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Bis-bibenzyls from the Cameroon Liverwort *Marchantia debilis*

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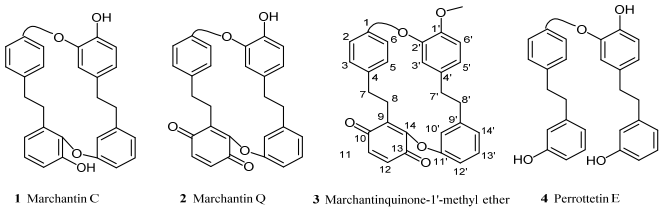
Liverworts are rich sources of terpenoids and aromatic compounds among which bis-bibenzyls are well known for their wide spectrum of biological activities. This is the first report of chemical analysis of the African liverwort *Marchantia debilis* Goebel. From the methanol extract marchantinquinone-1'-methyl ether was newly isolated together with three known bis-bibenzyls, marchantin C, marchantinquinone and perrottetin E. The presence of bis-bibenzyls with a quinone moiety is noted for the first time in the *Marchantia* genus.

Keywords: Bis-bibenzyls, *Marchantia debilis*, Isolation, Marchantinquinone-1'-methyl ether.

Marchantiophyta (liverworts) are divided into two subclasses Jungermanniidae and Marchantiidae which include more than 6000 species. The best known biologically active compounds isolated from liverworts are bis-bibenzyls. Naturally occurring bis-bibenzyls are either macrocyclic molecules obtained from two biphenyl ether C–O bonds (for example marchantins [1a]), one biphenyl ether C–O and one biaryl C–C bond (e.g. riccardins [1a] and plagiochins [1b] and two biaryl C-C bonds (e.g. isoplagiochin [1c]). Acyclic bis-bibenzyls such as perrottetins are found in liverworts in the genus *Radula* [1d]. The spectrum of biological activities of these compounds is really wide: anti-viral, antibacterial, antifungal, cytotoxic, muscle-relaxing, and antioxidant [2-5]. The most investigated thalloid liverwort, *Marchantia. polymorpha* L., is known for its antipyretic, antihepatic, antidotal, and diuretic activities, for curing cuts, fractures, and external wounds [5].

M. debilis Goebel is an African liverwort species with distribution in Cameroon, Ivory Coast, South Africa and Madagascar. The thallus is small to medium size, green or purplish, when exposed to bright sun [6a]. The aim of this study was the isolation and structure elucidation of bis-bibenzyls of *M. debilis* from Cameroon. This investigation represents the first report from this species of the bis-bibenzyls, marchantin C (**1**), marchantinquinone (**2**), marchantinquinone-1'-methyl ether (**3**), and perrottetin E (**4**). This is also the first record of marchantinquinone-1'-methyl ether (**3**).

The newly isolated bis-bibenzyl (**3**) showed the presence of a *p*-quinone moiety (1674, 1653 cm^{-1}) in the IR and (236, 262 nm) UV spectra. Its HRESIMS data (*m/z* 452.1626) showed the molecular formula $C_{29}H_{24}O_5$. The ^1H and ^{13}C NMR data of **3** were very similar to those of marchantinquinone (**2**) and marchantin N (=marchantinquinone 11-methyl ether) [6b]. Doublets at δ 6.67 and 7.05 {Table 1, Figure S1 (Supporting Material)} refer to *para* substitution of the A ring and are characteristic of all marchantins. Like marchantinquinone (**2**) and marchantin N, two carbonyl C-atoms appeared at δ 181.0 and 187.9 in the ^{13}C NMR spectrum of compound **3**, suggesting a quinone moiety as part of its structure. Doublets at δ 6.71 and 6.84, both with a coupling constant



1 Marchantin C **2** Marchantin Q **3** Marchantinquinone-1'-methyl ether **4** Perrottetin E

Figure 1: Bis-bibenzyls from *Marchantia debilis*.

Table 1: NMR data of marchantinquinone-1'-methyl ether (**3**) ($CDCl_3$, 125 MHz for ^{13}C, 500 MHz for ^1H).

Atom no.	C (δ, ppm)	H (δ, ppm)	Atom no.	C (δ, ppm)	H (δ, ppm)
1	153.3	-	1'	147.1	-
2	121.6	6.67 d (8.5)	2'	147.6	-
3	129.6	7.05 d (8.5)	3'	116.3	5.56 d (2.0)
4	137.3	-	4'	133.1	-
5	129.6	7.05 d (8.5)	5'	121.9	6.78 dd (8.0, 2.0)
6	121.6	6.67 d (8.5)	6'	111.6	6.84 d (8.0)
7	33.8	2.90 m	7'	34.9	2.86 m
8	25.8	2.95 m	8'	36.3	2.78 m
9	134.3	-	9'	142.7	-
10	187.9	-	10'	116.0	6.55 dd (2.5, 2.0)
11	136.9	6.84 d (10.0)	11'	156.9	-
12	135.1	6.71 d (10.0)	12'	113.7	6.39 m*
13	181.1	-	13'	128.3	6.93 t (8.0)
14	152.4	-	14'	124.3	6.40 m*
			1'-OMe	56.0	3.90 s

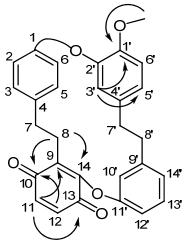


Figure 2: Key correlations in the HMBC spectrum of marchantinquinone-1'-methyl ether (**3**).

