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GONIOTRIOL FROM *GONIOTHALAMUS GIGANTEUS*

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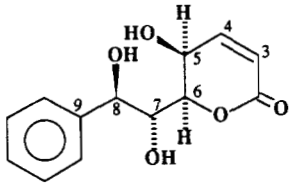
ABSTRACT.—The known styrylpyrone, goniotriol, has been isolated from *Goniothalamus giganteus*. Its bioactivities are reported, and its structure and relative stereochemistry have been determined by X-ray crystallography as 6*R*-(7*R*,8*R*-dihydro-7,8-dihydroxystyryl)-5*S*,6*R*-dihydro-5-hydroxy-2-pyrone [**1**].

In previous investigations of the bark of *Goniothalamus giganteus* Hook. f. and Thomas (Annonaceae) as a source of biologically active secondary metabolites, the tetrahydrofuranopyrone, altholactone (goniothalenol), and the monotetrahydrofuranoid acetogenins, annonacin and goniothalamicin, were isolated while using brine shrimp lethality as a bioassay (1,2). We have now isolated another styrylpyrone compound that is identified as goniotriol [**1**]. Goniotriol [**1**] was first isolated from *Goniothalamus sesquipedalis* Wall (3). Its stereochemistry was proposed based on biogenetic considerations; however, the configuration at C-5 in this compound remained unsolved. Using single crystal X-ray diffraction, we now report that the structure with relative configuration



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of goniotriol is 6*R*-(7*R*,8*R*-dihydro-7,8-dihydroxystyryl)-5*S*,6*R*-dihydro-5-hydroxy-2-pyrone (Figure 1), as suggested by Gesson *et al.* (4). This compound showed some activities in the brine shrimp lethality test (BST) (5) and the potato disc assay (PD) (6) and mild activities to human tumor cells (Table 1).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The mp was uncorrected. Optical rotation was taken with a Perkin Elmer 241 polarimeter. The ir spectrum was obtained with a Beckman IR-33. ^{1}H-*nmr* and ^{13}C-*nmr* spectra were recorded on Chemagnetics A-200 in CD_3OD. Low resolution

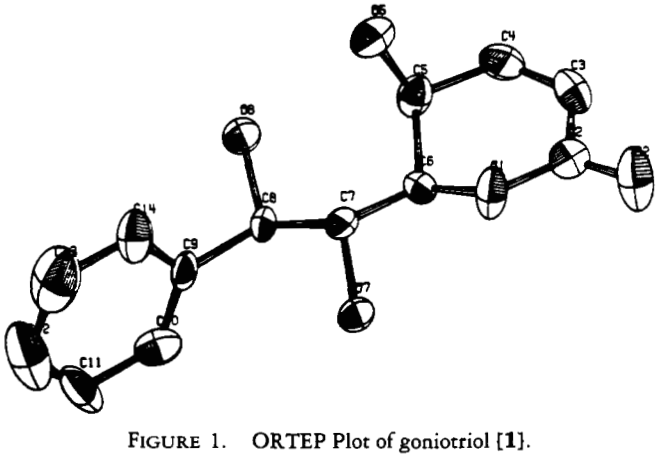

FIGURE 1. ORTEP Plot of goniotriol [**1**].

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TABLE 1. Bioactivities of Goniotriol [1].

BST[a] LC_{50} (ppm)	PD[b] % tumor inhibition	A-549[c] ED_{50} (μg/ml)	MCF-7[d] ED_{50} (μg/ml)	HT-29[e] ED_{50} (μg/ml)
269(182/412)	38	>10	5.9	>10

[a]Brine shrimp lethality test.
[b]Potato disc assay.
[c]Human lung carcinoma.
[d]Human breast carcinoma.
[e]Human colon adenocarcinoma.

eims and cims were obtained on a Finnigan 4000, and high resolution ms was measured on a Kratos MS50 through peak matching.

