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Absolute Structure of Ionol Glucoside: A Single-Crystal X-Ray Analysis of Dendranthemoside A Pentaacetate

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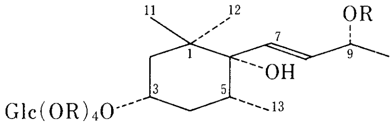
By means of single crystal X-ray analysis of dendranthemoside A pentaacetate, the absolute configuration of the asymmetric center at the 9-position was determined to be *R*. The configurations of three other positions, which had been determined to be 3*S*, 5*R* and 6*S* by application of β-D-glucosylation induced shift trends, were verified.

Keywords *Dendranthema shiwogiku*; Asteraceae; dendranthemoside A pentaacetate; megastigmane; ionol glucoside; X-ray analysis

Dendranthemoside A (**1**) was first isolated from the aerial parts of *Dendranthema shiwogiku* (Asteraceae), collected on Shikoku Island. The planar and relative structures of dendranthemoside A were determined by a combination of one- and two-dimensional NMR spectroscopies.[1)] The absolute stereochemistry of the 3-position was deduced to be *S* from an empirical rule described by Kasai *et al.*[2)] and that of the 5-position was concluded to be *R* from the relative relationships of protons revealed by NMR spectral examinations. By the precise inspection of nuclear Overhauser effects between the protons around the 6-position, the configuration at the 6-position was concluded to be *S*. As the range of applicability of the rule has not been fully established, some ambiguity remained in the absolute stereochemistry of the substituents on the six-membered ring, and the absolute configuration of the 9-position also remained to be determined. Thus, we decided to solve the structure by X-ray diffraction analysis.



Glc : β-D-glucopyranosyl
1 : R=H (dendranthemoside A)
2 : R=Ac

Dendranthemoside A was acetylated in a usual manner to give the corresponding pentaacetate (**2**) and a suitable crystal was grown by slow evaporation of an EtOH solution. Crystal data are as follows: monoclinic, space group $P2_1$; $a=5.934$ (3), $b=21,096$ (3), $c=13.236$ (2) Å; $\beta=101.17$ (2)°; $V=1625.6$ (8) Å^3; $Z=2$; $D_X=1.227$ g/cm^3.

A computer-generated perspective drawing is shown in Fig. 1. Since the absolute structure of the glucose has already been determined to be in the D-series, the absolute configurations of the 3-, 5- and 6-positions were respectively determined to be *S*, *R* and *S*, which are consistent with those deduced from the NMR spectra.[1)] Finally, the absolute configuration of the remaining 9-position was found to be *R*. The fractional atomic coordinates with equivalent isotropic thermal parameters, bond lengths and bond angles are listed in Tables I, II and III.

Experimental

The melting point was determined with a Yanagimoto micro melting apparatus and is uncorrected. UV and IR spectra were taken with a Shimadzu UV-160S spectrophotometer and a Shimadzu IR-408 spectrophotometer, respectively. NMR spectra were recorded with a JEOL GX-400 spectrometer. Chemical shifts are given in δ values using tetramethylsilane as an internal standard. Optical rotation was determined with a Union Giken PM-101 digital polarimeter. Mass spectra were determined with a JEOL SX-102 spectrometer.

Dendranthemoside A Pentaacetate (2) Dendranthemoside A used was obtained previously.[1)] Dendranthemoside A (**1**) (30 mg) was treated with 0.5 ml each of acetic anhydride and pyridine for 18 h at 20 °C. The reaction mixture was poured into iced water and triturated to give a solid. The precipitates were collected by filtration (37 mg) and crystallized from EtOH to give colorless plates. mp 123—124 °C, $[\alpha]_D^{25}$ +23.0° ($c=0.43$, MeOH). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3500, 2950, 1750, 1725, 1440, 1370, 1225, 1040. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm (log ε): 202 (3.64). ^{1}H-NMR (CDCl$_3$, 400 MHz) δ: 0.77 (3H, d, $J=7$ Hz, 13-H$_3$), 0.85 (3H, s, 11- or 12-H$_3$), 0.96 (3H, s, 12- or 11-H$_3$), 1.32 (3H, d, $J=6$ Hz, 9-H$_3$), 1.44 (H, ddd, $J=2, 5, 12$ Hz, 2-H$_{eq}$), 1.45 (H, q, $J=12$ Hz, 4-H$_{ax}$), 1.59 (H, t, $J=12$ Hz, 2-H$_{ax}$), 1.90 (H, ddd, $J=4, 7, 12$ Hz, 5-H),

