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THE ABSOLUTE CONFIGURATION OF DIARYLHEPTANOID XYLOSIDE, OREGONIN, ISOLATED FROM THE FEMALE FLOWERS OF *ALNUS SERRULATOIDES*

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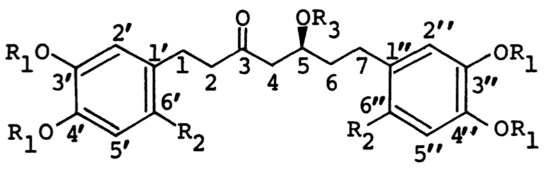
It was found that (-)-diarylheptanoid xyloside isolated from the female flowers of *Alnus serrulatoides* is 1,7-bis(3,4-dihydroxyphenyl)-5-(β-D-xylopyranosyloxy)-3-heptanone, and its spectral data and chemical behaviors coincides perfectly with those of previously reported oregonin whose absolute configuration had not been clarified yet. Then, the absolute configuration of the diarylheptanoid xyloside was investigated by a combination of the ^{13}C NMR spectroscopy and the X-ray crystallography, and established to be *S*.

In our previous studies, we have isolated novel five C_{31}-dammarane-type triterpenoids, such as alnuserol,[1)] alnuseric acid,[2)] alnuselide,[2)] alnuserrudiolone,[3)] and alnuserrutriol,[4)] from the male flowers of *Alnus serrulatoides* CALL. (Japanese name: Kawara-hannoki) and four monoglycosides of alnustic acid[5)] from the female flowers of that plant, and elucidated their structures. In a continuation of the structural elucidation of the chemical constituents, we newly isolated a diarylheptanoid glycoside (1) from the female flowers, and found all the spectral data and chemical behaviors of the diarylheptanoid glycoside to be coincident with those of previously reported oregonin[6)] whose absolute configuration had not been clarified yet. We have now established the absolute configuration as well as the structure of the diarylheptanoid glycoside (1), and here wish to communicate the evidence.

The diarylheptanoid glycoside (1) was isolated from the acetone extract of the female flowers (444 g) by centrifugal chromatography on a silica-gel plate (5 mm in thickness and 30 cm in diameter) with $CHCl_3$-MeOH-H_2O (85:14:1 v/v), as a pale yellow oil: 14.9 g; R_f 0.30 on an analytical silica-gel plate (0.25 mm thick) with $CHCl_3$-MeOH-H_2O (30:9:1 v/v); $[\alpha]_D^{25}$ $-19.6° \pm 0.1°$ (*c* 13.0, MeOH); UV_{max} (EtOH) 222 (log ε 4.07) and 283 nm (3.75); IR (neat) 3360 (OH), 1702 (C=O), and 1608 and 1510 cm^{-1} (aromatic ring); ^1H NMR (C_5D_5N) δ=2.0 and 2.8 (2H and 8H, each



1 $R_1=R_2=H$, R_3=β-D-xylopyranose
2 $R_1=R_2=R_3=H$
3 R_1=Me, R_2=H, R_3=β-D-xylopyranose
4 R_1=Me, R_2=H, R_3=H
5 R_1=Me, R_2=Br, R_3=H

m, >CH_2 × 5), 4.63 (1H, d, J=7 Hz, anomeric H), and 6.58—7.15 (6H, m, aromatic protons); ^{13}C NMR (C_5D_5N) δ_C=209.1 (s, C-3), 103.7 (d, anomeric C), 75.2 (d, C-5), 47.8 (t, C-4), and 37.8 (t, C-6); FD-MS m/z 501 ($[M + Na]^+$) and 328 ($[M - 150]^+$). Hydrolysis of **1** with Taka-diastase$^{7)}$ (Sankyo Co. Ltd.) gave xylopyranose and its aglycone (**2**): $[\alpha]_D^{25}$ -1.7° ± 0.3° (*c* 0.78, MeOH); ^{13}C NMR (C_5D_5N) δ_C=67.3 (d, C-5), 51.2 (t, C-4), and 40.5 (t, C-6). The above-described spectral data and the chemical behaviors indicate that the aglycone (**2**) is 1,7-bis(3,4-dihydroxyphenyl)-5-hydroxy-3-heptanone and the xylopyranose links to the 5-position of **2**. On the basis of the application of Klyne's rule$^{8)}$ to the $[M]_D$ value (-87.7 °) of the xylopyranose evaluated by use of the $[M]_D$ values of **1** and **2**, it became clear that D-xylopyranose links to the aglycone (**2**) by the β-glycosidic linkage.$^{9)}$ The diarylheptanoid glycoside (**1**) was thus found to be 1,7-bis(3,4-dihydroxyphenyl)-5-(β-D-xylopyranosyloxy)-3-heptanone. Then, comparisons of the spectral data were made, and the spectra (UV, IR, ^1H NMR, and EI- and/or FD-MS) of its tetramethyl ether (**3**) [$[\alpha]_D^{25}$ -20.2° ± 0.7° (*c* 0.59, MeOH)$^{10)}$] and its aglycone (**2**) were found to be coincident with the spectral data of oregonin tetramethyl ether$^{6)}$ and hirsutanonol.$^{11)}$ Although oregonin and hirsutanonol have an asymmetric carbon, however, even the optical rotation, needless to mention the absolute configuration, has not been given in Refs. 6 and 11.$^{12)}$

