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Structures of Four Novel Macrocyclic Bis(Bibenzyl) Dimers, Pusilatins A-D from the Liverwort *Blasia pusilla*

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Abstract : Four novel macrocyclic bis(bibenzyl) dimers, named pusilatins A-D have been isolated from the liverwort, *Blasia pusilla*, and their structures established by a combination of high resolution NMR spectra, X-ray crystallographic analysis and chemical degradation.

Liverworts are rich sources of both terpenoids and aromatic compounds with biological activities. We have reported the distribution of a numer of new terpenoids and aromatic compounds in more than 100 species of the liverworts.[1] For example, marchantin A, a novel macrocyclic bis(bibenzyl) ether, isolated from the liverwort *Marchantia* species, possesses cytotoxic, 5-lipoxygenase and calmodulin inhibitory activities, and d-tubocurarine-like muscule relaxing activity.[2] In the course of the isolation of the biologically active substances from the liverworts, we isolated four novel macrocyclic bis(bibenzyl) dimers, pusilatins A-D (**1-4**) from the MeOH extract of *Blasia pusilla* belonging to the Blasiaceae. Here we wish to report on the isolation and structure elucidation of **1-4**.

The MeOH extract (27.4 g) of fresh material (1.69 kg) of *B. pusilla* collected in Tokushima in 1992 was subjected repeatedly to column chromatography of Sephadex LH-20 ($CHCl_3$: MeOH = 1 : 1) and of silica gel ($CHCl_3$-MeOH, gradient) to afford pusilatins A (**1**)[3] (29 mg), B (**2**)[4] (146 mg), C (**3**)[5] (246 mg), and D (**4**)[6] (14 mg) as well as known bis(bibenzyls) riccardins C (**5**) (667 mg) and F (**6**) (183 mg).

The IR spectrum of pusilatin A (**1**) ($C_{56}H_{46}O_8$) indicated the presence of phenolic hydroxyl groups (3387 cm^{-1}). The ^{13}C NMR spectrum of **1** showed 28 signals including four benzyl methylene signals (δ 35.7, 37.9, 38.6 and 38.8), which were quite similar to those of riccardin C (**5**). As **1** gave a parent ion peak in the FAB (positive)-MS spectrum at *m/z* 869 $(M+Na)^+$ and 846 $(M)^+$, **1** must be a symmetrical dimer of **5**. The acetylation (Ac_2O, pyridine) of **1** afforded a hexaacetate (**7**), and the methylation gave a hexamethyl ether (**8**). The srructure of **1** was deduced from careful analysis of the 2D NMR spectra including DQF-COSY, HMQC, HMBC and NOESY, and finally established by X-ray crystallography[7] of **7** as shown in Fig. 1. Similarly, the structures of pusilatins B-D (**2-4**) were established by the detailed 2D NMR analyses of them and their derivatives (**9-13**).

Pusilatins A-D is the first example of isolation of macrocyclic bis(bibenzyl) dimers in Nature, which might be one of the important chemical markers of the Blasiaceae.