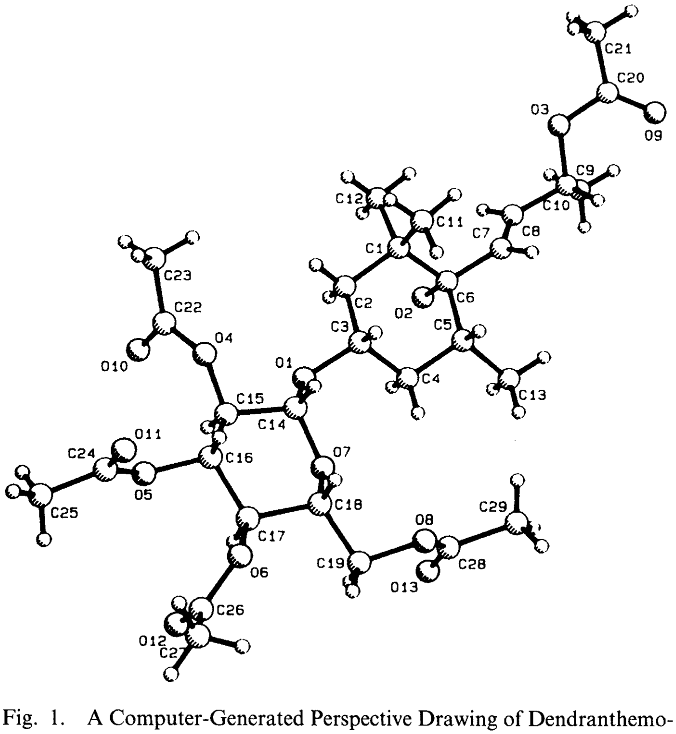


Fig. 1. A Computer-Generated Perspective Drawing of Dendranthemoside A Pentaacetate (**2**)

Table I. Fractional Atomic Coordinates and Equivalent Isotropic Thermal Parameters of Non-H Atoms with e.s.d.'s in Parentheses

Atom	x	y	z	B_{eq}
O(1)	0.870 (1)	0.6940 (5)	1.1250 (6)	4.3 (4)
O(2)	0.841 (1)	0.7405	1.4566 (6)	3.8 (4)
O(3)	0.317 (2)	0.8994 (5)	1.5971 (6)	4.4 (5)
O(4)	0.926 (2)	0.7474 (5)	0.9348 (6)	4.2 (5)
O(5)	1.036 (1)	0.6433 (6)	0.8010 (6)	4.0 (4)
O(6)	0.658 (2)	0.5528 (6)	0.7741 (7)	5.4 (5)
O(7)	0.723 (2)	0.6039 (6)	1.0392 (7)	4.8 (5)
O(8)	0.343 (2)	0.5181 (6)	1.0247 (8)	7.0 (7)
O(9)	0.003 (2)	0.8921 (6)	1.6649 (8)	6.0 (6)
O(10)	1.297 (2)	0.7592 (7)	0.980 (1)	9.8 (9)
O(11)	0.817 (2)	0.6813 (7)	0.6590 (7)	7.8 (7)
O(12)	0.952 (3)	0.492 (1)	0.760 (2)	15 (1)
O(13)	0.564 (3)	0.469 (1)	1.151 (1)	13 (1)
C(1)	0.668 (2)	0.8055 (7)	1.312 (1)	3.3 (6)
C(2)	0.818 (2)	0.7767 (7)	1.2423 (9)	3.5 (6)
C(3)	0.714 (2)	0.7180 (7)	1.1890 (9)	3.8 (7)
C(4)	0.676 (2)	0.6670 (7)	1.269 (1)	4.2 (7)
C(5)	0.521 (2)	0.6945 (8)	1.336 (1)	4.4 (7)
C(6)	0.617 (2)	0.7572 (7)	1.3909 (9)	3.1 (6)
C(7)	0.464 (2)	0.7805 (7)	1.459 (1)	3.3 (6)
C(8)	0.518 (2)	0.8117 (7)	1.545 (1)	3.8 (7)
C(9)	0.362 (2)	0.8324 (8)	1.613 (1)	4.2 (8)
C(10)	0.465 (3)	0.8207 (9)	1.725 (1)	6.5 (9)
C(11)	0.449 (2)	0.8321 (8)	1.248 (1)	4.7 (7)
C(12)	0.805 (2)	0.8620 (7)	1.367 (1)	4.4 (7)
C(13)	0.474 (3)	0.6414 (9)	1.412 (1)	6.3 (8)
C(14)	0.765 (2)	0.6703 (8)	1.0291 (9)	3.7 (7)
C(15)	0.931 (2)	0.6798 (7)	0.956 (1)	3.7 (7)
C(16)	0.847 (2)	0.6462 (8)	0.8564 (9)	3.3 (6)
C(17)	0.777 (2)	0.5769 (7)	0.872 (1)	4.3 (7)
C(18)	0.603 (3)	0.5756 (8)	0.946 (1)	5.1 (8)
C(19)	0.525 (3)	0.5101 (9)	0.965 (1)	7 (1)
C(20)	0.129 (3)	0.924 (1)	1.626 (1)	5.4 (9)
C(21)	0.106 (4)	0.992 (1)	1.607 (2)	10 (1)
C(22)	1.114 (3)	0.783 (1)	0.956 (1)	5.3 (9)
C(23)	1.071 (3)	0.8510 (9)	0.941 (1)	8 (1)
C(24)	0.995 (3)	0.6611 (7)	0.702 (1)	4.1 (8)
C(25)	1.195 (3)	0.649 (1)	0.653 (1)	7 (1)
C(26)	0.770 (5)	0.509 (1)	0.724 (2)	8 (1)
C(27)	0.616 (5)	0.496 (1)	0.627 (2)	12 (2)
C(28)	0.398 (4)	0.497 (1)	1.117 (2)	8 (1)
C(29)	0.212 (3)	0.507 (1)	1.178 (1)	7 (1)

