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Two Novel Macrocyclic Bis(Bibenzyls), Isoplagiochins A and B from the Liverwort *Plagiochila fruticosa*

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Abstract : Two novel macrocyclic bis(bibenzyls) named isoplagiochins A and B have been isolated from the liverwort *Plagiochila fruticosa*, and their structures established by a combination of two dimension NMR spectra, X-ray crystallographic analysis and chemical degradation.

Plagiochila species (liverworts) are rich sources not only of sesquiterpenoids but also bibenzyl and cyclic bis(bibenzyl) derivatives with biological activities.[1,2] In our previous paper, we have reported on the isolation and structure elucidation of new 2,3-secoaromadendrane-type sesquiterpenoids having strong pungent taste from *Plagiochila fruticosa*.[3] Further fractionation of the MeOH extract of *P. fruticosa* resulted in the isolation of two novel macrocyclic bis(bibenzyls), named isoplagiochins A (**1**) and B(**2**). We now report on elucidation of their structure.

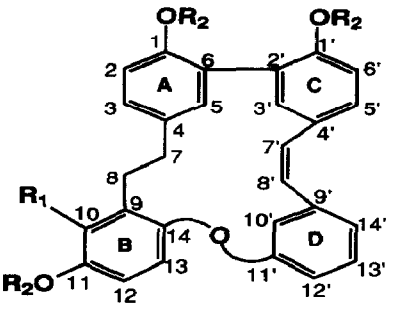
The MeOH extract (27.4 g) of fresh material (1.64 kg) of *P. fruticosa* collected in Yakushima in 1985 was subjected repeatedly to column chromatography using Sephadex LH-20 ($CHCl_3$: MeOH = 1 : 1) and silica gel ($CHCl_3$-MeOH, gradient) to afford isoplagiochin A (**1**)[4](365mg) and B (**2**)[5] (194 mg).

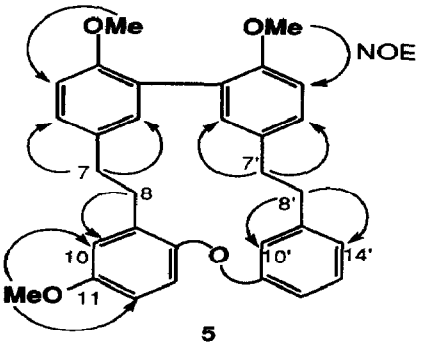
Isoplagiochin A (**1**)($C_{28}H_{22}O_4$) (HRMS: $[M]^+$ m/z 422.1494) indicated the presence of a phenolic hydroxyl group (ν 3194 cm^{-1}) and a benzene ring (ν 1572 cm^{-1}), which was conjugated with a double bond [λ_{max}290 nm (log ε=3.92)]. The ^1H and ^{13}C NMR spectra of **1** showed two benzyl methylene signals [δ2.66(4H, m, 7' and 8'-H_2), δ35.2(C-7), 37.6(C-8)] and *cis*-olefinic protons [δ 6.59, 6.63(each 1H, d, J=9.1Hz, 7 and 8-H)]. The acetylation (Ac_2O, pyridine) and methylation (MeI, K_2CO_3) of **1** afforded a triacetate **3** and a trimethyl ether **4** respectively, indicating the presence of three phenolic hydroxyl groups. The hydrogenation (10%Pd-C/H_2) of **4** afforded a dihydro derivative **5** . The structure of **1** was deduced from careful analysis of the 2D NMR spectra including COSY, HMQC and HMBC of **1**, NOE difference spectra of **4** and **5** , and finally established by X-ray crystallography[6]of **3** as shown in Fig. 1.

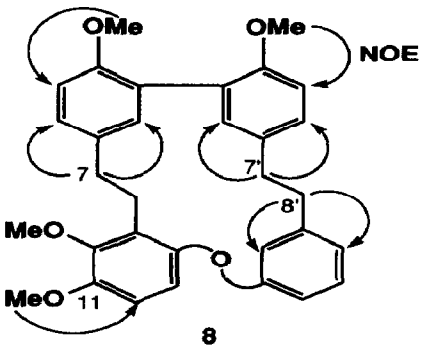
Isoplagiochin B (**2**)($C_{28}H_{22}O_5$) (HRMS: $[M]^+$ m/z 438.1488), has spectral data very similar to those of **1**. Compound **2** gave the tetraacetate **6** on acetylation and methylation affored the tetramethyl ether **7**, which was further converted to **8** by hydrogenation. From the 2D NMR spectra of **2** and NOE experiments on **7** and **8**, the structure of **2** was determined as C-10 hyroxylated derivative of compound **1**.

Plagiochin-type bis(bibenzyls)[7] isolated from *Plagiochila sciophylla* possess a C_1-$C_{2'}$ ether linkage and a C_{14}-$C_{10'}$ biphenyl bond, whereas isoplagiochins A (**1**) and B (**2**) do a C_{14}-$C_{11'}$ ether linkage and a C_6-$C_{2'}$ biphenyl bond. This is the first report of the isolation of macrocyclic bis(bibenzyls) possesing a *cis*-stilbene

and the biphenyl linkage between rings A and C.







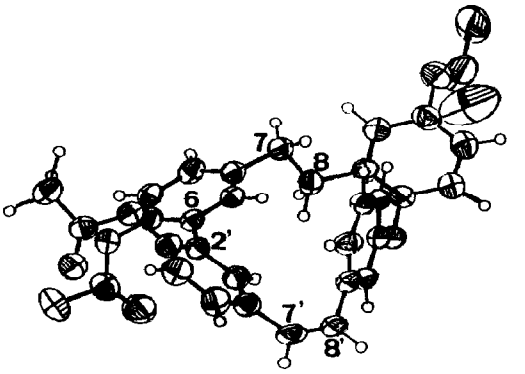


Fig. 1 ORTEP Drawing of 3

References and notes

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2. Y. Asakawa (1993) Biologically Active Terpenoids and Aromatic Compounds from Liverworts and the Inedible Mushroom *Cryptoporus volvatus* in "*Bioactive Natural Products: Detection, Isolation, and Structural Determination*" (S. M. Colegate and R. J. Molyneux eds.) p. 319, CRC Press, Florida.
3. Y. Fukuyama and Y. Asakawa, *Phytochemistry*, **30**, 4061 (1991).
4. HR-MS: *m/z* 422.1494, $C_{28}H_{22}O_4$ requires 422.1518; EI-MS: m/z 422(M^+, 100%), 404, 211; IR(KBr)cm^{-1}: 3194(OH), 1572, 1493, 1200; UV(EtOH) λ_{max}nm (logε): 211(4.51), 290(3.92)
5. HR-MS: *m/z* 438.1488 $C_{28}H_{22}O_5$ requires 438.1467; EI-MS: m/z 438(M^+, 100%), 420; IR(KBr)cm^{-1}: 3285(OH), 1603, 1572, 1235; UV(EtOH) λ_{max}nm (logε): 213(4.66), 282(3.95)
6. The crystal data for **3** are as follows : monoclinic; space group Cc with a=18.001 (3), b=18.688 (3), c=17.251 (4)Å, β=96.95(2)°, V=5761(2)Å^3, Z=8, and μ(Cu K-α)=6.38cm^{-1} by Mac Science MXC 18 instrument. Final R value was 0.054 for 5201 reflections. The supplementary materials have been deposited at the Cambridge Crystallographic Data Centre.
7. T. Hashimoto, M. Tori, Y. Asakawa, and Y. Fukazawa, *Tetrahedron Lett.*, **28**, 6295 (1987).

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