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Trifarienols A and B, Isolated from the Liverwort *Cheilolejeunea trifaria*. Sesquiterpenes having a New Carbon Skeleton, Trifarane

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***Abstract*:**. Two novel bicyclic sesquiterpenoids, trifarienols A and B with a new carbon skeleton, trifarane, have been isolated from the Malaysian liverwort, *Cheilolejeunea trifaria* , and their absolute structures established by a combination of NMR, CD, and X-ray crystallographic analysis.

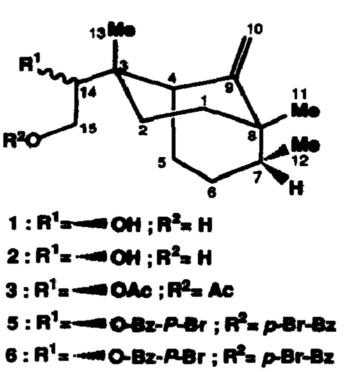
Liverworts are rich source of terpenoids and lipophilic aromatic compounds. We have reported the distribution of a number of new terpenoids and aromatic compounds in more than 100 species of the liverworts.[1] In the course of our investigation of the Malaysian liverworts, two new sesquiterpenoids, named trifarienols A (**1**) and B (**2**), have been isolated from the ether extract of *Cheilolejeunea trifaria* belonging to the Lejeuneaceae. Here we wish to report the isolation and the structure elucidation of **1** and **2**.

The ether extract (1.3 g) of dry material (19 g) of *C. trifaria* collected in Malaysia in 1992 was subjected repeatedly to column chromatography of Sephadex LH-20 ($CHCl_3$: MeOH = 1 : 1) and of silica gel (hexane : EtOAc, gradient) to afford **1** (271mg)[2] and **2** (73mg)[3].

The molecular formula of **1** was determined to be $C_{15}H_{20}O_2$ by HRMS. The presence of primary and secondary hydroxyl groups was confirmed by IR (3350 cm^{-1}) and ^{13}C NMR spectra [δ 76.7 (d), 63.7 (t)], and the formation of the diacetate (**3**) [^1H NMR ($CDCl_3$): δ 2.04, 2.09 (each s, 3H)]. These two hydroxyl groups are in a *vic* diol system, as confirmed by the $NaIO_4$ oxidation to give an aldehyde (**4**) [δ 9.49 (s)]. The ^1H NMR spectrum of **1** showed the presence of two tertiary [δ 0.84 (s), 0.92 (s)] and one secondary methyl groups [δ 0.86 (d, J=7.3 Hz)], and an exomethylene group [δ 4.63 (d, J=2.2 Hz), 4.79 (d, J=2.2 Hz)]. The planar structure and relative configuration of **1** was deduced from careful analysis of the 2D NMR spectra including DQF-COSY, HMQC, HMBC and NOESY, and was finally established by X-ray crystallography[4] (Fig. 1). The spectral data[3] and chromatographic behaviour of **2** resembled those[2] of **1**, indicating that **2** might be the C-14 epimer of **1**. In fact, the $NaIO_4$ oxidation of **2** furnished the aldehyde **4** .

The absolute stereochemistry of the secondary hydroxyl group at C-14 of **1** and **2** was elucidated by their CD spectra in the presence of the shift reagent [$Eu(fod)_3$], and by those of the dibenzoates, **5** and **6**. The CD spectra of **1** and **5** showed the positive first Cotton effects at 307 and 250 nm, respectively, while those of **2** and **6** showed the negative first Cotton effects at 304 and 250 nm, respectively, indicating that the C-14 has *S* configuration in **1** and *R* in **2**. Thus, the structures of trifarienols A and B including the absolute configuration were established as shown in the formula **1** and **2**, respectively.

Compounds **1** and **2** might be biosynthesized through **7**, which is an intermediate to pinguisane-type sesquiterpenes[5], by a series of rearrangements as shown in Fig. 2. This is the first sesquiterpenoids having a new skeleton, to which we propose trifarane.



