FIVE NEW DIARYLHEPTANOIDs FROM THE MALE FLOWERS OF ALNUS SIEBOLDIANA

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Five new diarylheptanoids, yashabushidiol A and B, yashabushiketodiol A and B, and yashabushitriol, have been isolated from the male flowers of Alnus sieboldiana MATSUM. and their absolute structures determined by spectral methods and chemical transformations to known yashabushiketol and dihydroyashabushiketol.

KEYWORDS—Alnus sieboldiana; yashabushidiol A; yashabushidiol B; yashabushiketodiol A; yashabushiketodiol B; yashabushitriol; structure elucidation; diarylheptanoid

The isolation of diarylheptanoids, stilbenes, flavonoids, and triterpenes from the male flowers of Alnus sieboldiana MATSUM. (Betulaceae) has been recorded.1-6 We are interested in the characteristic aroma and the viscous nature of this plant. In a continuation of the chemical study of this family of plants, we have isolated five new diarylheptanoids (1-5) from the male flowers of A. sieboldiana, which were collected in Tokushima prefecture just before the flowering season. This paper describes the structures of 1-5.

The fresh male flowers of A. sieboldiana (9.2 kg) were homogenized with hexane and the hexane extract was subjected to silica-gel column chromatography to give 1 (257 mg), 2 (309 mg), 3 (4.4 g), 4 (143 mg), and 5 (252 mg).

Yashabushidiol A (1) [mp 80-81°C, [α]D=+0° (CHCl_3)] and yashabushidiol B (2) [mp 92-93°C, [α]D=+7.2° (CHCl_3)] showed the molecular formula, C_{19}H_{24}O_{2} [m/z 285.1855 (M+1)^+ for 1, m/z 285.1844 (M+1)^+ for 2], by chemical ionization high resolution mass spectrometry (CI-HRMS).7 The 1H NMR and 13C NMR spectra8 of 1 and 2 revealed two oxygen-bearing methine groups [1: δ_H 3.84 (H-3 and H-5), δ_C 72.3 (C-3 and C-5); 2: δ_H 3.97 (H-3 and H-5), δ_C 68.9 (C-3 and C-5)]. These data are very similar to those of dihydroyashabushiketol (6)3,5 and indicate that both 1 and 2 are 1,7-diphenylheptane-3,5-diols. In order to determine the stereochemistries, 6 was reduced with NaBH_4 to give 1 and 79 after chromatographic separation. As the specific rotation of 1 is [α]D=+0°, 1 must be a meso compound and therefore 7 [mp 91-92°C, [α]D=−7.3°(CHCl_3)] should have the
Table. $^{13}$C NMR Data of Compounds 1-6 and 9-10

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<th>4</th>
<th>5</th>
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<th>9</th>
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<td>68.0$^*$</td>
<td>67.6$^*$</td>
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$^*$,$^+$ Assignments may be interchanged in each vertical column.

![Chemical structures](attachment:image.png)
structure shown,\textsuperscript{10} because the absolute stereochemistry of 6 has been established to be $\pm$.\textsuperscript{3,5} The spectral data of 2 were in fair agreement with those of 7 except for the sign of the rotation. Thus, 1 is meso-1,7-diphenylheptane-3,5-diol and 2 was established to be 1,7-diphenylheptane-$(3R),(5S)$-diol.

The molecular formula of both yashubushiketodiol A (3) [mp 62-63°C, $[\alpha]_D^{15}=+57.5^\circ$(CHCl$_3$) and $+21.4^\circ$(MeOH)] and yashubushiketodiol B (4) [mp 60-61°C, $[\alpha]_D^{15}=-28.6^\circ$(CHCl$_3$) and $-16.3^\circ$(MeOH)] was determined by Cl-HRMS to be C$_{19}$H$_{22}$O$_3$ [m/z 299.1592 (M+1)$^+$ for 3 and m/z 299.1660 (M+1)$^+$ for 4]. The IR spectra of 3 and 4 indicated the presence of hydroxyl (3520 and 3380 cm$^{-1}$) and carbonyl (1695 cm$^{-1}$) groups. The $^1$H and $^{13}$C NMR spectra of 3 and 4 showed two oxygen-bearing methine groups [3: $\delta_H$ 4.05 (m, H-5) and 5.12 (dd, J=9.5 and 3.2 Hz, H-1), $\delta_C$ 66.8 (d, C-5) and 69.8 (d, C-1); 4: $\delta_H$ 4.05 (m, H-5) and 5.15 (dd, J=9.5 and 3.2 Hz, H-1), $\delta_C$ 67.0 (d, C-5) and 70.2 (d, C-1)]. Comparison of the $^{13}$C NMR spectra of 3 and 4 with that of dihydroyashubushiketol (6) (Table) suggests that the diols are the C-1 epimers of 1,7-diphenylheptan-3-one-1,5(S)-diol. This is confirmed by the formation of yashubushiketol acetate (8) ($[\alpha]_D^{15}=-15.2^\circ$(CHCl$_3$)$^5$) upon acetylation (Ac$_2$O/Py/rt) of either 3 or 4. Hydrogenolysis (H$_2$/Pd-C) of both 3 and 4 afforded dihydroyashubushiketol (6) ($[\alpha]_D^{15}=+16.1^\circ$ from 3 and $+15.1^\circ$ from 4). The stereochemistries of the C-1 of 3 and 4 were established as follows.

Reduction of 3 with NaBH$_4$ gave a mixture of two triols, which was further treated with 2,2-dimethoxypropane in the presence of p-TsOH affording two acetones, 9 and 10, after chromatographic separation. As it is expected that only two acetones, in which the large substituents occupy the equatorial positions, will be formed as illustrated in the Fig., 9 and 10 are inferred to have the structures as shown. When the proton at C-1 ($\delta_H$ 4.92) of 9 was irradiated, H-3 ($\delta_H$ 4.36) and the methyl group (H 1.57) showed a large NOE. Similar NOE's were detected between H-3, H-5, and the axial methyl group of 10. The final evidence was obtained by hydrogenolysis (H$_2$/Pd-C) of 9 and 10 in ACOH giving 7 and 1, respectively. Thus, the stereochemistries of C-1 of 3 and 4 were unambiguously established to be $R$ and $S$, respectively.

The $^1$H and $^{13}$C NMR spectra of yashubushitriol (5) (mp 89-90°C, $[\alpha]_D^{15}=-30.3^\circ$(CHCl$_3$), C$_{19}$H$_{24}$O$_3$, m/z 300.1728 (M)$^+$ by HRMS) showed three oxygen-bearing methine
groups ($\delta_H$ 4.92 (dd, J=10.3 and 2.4 Hz, H-1), 4.30 (m, H-3), and 3.96 (m, H-5); $\delta_C$ 74.6 (C-1), 69.6 (C-3), and 68.1 (C-5)). The acetonide 2 obtained from 1 (vide supra) afforded 5 [mp 88.5-90°C, [$\alpha$]D=+29.5°(CHCl3)] on treatment with 60% AcOH. From these results the structure of 5 was determined to be 1,7-diphenylheptane-(1R),(3R),(5S)-triol.

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REFERENCES AND NOTES
7) High resolution mass spectra were measured on a JEOL JMS HX-100 spectrometer.
8) NMR spectra were taken on a JEOL JNM GX-400 spectrometer.
10) Although the isolation of compound 7 ($[\alpha]$D=--10°(CHCl3) has been reported, the stereochemistry was not determined.

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