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8(14),15-SANDARACOPIMARADIENE-2α,18-DIOL, A MINOR CONSTITUENT OF THE RWANDESE MEDICINAL PLANT *TETRADENIA RIPARIA*

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Key Word Index—*Tetradenia riparia*; Labiatae; diterpenediol; 8(14),15-sandaracopimaradiene-2α,18-diol.

Abstract—An investigation directed towards minor constituents of *Tetradenia riparia* (previously named *Riboza riparia*) resulted in the isolation of 8(14),15-sandaracopimaradiene-2α,18-diol, a new natural diterpenediol.

INTRODUCTION

Recently [1], the active principle of *Tetradenia riparia* (Hochst) Codd. (previously named *Iboza riparia*), an important plant in the traditional medicine of Rwanda (Central Africa), was identified as 8(14),15-sandaracopimaradiene-7α,18-diol (**1**). This diterpenediol showed substantial antispasmodic [2] and antimicrobial (unpublished work) activity. Further investigation of the petrol extract of *T. riparia* for minor constituents resulted in the isolation and characterization of an isomeric diterpenediol, i.e. 8(14),15-sandaracopimaradiene-2α,18-diol (**2**).

RESULTS AND DISCUSSION

The identity of **2** as a diterpenediol was immediately clear from its mass spectrum, which revealed a molecular ion at *m/z* 304 and a fragmentation pattern almost identical to that of diterpenediol **1** [1].

Comparison of the 360 MHz ^{1}H NMR spectra of diterpenediol **1** and the new natural diterpenediol indicated that the same substitution pattern was present except for the absence of hydroxylation at C-7. The characteristic three methyl singlets, the hydroxymethyl group at C-4, the position of the endocyclic olefinic double bond and the vinyl substituent led to the conclusion that the diterpene compound was substituted with a hydroxyl group on the ring skeleton of the diterpenediol. The typical splitting pattern of the hydroxyl-substituted methine moiety, characteristic for a proton having two methylene substituents, established the presence of a hydroxyl group at C-2.

The unambiguous assignments by ^{1}H NMR (360 MHz) of 27 of the 32 protons of 8(14),15-sandaracopimaradiene-2α,18-diol (**2**) was achieved using a combination of one-dimensional (1D) and two-dimensional (2D) proton NMR techniques, such as COSY [3] and delayed COSY [4]. The results are presented in Table 1.

The vicinal coupling constant (^3J) of 11.5 and 4.1 Hz observed along the 1–2 and 2–3 fragments of the A-ring are typical for an equatorial 2-(α)-hydroxy substituent in a rigid chair conformation [5]. The chair form of the B-ring with an exocyclic double bond is indicated by (a) the value of −14.2 Hz of the geminal coupling (^2J) of the allylic 7-CH_2 group [6], (b) the vicinal axial–equatorial coupling ^3J(ae) of 4.2 Hz and ^3J(ee) of 2.0 Hz along the 6–7 bond, and (c) the cross-peaks of H-14 to H-9 and H-7α in the COSY-2D spectra, but not to H-7β which resides in the plane of the double bond [7]. The (averaged) vicinal couplings along the 9–11 bond are consistent with a non-chair C-ring containing the double bond.

8(14),15-Sandaracopimaradiene-2α,18-diol (**2**) is a new natural product. It has, however, already been obtained as a chemical degradation product of the naturally occurring diterpenetetrol hallol (**4**), which was isolated from the New Zealand podocarp *Podocarpus halii* Kirk [8]. The tetrol **4** was chemically modified by periodic acid oxidation and subsequent olefination of the intermediate aldehyde into the diterpenediol **2** using methylene-triphenylphosphorane. The data for the natural and

Table 1. ^{1}H NMR data for compound **2** (360 MHz, $CDCl_3$, TMS as internal standard)

H	δ	H	δ	H	δ
1α	1.006	7α	2.076	16	4.915
1β	2.061	7β	2.26		4.890
2	3.917	9	1.837	17	1.046
3α	1.394	11	1.63	18	3.420
			1.53		3.159
3β	1.678	12	1.3–1.6	19	0.851
5	1.2–1.5	14	5.258	20	0.883
6α	1.49	15	5.775		
6β	1.30				

J(Hz): 1α,1β = −11.8; 1α,2 = 11.5; 1β,2 = 4.1; 1β,3β = 2.3; 2,3α = 11.5; 2,3β = 4.1; 3α,3β = −12.0; 6α,7β = 2.0; 6β,7β = 4.2; 7α,7β = −14.2; 9,11α = ~7.7; 9,11β = ~7.7; 15,16 = 17.5, 10.6; 16,16′ = 1.4; 18,18′ = 10.8.