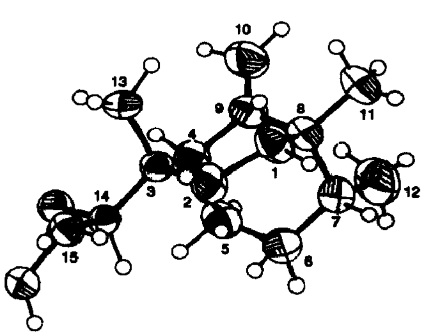
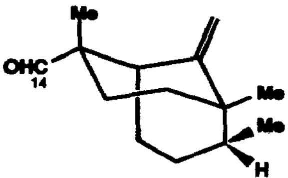


Fig. 1. ORTEP Drawing of Trifarienol A (1)



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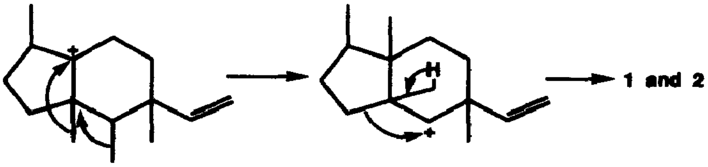

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Fig. 2. Possible Biogenetic Pathways for 1 and 2

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2. 1; mp 59.0-60.0°, $[\alpha]_D^{20}$ +10.2°(*c* 0.63, $CHCl_3$); CD $[CCl_4$+Eu(fod)$_3]$: λ_{max} 307 nm (Δε+79.8), 282 nm (Δε -55.9); HRMS: *m/z* 238.1930, $C_{15}H_{26}O_2$ requires 238.1932; IR (KBr) cm^{-1}: 3354 (OH), 1644, 1078, 1011; ^{1}H NMR ($CDCl_3$): δ 4.79 (1H, d, J=2.2 Hz, H-10a), 4.63 (1H, d, J=2.2 Hz, H-10b), 3.80 (1H, dd, J=9.5, 2.4 Hz, H-14), 3.70 (1H, dd, J=11.0, 2.4 Hz, H-15a), 3.54 (1H, dd, J=11.0, 9.5 Hz, H-15b), 2.23 (1H, m, H-4), 0.92 (3H, s, H-11), 0.86 (3H, d, J=7.3 Hz, H-12), 0.84 (3H, s, H-13); ^{13}C NMR ($CDCl_3$): δ 152.7 (C-9), 106.8 (C-10), 76.6 (C-14), 63.7 (C-15), 46.9 (C-4), 41.0 (C-7), 40.7 (C-3), 39.7 (C-8), 38.5 (C-1), 32.9 (C-2), 29.7 (C-6), 25.8 (C-11), 24.4 (C-5), 19.1 (C-13), 17.7 (C-12).
3. 2; mp 105-105.5°, $[\alpha]_D^{20}$ -3.6° (*c* 1.62, $CHCl_3$); CD $[CCl_4$+Eu(fod)$_3]$: λ_{max} 304 nm (Δε-53.9), 280 nm (Δε +38.7); HRMS: *m/z* 238.1925, $C_{15}H_{26}O_2$ requires 238.1932; IR (KBr) cm^{-1}: 3383 (OH), 1641, 1161, 1055; ^{1}H NMR ($CDCl_3$): δ 4.75 (1H, d, J=2.0 Hz, H-10a), 4.59 (1H, d, J=2.0 Hz, H-10b), 3.80 (1H, dd, J=9.5, 2.6 Hz, H-14), 3.71 (1H, dd, J=11.2, 2.6 Hz, H-15a), 3.49 (1H, dd, J=11.2, 9.7 Hz, H-15b), 2.33 (1H, m, H-4), 0.92 (3H, s, H-11), 0.85 (3H, d, J=7.1 Hz, H-12), 0.81 (3H, s, H-13); ^{13}C NMR ($CDCl_3$): δ 152.7 (C-9), 106.6 (C-10), 78.4 (C-14), 62.0 (C-15), 48.2 (C-4), 41.0 (C-7), 40.9 (C-3), 39.7 (C-8), 38.2 (C-1), 33.7 (C-2), 29.5 (C-6), 25.9 (C-11), 24.4 (C-5), 18.9 (C-13), 17.7 (C-12).
4. The crystal data for 1 are as follows: monoclinic; space group P21 with a=18.538 (4), b=7.062 (2), c=18.427 (4) Å, b=95.02(2)°, V=2403.1Å^3, Z=8, and μ (Cu Kα)=5.74cm^{-1} by Mac Science MXC 18 instrument. Final R value was 0.051 for 3972 reflections. The supplementary materials have been deposited at the Cambridge Crystallographic Data Centre.
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