CRYSTAL DATA.[2]—$C_{13}H_{14}O_5$, MW = 250, orthorhombic, $a = 15.52(1)$ Å, $b = 9.303(7)$ Å, $c = 8.336(7)$ Å, $V = 1204(2)$ Å^3, $Z = 4$, ρ calcd = 1.38 g·cm^{-3}, F(000) = 528, μ(CuKα) = 8.00, space group $P2_12_12_1$ from systematic absences. The cell parameters of the colorless crystal (0.35 × 0.35 × 0.71 mm) were determined by centering 15 reflections (2θ range of 14° to 25°) by the half-height method. Crystallographic data were collected at room temperature using CuKα X-rays (λ = 1.5418 Å) and a monochromator on a Nicolet P3 four-circle diffractometer, with the θ–2θ scan technique out to a 2θ of 116.0°. A variable scan rate was used with a maximum of 29.30° per min, and a minimum of 7.23° per min. The scan range was from $1.2° < K\alpha_1$ to $1.2° > K\alpha_2$; the time that backgrounds at both ends of the scan range were counted was equivalent to the scan time. Three standard reflections, measured every 50 reflections, showed less than a 6% change during data collection; the data were corrected for Lorentz-polarization effects. Of the 988 reflections collected, 18 reflections were rejected as systematically absent, leaving 970 unique reflections, of which 901 met the condition of $F_o > 5\sigma(F_o)$ and were considered observed. The structure was solved using the MULTAN80 program and refined by SHELX76 to a final unweighted R of 0.1062 with all the hydrogens fixed in their calculated positions (except for the OH hydrogens: H-55 and H-77, bonded to O-5 and O-7, respectively, were found on a difference map; H-88 bonded to O-8 was not found and therefore not included in the calculation), with C-H bond distance fixed at 1.08 Å, and the isotropic temperature factor at 0.05. (The cause of the relatively high R factor value is apparently poor crystal quality; attempts to collect data on a second crystal failed; however, from the previous spectral data it is obvious that the X-ray structure is correct and clarified previously unknown stereochemistry at C-5.) A final difference map showed no peaks greater than 0.60 ē/Å^3. The maximum shift divided by the estimated standard deviation for the final refinement cycle was −0.009. One intramolecular H-bond was found: O-5. . .O-8 (2.70 Å); one intermolecular H-bond was found: O-2. . .O-7 (by translated SYMM2: $1.5-x$, $1-y$, $0.5+z$) (2.75 Å). Atomic coordinates are given in Table 2.

PLANT MATERIAL.—Bark of *G. giganteus* was collected in Thailand (B-826538, PR-50604) under the auspices of Dr. Robert E. Perdue, Medicinal Plant Laboratory, USDA, Beltsville, Maryland, where voucher specimens are maintained.

ISOLATION AND IDENTIFICATION.—The plant material was extracted as previously described (2) with 95% EtOH; the EtOH residue was partitioned between $CHCl_3$ and H_2O, and the $CHCl_3$ residue was partitioned between hexane and 10% H_2O in MeOH. The MeOH residue was subjected to Si gel cc eluted with a gradient of hexane, CH_2Cl_2, and MeOH. Goniotriol [1] was crystallized from fraction 59. Recrystallization in a mixture of hexane and EtOH afforded goniotriol as white flakes: mp 170°; [α]D 121° (MeOH); ir (KBr) cm^{-1} 3360, 2890, 2825, 1710, 1370, 1250, 755, 680; eims *m/z* (%) 251 (5.6), 233 (41), 215 (17), 143 (40), 126 (51), 107 (99), 79 (100); cims (isobutane) *m/z* 251; hr eims $[M]^+$ found *m/z* 250.0836 for $C_{13}H_{14}O_5$ (calcd 250.0840); uv (MeOH) 215 nm (log ε 3.82); ^{1}H nmr (CD_3OD) 7.33–7.44 (5H, m, aromatic protons), 7.00 (1H, q, $J = 9.6, 5.8$, H-4), 6.08 (1H, d, $J = 9.6$, H-3), 4.74 (1H, d, $J = 7.9$, H-8), 4.59 (1H, t, $J = 3.8, 3.2$, H-6), 4.42 (1H, q, $J = 5.8, 3.2$, H-5), 4.20 (1H, q, $J = 7.9, 3.8$, H-7); ^{13}C nmr (CD_3OD) 166.13 (C-2), 146.48 (C-4), 143.38 (C-9), 129.14 (C-11, C-13), 128.81 (C-10, C-14), 128.75 (C-12),

[2]Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.

TABLE 2. Atomic Coordinates of Goniotriol [**1**].

Atom	*x*	*y*	*z*
O-1	0.7820(7)	0.327(1)	0.403(1)
C-2	0.743(1)	0.381(2)	0.529(2)
O-2	0.6914(7)	0.478(1)	0.516(1)
C-3	0.759(1)	0.311(2)	0.691(2)
C-4	0.803(1)	0.190(2)	0.699(2)
C-5	0.8460(9)	0.122(2)	0.557(2)
O-5	0.7956(7)	0.004(1)	0.507(1)
C-6	0.862(1)	0.236(2)	0.426(2)
C-7	0.8783(9)	0.182(1)	0.257(2)
O-7	0.9009(6)	0.3034(9)	0.158(1)
C-8	0.9630(9)	0.088(1)	0.252(2)
O-8	0.9419(7)	−0.043(1)	0.340(1)
C-9	0.985(1)	0.049(1)	0.080(2)
C-10	1.057(1)	0.104(2)	0.010(2)
C-11	1.081(1)	0.064(2)	−0.147(2)
C-12	1.032(2)	−0.033(3)	−0.228(2)
C-13	0.959(2)	−0.086(2)	−0.162(2)
C-14	0.936(1)	−0.045(2)	−0.006(2)
H-55	0.8451	−0.0659	0.4698
H-77	0.8524	0.3681	0.1158

123.03 (C-3), 80.33 (C-6), 75.70 (C-5), 73.97 (C-8), 63.54 (C-7).

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