of 10.0 Hz, exhibited in the HMBC spectrum showed strong correlation with the carbonyl carbons, this being the difference from marchantin N with a methoxy group at C-11. In the same way, a significant difference in the chemical shift of the methoxy group of the quinone moiety (0.4 ppm) in marchantin N [6b] and compound

3, together with the multiplicity of protons 11 and 12 (doublets), confirm that the methoxy group is not on the quinone moiety as in marchantin N. The methoxy group observed at δ 3.90 in the ^{1}H NMR spectrum of **3** exhibited strong correlation with C-3' (Figure 2). The chemical shifts and multiplicity of other signals from ring C of **3** were almost the same as those of marchantinquinone (**2**) and marchantin N, thus revealing that the methoxy group is in position 1'. Signals for protons and carbons of the D ring were very similar to those of marchantinquinone (**2**) [6b]. Thus the structure of **3** was established to be marchantinquinone-1'-methyl ether.

The various marchantin-type macrocyclic bis-bibenzyls have been isolated from only liverworts, especially *Marchantia* species belonging to the Marchantiaceae. *M. polymorpha* produces marchantin A, 6'-hydroxymarchantin C, as the major component, together with marchantins B-H, and J-L, and *M. paleaceae* subsp. *diptera* also elaborates marchantins A-H [2b-4]. The Indian *M. palmata* and the Japanese *M. tosana* biosynthesize marchantin A-C and the latter species produces marchantin F [2b-4]. Marchantin C was also found in *M. chenopoda* and *M. foliacea* [2b-4,6c]. The present Cameroon species predominantly produces marchantin C (**1**), like *M. chenopoda,* but it is noteworthy that marchantinquinone type bis-bibenzyls (**2**, **3**) and 11-methoxymarchantinquinone (=marchantin N) have not yet been found in any *Marchantia* species although they are secondary metabolites of the liverwort *Reboulia hemisphaerica*, family Aytoniceae [6b].

The acyclic bis-bibenzyl perrottetin E (**4**) and its related bis-bibenzyls, which may be the precursors of cyclic bis-bibenzyls such as the marchantin series, are widely distributed in liverworts, and not only in the stem-leafy ones, such as *Frullania*, *Jungermannia, Nardia, Plagiochila* and *Radula*, species, but also in thalloid liverworts, *Lunularia, Marchantia, Monocolea* and *Pellia* species [2b,3a,3b].

Experimental

Liverwort material: The liverwort was collected on the banks of streams around raffia bushes at w3Mendakwe, Bamenda, north west region of Cameroon. *Marchantia debilis* Goebel was identified by Catherine Reeb from the Institut de Systématique, Évolution, Biodiversité, ISYEB - UMR 7205 - MNHN, UPMC, CNRS, EPHE Muséum National D' histoire Naturelle, 75005 Paris, France and Y.A. Voucher samples of *M. debilis* have been deposited in the Museum National D' histoire Naturelle, Paris, France and at the Phytobiotechnology Research Foundation Botanical Laboratory (Project no code: PRFYONG0314).

General: NMR, Varian 500-PS spectrometer; HRESIMS, JEOL JMS-700 instrument; UV, GBC Cintra 40 UV/Vis spectrometer; IR, ThermoScientific Nicolet 6700 FTIR spectrometer; Optical rotations, Rudolph Research Analytical AUTOPOL IV automatic polarimeter. CC, silica gel 60; TLC silica gel 60 GF254 20 × 20 cm plates, layer thickness 0.25 mm (Merck).

Extraction and isolation: Dried material (29.7 g) was milled and extracted first with *n*-hexane, to remove the majority of lipid components, then 4 times with 400 mL of methanol for 24 h (including 2 times usage of ultrasonic bath for 30 min); 3.05 g of methanol extract was obtained (yield 10.3%).

The methanol extract was subjected to silica gel CC (260 × 45 mm) with gradient elution with a solvent system of *n*-hexane/EtOAc according to Table S1 (Supporting Material). Similar fractions were joined together according to TLC analyses and final separation was made using preparative TLC and *n*-hexane/EtOAc 60:40 (marchantin C, marchantinquinone and marchantinquinone methyl ether) and *n*-hexane/EtOAc 50:50 (perrottetin E). Marchantin C (**1**) was obtained in a quantity of 30 mg, marchantin Q (**2**) 11 mg, marchantinquinone-1'-methyl ether (**3**) 5 mg, and perrottetin E (**4**) 5 mg.

Marchantinquinone-1'-methyl ether (**3**)
$[\alpha]_D$: +1.0 (*c* 1.00, $CHCl_3$), +1.0 (*c* 1.00, CH_3OH).
IR (KBr): 3437, 2924, 2853, 1674, 1653, 1584, 1507, 1447, 1309, 1267, 1236, 1166, 1127, 1045, 841 cm^{-1}.
UV/Vis λ_{max} (MeOH) nm (log ε): 227 (4.39), 236 (4.32), 262 (3.88).
^{1}H NMR (500 MHz, $CDCl_3$): Table 1
^{13}C NMR (125 MHz, $CDCl_3$): Table 1
HRESIMS: *m/z* found: 452.1626 [M^+] (calcd. for $C_{29}H_{24}O_5$: 452.1624).

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