e.s.d., estimated standard deviations. $B_{eq}=(8/3)\pi^2\Sigma_i\Sigma_jU_{ij}\boldsymbol{a}_i^*\boldsymbol{a}_j^*a_ia_j$.

1.82 (H, br d, $J=12$ Hz, 4-H_{eq}), 2.00, 2.02, 2.03, 2.04, 2.08 (3H each, each s, $C\underline{H}_3CO$– ×5), 3.70 (H, ddd, $J=2$, 5, 10 Hz, 5′-H), 3.81 (H, tt, $J=5$, 12 Hz, 3-H), 4.14 (H, dd, $J=2$, 12 Hz, 6′-H_b), 4.25 (H, dd, $J=5$, 12 Hz, 6′-H_a), 4.58 (H, d, $J=8$ Hz, 1′-H), 4.94 (H, dd, $J=8$, 10 Hz, 2′-H), 5.07 (H, t, $J=10$ Hz, 4′-H), 5.20 (H, t, $J=10$ Hz, 3′-H), 5.36 (H, qui, $J=6$ Hz, 9-H), 5.61 (H, d, $J=16$ Hz, 7-H), 5.67 (H, dd, $J=6$, 16 Hz, 8-H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 15.76 (13-C), 20.55, 20.56, 20.65, 20.67 (×2) ($\underline{C}H_3CO$– ×5), 21.27 (9-C), 24.48 (11-C),[a)] 25.10 (12-C),[a)] 34.12 (5-C), 36.75 (4-C), 39.39 (1-C), 41.71 (2-C), 62.45 (6′-C), 69.04 (4′-C), 70.82 (9-C), 71.87 (2′-C),[b)] 71.95 (3′-C),[b)] 73.16 (5′-C), 75.11 (3-C), 76.91 (6-C), 99.45 (1′-C), 130.28 (7-C), 135.90 (8-C), 169.14, 169.36, 170.20, 170.23, 170.51 ($CH_3\underline{C}O$–×5), assignments with the same superscripts may be interchanged. FAB-MS (*m*-nitrobenzyl alcohol) *m*/*z*: 661 $[M+H]^+$, 623 $[M+Na]^+$ (+NaI), 639 $[M+K]^+$ (+KI). *Anal.* Calcd for $C_{29}H_{44}O_{13}$: C, 57.99; H, 7.38. Found: C, 58.44; H, 7.27.

Single-Crystal X-Ray Analysis A suitable crystal was grown in EtOH by slow and spontaneous evaporation of the solvent. A colorless plate crystal with dimensions of 0.40×0.40×0.10 mm was used for X-ray measurements on a Rigaku AFC5S diffractometer with graphite monochromated MoK_α radiation [$\lambda=0.71069$ Å, $\mu=0.90\ \text{cm}^{-1}$, $F(000)=644$]. Cell constants were determined from 25 well-centered reflections in the range of $25.0<2\theta<28.6°$. Intensity data were collected to a maximum 2θ of 45.1° by the $\omega/2\theta$ scan technique with the ω scan range $(0.84°+0.30° \tan\theta)$ at a rate of 32.0°/min (in ω). The total number of independent reflections measured was 2228, of which 1344 were considered to be observed [$I\geqq 2.0\,\sigma(I)$]. The data were corrected for Lorentz polarization factors, but not for absorption. The structure was solved by direct methods using MITHRIL[3)] and DIRDIF,[4)] and the positions of all H atoms were calculated geometrically. $\Sigma\omega\ (|F_O|-|F_C|)$ was minimized with $\omega=4|F_O|^2/\sigma^2(|F_C|^2)$. The hydrogens were included in the calculation of the structure factors, but their parameters were not refined. The structure