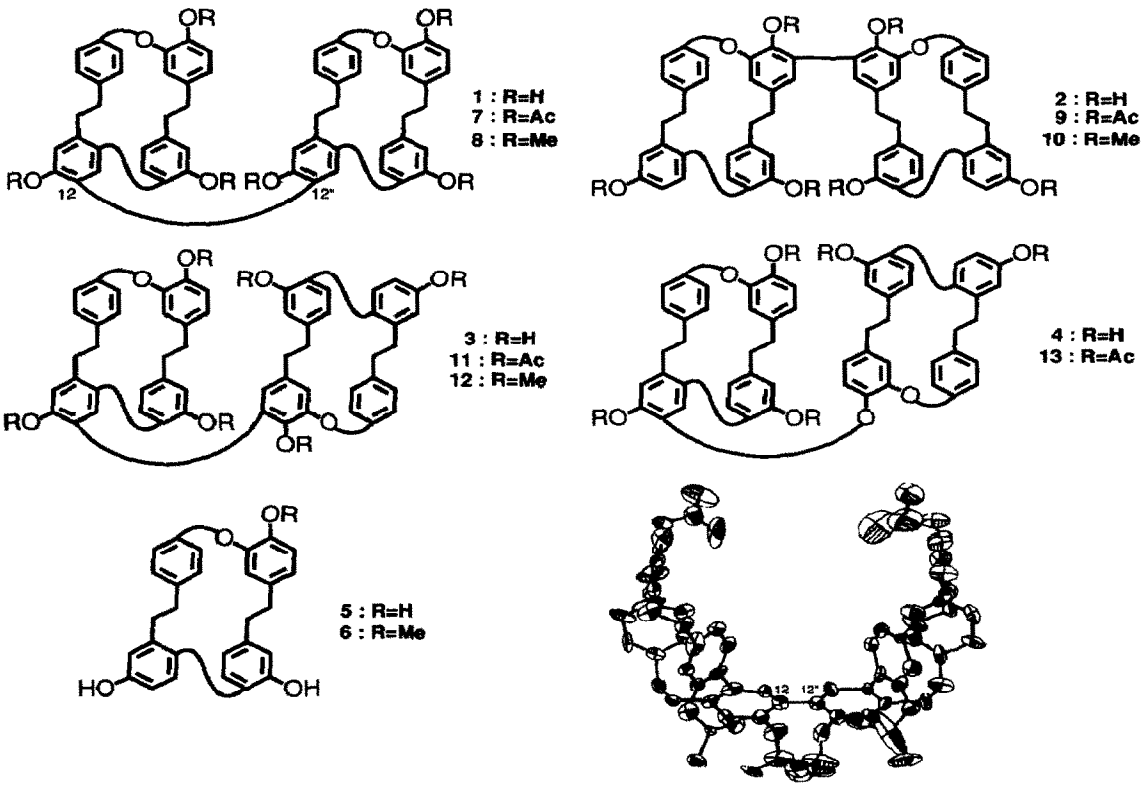

Fig.1 ORTEP Drawing of 7

Acknowledgements We thank Dr. M. Mizutani (The Hattori Botanical Laboratory, Nichinan, Japan) for the identification of *B.pusilla*.

References and notes

1. Y. Asakawa (1982) Chemical Constituents of Hepaticae in "*Progress in the Chemistry of Organic Natural Products*"(W. Herz, H. Grisebach, and W. G. Kirby eds.) Vol. **42**, P. 1, Springer, Wien.
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. FAB-MS: *m/z* 869(M+Na)$^+$, 846(M)$^+$; UV(EtOH) λ_{max} nm (logε): 212(4.62), 240(4.49), 288(4.10); IR(KBr)cm^{-1}: 3387(OH), 1611, 1562, 1504, 1223, 1111.
4. mp 293.0-293.5°; FAB-MS: *m/z* 869(M+Na)$^+$, 846(M)$^+$; UV(EtOH) λ_{max} nm (logε): 227(4.12), 285(2.81); IR(KBr)cm^{-1}: 3399(OH), 1616, 1504, 1423, 1336, 1223.
5. FAB-MS: *m/z* 869(M+Na)$^+$, 846(M)$^+$; UV(EtOH) λ_{max} nm (logε): 215(4.11), 240(4.72); IR(KBr)cm^{-1}: 3433(OH), 1711, 1608, 1505, 1433, 1221.
6. FAB-MS: *m/z* 846(M)$^+$; IR(KBr)cm^{-1}; UV(EtOH) λ_{max} nm (logε): 214(4.66), 285(3.91); 3437(OH), 1605, 1507, 1433, 1271, 1227.
7. The crystal data for **7** are as follows : monoclinic; space group Cc with a=30.483 (6), b=14.330 (3), c=17.106 (3)Å, β=122.86(1)°, V=6277(2)Å^3, Z=4, and μ(Cu K-α)=5.86cm^{-1} by Mac Science MXC 18 instrument. Final R value was 0.102 for 3759 reflactions. The supplementary materials have been deposited at the Cambridge Crystallographic Data Centre.

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