Then, the absolute configuration of the diarylheptanoid xyloside (**1**) was first investigated by the ^{13}C NMR spectroscopy. On comparison of the ^{13}C NMR chemical shifts of **1** with those of **2**, the larger glycosidation shift (-3.4 ppm) at C-4 than that (-2.7 ppm) at C-6 was observed. Application of the glycosidation shift rule$^{13)}$ to these shifts indicated the configuration at C-5 of **1** to be *S*.$^{13)}$ The similar glycosidation shifts were also observed in comparison of the chemical shifts at C-4 and C-6 of **3** with those of its aglycone (**4**) [$[\alpha]_D^{25}$ -2.3°±0.1° (*c* 1.85, MeOH)$^{10)}$]. This observation further supported the *S*-configuration at C-5 of **1**.

The absolute configuration of **1** was finally established by the X-ray crystallography of the dibromo tetramethyl ether (**5**) [mp 93°C; $[\alpha]_D^{25}$ -1.3° ± 0.2°(*c* 0.92, MeOH)$^{10)}$; Found: C, 49.11; H, 5.03; Br, 28.50%.] derived from **4** by bromination with $Br_2/CHCl_3$.$^{14)}$ Occurrence of the bromination at C-6' and C-6'' on the aromatic rings was indicated by the ^1H NMR ($CDCl_3$) signals at δ 6.78 and 7.00 (each 2H, brs and s, aromatic H) and the ^{13}C NMR ($CDCl_3$) signal at δ_C 113.8 (s, C-6' and C-6''). This dibromo tetramethyl ether (**5**) was crystallized from benzene-hexane to give the single-crystals for the X-ray analysis. Crystal data: $C_{23}H_{28}O_6Br_2$; *M*=560.35; monoclinic (space group $P2_1$); *Z*=2 per unit cell with dimensions *a*=4.720(1), *b*=18.806(7), *c*=13.651(6) Å, β=98.65(3)°; *U*=1198 $Å^3$; *Dc*=1.55 $g\cdot cm^{-3}$; *Dm*=1.52 $g\cdot cm^{-3}$; μ(Mo-Kα)=36.0 cm^{-1}. A total of 2355 reflections were collected on a Syntex R3 diffractometer with graphite-monochromated radiation by use of the ω-scan technique ($2\theta_{max}$=50.0°); 1860 reflections with intensities greater than 1.96 times of the standard deviations were used in the structure determination. The structure was solved by the heavy atom method on the basis of the bromine position derived from a sharpened Patterson function, and the positions of oxygen, carbon, and hydrogen atoms were determined by difference-Fourier syntheses. A least-squares refinement was carried out by use of anisotropic

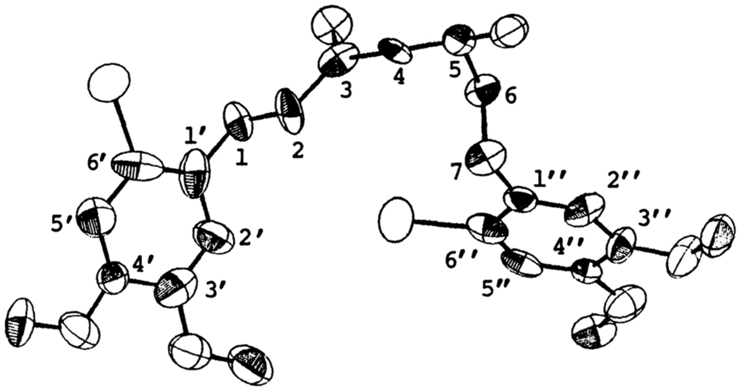


Fig. 1. ORTEP drawing[17] of the molecular structure of dibromo tetramethyl ether (5). The atoms indicated with ◐, ⊕, and ○ denote carbon, oxygen, and bromine atoms, respectively.