Table II. Bond Lengths (Å) of Non-H Atoms with e.s.d.'s in Parentheses

Atom	Atom	Distance	Atom	Atom	Distance
O1	C3	1.46 (1)	C1	C11	1.52 (2)
O1	C14	1.39 (1)	C1	C12	1.54 (2)
O2	C6	1.48 (1)	C2	C3	1.50 (2)
O3	C9	1.44 (2)	C3	C4	1.55 (2)
O3	C20	1.35 (2)	C4	C5	1.52 (2)
O4	C15	1.45 (2)	C5	C6	1.56 (2)
O4	C22	1.32 (2)	C5	C13	1.56 (2)
O5	C16	1.45 (1)	C6	C7	1.49 (2)
O5	C24	1.34 (1)	C7	C8	1.30 (2)
O6	C17	1.44 (2)	C8	C9	1.48 (2)
O6	C26	1.38 (2)	C9	C10	1.51 (2)
O7	C14	1.44 (2)	C14	C15	1.52 (2)
O7	C18	1.43 (2)	C15	C16	1.50 (2)
O8	C19	1.47 (2)	C16	C17	1.55 (2)
O8	C28	1.28 (2)	C17	C18	1.55 (2)
O9	C20	1.20 (2)	C18	C19	1.49 (2)
O10	C22	1.18 (2)	C20	C21	1.45 (2)
O11	C24	1.18 (1)	C22	C23	1.46 (2)
O12	C26	1.15 (3)	C24	C25	1.48 (2)
O13	C28	1.16 (2)	C26	C27	1.46 (3)
C1	C2	1.53 (2)	C28	C29	1.50 (2)
C1	C6	1.53 (2)			

Table III. Intramolecular Bond Angles (°) of Non-H Atoms with e.s.d.'s in Parentheses

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
C3	O1	C14	115.4 (9)	C8	C9	C10	112 (1)
C9	O3	C20	118 (1)	O1	C14	O7	109 (1)
C15	O4	C22	122 (1)	O1	C14	C15	108 (1)
C16	O5	C24	118 (1)	O7	C14	C15	110 (1)
C17	O6	C26	118 (1)	O4	C15	C14	105 (1)
C14	O7	C18	113 (1)	O4	C15	C16	108 (1)
C19	O8	C28	113 (1)	C14	C15	C16	111 (1)
C2	C1	C6	111 (1)	O5	C16	C15	108 (1)
C2	C1	C11	110 (1)	O5	C16	C17	106 (1)
C2	C1	C12	106 (1)	C15	C16	C17	113 (1)
C6	C1	C11	112 (1)	O6	C17	C16	108 (1)
C6	C1	C12	110 (1)	O6	C17	C18	107 (1)
C11	C1	C12	107 (1)	C16	C17	C18	109 (1)
C1	C2	C3	112 (1)	O7	C18	C17	105 (1)
O1	C3	C2	108 (1)	O7	C18	C19	111 (1)
O1	C3	C4	110 (1)	C17	C18	C19	113 (1)
C2	C3	C4	111 (1)	O8	C19	C18	106 (1)
C3	C4	C5	109 (1)	O3	C20	O9	121 (2)
C4	C5	C6	113 (1)	O3	C20	C21	113 (2)
C4	C5	C13	108 (1)	O9	C20	C21	126 (2)
C6	C5	C13	114 (1)	O4	C22	O10	120 (2)
O2	C6	C1	106.8 (9)	O4	C22	C23	114 (2)
O2	C6	C5	106 (1)	O10	C22	C23	125 (2)
O2	C6	C7	108.0 (9)	O5	C24	O11	123 (1)
C1	C6	C5	111 (1)	O5	C24	C25	112 (1)
C1	C6	C7	115 (1)	O11	C24	C25	125 (1)
C5	C6	C7	110 (1)	O6	C26	O12	121 (2)
C6	C7	C8	128 (1)	O6	C26	C27	106 (2)
C7	C8	C9	127 (1)	O12	C26	C27	133 (2)
O3	C9	C8	108 (1)	O8	C28	O13	126 (2)
O3	C9	C10	109 (1)	O8	C28	C29	113 (2)

was refined by the full-matrix least-squares method, with anisotropic temperature factors for non-H atoms. The refinement converged to $R=0.056$ $[R=\Sigma(|F_O|-|F_C|)/\Sigma|F_O|]$, $\omega R=0.070$ $\{\omega R=[\Sigma\omega(|F_O|-|F_C|)^2/\Sigma\omega|F_O|^2]^{1/2}\}$, $S=1.91$ $\{S=[\Sigma\omega(|F_O|-|F_C|)^2/(n-m)]^{1/2}\}$, $|\text{shift}/\sigma|_{\max}<0.57$, and $-0.22\leqq\Delta\rho\leqq0.19\,e\text{Å}^{-3}$, where n and m are the numbers of reflections and parameters, respectively. All calculations were performed using the TEXSAN[5)] crystallographic software package (Molecular Structure Corporation).

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