–	21.9 Q

spectrum of **2**. The structure of **2**, $C_{15}H_{18}O_3$, followed from the ^{1}H NMR data. While most signals were similar to those of **1**, the biggest differences in the ^{1}H spectrum of **2** were the disappearance of the furan signal, the presence of an additional broad singlet at δ 4.51, the upfield shift of H-9 to δ 1.63 as well as a slight downfield shift of the 8a-methyl group. A big downfield shift of C-2 from 137.6 to 172.2 ppm in the ^{13}C NMR spectrum (Table 2) was also observed. Hydroxylation in the 2 position has a big influence on the electron distribution in the furan ring as shown by the change in the chemical shifts of C-3 (-15.5), C-3a (+7.7) and C-9a (+9.2) when compared with the corresponding values in **1**. It effects C-9 (+11.7 ppm and $J_{9A,9B}$ = 14.4 Hz vs 16.9 Hz in **1**) and it also has a subtle influence on the preferred conformation of **2**, because the substantial long range proton-proton coupling constants observed between C-4 and C-9 protons in **1** are no longer detected. A change in the conformation of the cyclohexenone ring due to the buttressing effect of substituents may result in orientation of the C-8 carbonyl group parallel with the C-9 equatorial proton, thus explaining the big upfield shift of the C-9 equatorial proton in **2**.



1 R = H
2 R = OH
3 R = $OCOCH_3$

Reaction of **2** with acetic anhydride and triethylamine resulted in the expected *O*-acetylation on the 2-position and are confirmed by the data obtained from the ^{1}H and ^{13}C NMR and COSY experiments.

The two new compounds **1** and **2** are members of the eudesmane family of sesquiterpenoids. These classes of compounds are produced by other plants and marine organisms and display a significant variance in stereochemistry (Miller and Behare, 1974; Yamakawa et al., 1975; Al-Said et al., 1989), e.g. tuberiferine from Sonchus Tuberifer Svent (Barrera et al., 1967) and tubipofuran from *Tubipora musica* Linnaeus (Iguchi et al., 1986), respectively.

3. Experimental

3.1. General

^{1}H (300.06 MHz) and ^{13}C (75.46 MHz) NMR data were recorded on a Varian Gemini 2000 spectrometer and ^{1}H (500.06 MHz) and ^{13}C (125.46 MHz) NMR data were recorded on a Bruker AMR-500 NMR spectrometer using $CDCl_3$ as solvent unless otherwise stated. EI–MS and FAB–MS (glycerol matrix, Ar bombarding gas) were recorded on a VG-7070e spectrometer and optical rotations obtained on a Jasco DIP 370 digital polarimeter. Melting points were taken on a Reichert Kofler hot-stage apparatus and are uncorrected. CC was performed with silica gel (Merck, 230–400 mesh) and TLC using Merck silica gel plates ($60F_{254}$).

3.2. Plant material

Rhizomes and roots were collected from a commercial nursery. Since *S. aethiopicus* is the only indigenous member of the family in South Africa and since it has such a unique and distinctive morphology (see Van Wyk et al., 1997) no voucher specimen was collected.

3.3. Extraction and isolation

The fleshy crushed roots of several plants of *S. aethiopicus* were steam distilled for one hour to obtain a pale yellow semi-crystalline mixture which contained (TLC) compound **1** as main constituent. Extraction of the roots with cold EtOH for 5 days and evaporation of the solvent furnished a residue which again contained mainly **1**. Flash chromatography of a portion (0.5 g) of the residue on silica gel (100 g) in toluene and 2% triethylamine afforded two main compounds.

3.4. 4aαH-3,5α,8aβ-Trimethyl-4,4a,8a,9-tetrahydronaphtho[2,3b]-furan-8-one (*1*)

White crystals (78%); mp 60 °C. $[\alpha]_D^{22}$: +107.4° ($CDCl_3$, *c*, 1) ^{1}H NMR (Table 1). ^{13}C NMR (Table 2). EI–M *m*/*z* (rel. int.): 230 (100), 215 (90), 197 (13), 187 (56). HREI–MS *m*/*z*: 230.1312 ($C_{15}H_{18}O$ requires 230.1306).

3.5. 2-Hydroxy-4aαH-3,5α,8aβ-trimethyl-4,4a,8a,9-tetrahydronaphtho-[2,3b]-furan-8(5H)-one (*2*)

White crystals (14%); mp: 109 °C. $[\alpha]_D^{22}$: +84° (MeOH, *c*, 1.0). ^{1}H NMR (Table 1). ^{13}C NMR (Table 2). FAB–MS *m*/*z* (rel. int.): 247 ($M^+ + 1$, 100%).

3.6. 2-Acetoxy-4aαH-3,5α,8aβ-trimethyl-4,4a,8a,9-tetrahydronaphtho-[2,3b]-furan-8-one (*3*)

A solution of compound **2** (100 mg), Ac_2O (0.5 ml) and triethylamine (0.5 ml) in CH_2Cl_2 (3 ml) was stirred for 70 h at room temp. The solvent was removed under reduced pressure and the crude product chromatographed in EtOAc:$CHCl_3$ (1:1) to furnish the compound **3** as a colourless oil in a quantitative yield. ^{1}H NMR (Table 1). ^{13}C NMR (Table 2).

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