Table 1. Bijvoet inequalities

h	*k*	*l*	<|Fc|>	<|Fo|>	Δ|Fo|[a]	Δ|Fc|[b]	|S|[c]
0	1	2	68.5	66.0	12.9	12.3	34
0	4	0	88.8	99.2	9.4	8.9	20
0	6	0	35.2	36.1	-10.3	-8.7	19
1	1	1	65.9	73.8	10.7	8.8	18
0	5	2	65.7	73.8	-9.3	-5.8	17
1	1	3	45.8	55.9	9.2	7.3	16
1	1	-1	33.8	38.7	6.8	5.4	15
1	5	-3	50.0	55.9	-8.7	-7.9	15
0	8	0	42.5	46.7	-7.2	-6.0	14
1	3	0	33.1	40.4	7.3	6.1	13
2	1	1	29.8	35.2	5.0	4.5	13
2	1	5	54.0	59.5	7.8	5.5	13
0	4	1	74.3	82.8	4.1	3.4	12
1	2	-6	52.8	58.4	-7.9	-6.8	12
2	1	-6	28.3	30.3	5.3	4.5	12
0	4	3	90.6	105.0	4.3	3.9	11
0	6	2	14.3	14.9	-6.6	-4.7	10
1	1	4	54.0	58.4	5.6	4.5	10
1	7	-2	39.3	44.2	4.9	5.4	10
2	6	-2	51.3	56.6	7.8	6.5	10
0	2	5	47.3	48.2	-4.1	-3.4	9
1	2	-3	61.2	66.4	-5.2	-4.6	9
1	2	0	63.1	67.9	3.7	4.6	9
2	7	-4	31.3	35.6	-5.5	-5.5	9
2	7	0	31.1	34.3	-6.5	-5.5	9
0	3	7	68.1	71.9	4.3	3.7	8
1	1	-3	64.0	72.3	5.7	4.1	8
1	1	0	95.4	106.8	6.1	5.3	8
1	3	5	22.8	23.9	5.1	5.1	8
1	5	-4	32.3	37.5	3.9	4.2	8

a) $\Delta|Fo| = |Fo(hkl)| - |Fo(\bar{h}\bar{k}\bar{l})|$
b) $\Delta|Fc| = |Fc(hkl)| - |Fc(\bar{h}\bar{k}\bar{l})|$
c) $|S| = ||Fc(hkl)| - |Fc(\bar{h}\bar{k}\bar{l})||/\sigma(Fo)$

temperature factors for bromine, carbon, and oxygen atoms and isotropic ones for hydrogen atoms. The absolute configuration was determined by use of the anomalous dispersion effect of bromine and oxygen atoms for Mo-$K\alpha$ radiation.[15] The final refinements for two absolute configurations reduced the R factor to 0.068 for the *S* configuration and to 0.088 for the *R* configuration. The comparison of these R factors[16] indicated the absolute configuration of 5 to be *S*, as shown in Fig. 1. At the stage of the R factor of 0.068, the observed and calculated Bijvoet inequalities[18] for 30 pairs of reflections having the largest $||Fc(hkl)| - |Fc(\bar{h}\bar{k}\bar{l})||/\sigma(Fo)$ values were in good agreement with each other, as shown in Table 1. This observation established the absolute configuration of 5 to be *S*. Thus, the structure of the dibromo tetramethyl ether (5) derived from 1 was determined to be (5*S*)-1,7-bis(6-bromo-3,4-dimethoxyphenyl)-5-hydroxy-3-heptanone.

Consequently, the absolute configuration of the diarylheptanoid xyloside isolated from *Alnus serrulatoides* was established to be *S* and the structure was characterized as (5*S*)-1,7-bis(3,4-dihydroxyphenyl)-5-(β-D-xylopyranosyloxy)-3-heptanone (1).

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