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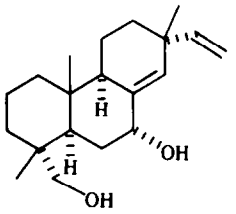

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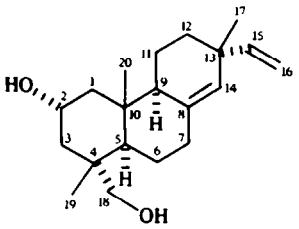

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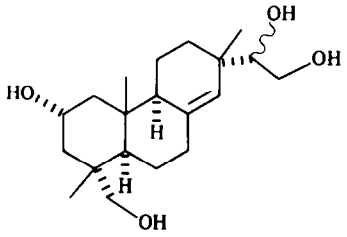

4 (Hallol)

Table 2. Comparison of the ^{13}C NMR data of the natural and synthetic diterpenediol (δ, $CDCl_3$)

C	Natural product (this paper)	Synthetic product [8]
1	48.2	48.1
2	65.3	65.1
3	44.7	44.7
4	39.5*	39.4†
5	47.0	47.0
6	22.1	22.1
7	35.5	35.5
8	136.2	136.2
9	50.5	50.4
10	39.7*	39.6†
11	18.86‡	18.9§
12	34.4	34.4
13	37.0	36.9
14	129.5	129.3
15	148.9	148.7
16	110.2	110.0
17	25.9	25.9
18	71.7	71.5
19	18.95‡	18.9§
20	16.5	16.5

*,†,‡,§Assignments may be interchanged.

synthetic **2** are in good agreement, although our ^1H NMR data (360 MHz) and mass spectral data are more complete. Final proof of the common identity of the natural compound and the synthetic compound came from a comparison of the ^{13}C NMR data (20 MHz), which were almost identical (Table 2).

EXPERIMENTAL

Plant material. Leaves of *T. riparia* were collected in the prefecture of Butare (South-West of Rwanda) in October 1984 and identified as previously described.

Extraction and isolation. Air-dried leaves (522 g) were ground to a fine powder, which was extracted in a percolator with petrol (40–60°) (12 l.). The extract was filtered, concentrated *in vacuo* and extracted with MeOH–H_2O (9:1). The petrol phase was then evaporated *in vacuo* to give a brown-green syrup (14.9 g, 2.8%), which was extracted with MeOH–H_2O. After evaporation of MeOH, the aq. phase was extracted with $CHCl_3$, which gave, after evaporation *in vacuo*, a brown residue (24.8 g, yield 4.5%). 12 g of the $CHCl_3$ extract was adsorbed on silica gel (50 g) and slurried onto the top of a column containing 550 g silica gel (Riedel de Haën, 230–400 mesh) in *n*-hexane and eluted with a *n*-hexane–toluene–$CHCl_3$–EtOAc–MeOH gradient.

8(14),15-*Sandaracopimaradiene*-2α,18-*diol* (**1**) was isolated from the EtOAc fraction (141 mg, yield 0.05%) and was recrystallized from cyclohexane to afford small white crystals, mp 203–204°, $[\alpha]_D^{20}$ −21.7° (*c* 0.35; $CHCl_3$) (589 nm). ^1H NMR (360 MHz) and ^{13}C NMR (20 MHz): see Tables 1 and 2; IR (KBr): 3600–3100 cm^{-1} (ν_{OH}, broad); MS *m/z* (rel. int.): 304 $[M]^+$ (9), 286 (40), 256 (33), 187 (100), 241 (16), 187 (100), 159 (41), 132 (32), 121 (70), 119 (51), 111 (27), 109 (32), 107 (41), 105 (43), 96 (36), 94 (45), 92 (45), 90 (41), 83 (36), 81 (58), 79 (34), 73 (30), 71 (30), 69 (51), 67 (32), 57 (55), 55 (72).

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