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GRAYATHOL A, A NEW DITERPENE FROM LEUCOTHOE GRAYANA MAX.

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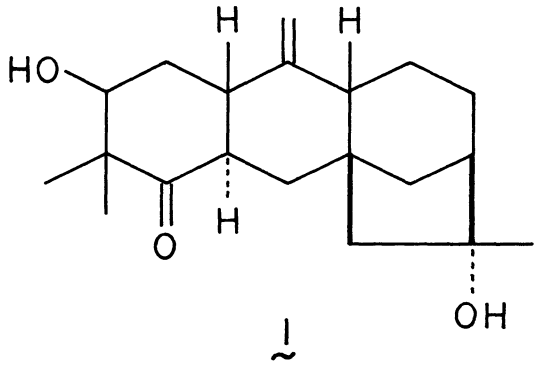
The structure of a new diterpene, grayathol A, has been shown to have a stereoisomeric grayanane skeleton by X-ray analysis.

Previously we reported structural elucidation of leucothols[1] (for example 1), minor diterpenes from L. grayana. Although the leucothane skeleton can be seemingly regarded as a rearranged grayanane skeleton, the absolute configuration at C-1 of the former is opposite to that of the latter. Therefore, co-occurrence of 1-epi-grayanoids in the plant has been thought probable, but it has not hitherto been confirmed. In this paper we describe the isolation and the X-ray structure of grayathol A, the first 1-epi-grayanoid[2] to be isolated from nature.

Careful chromatography (SiO_2, $CHCl_3$) of a grayanoid-leucothoid fraction[3,4] from the crude extract of L. grayana afforded grayathol A [$C_{20}H_{30}O_3$ (found: C, 75.88; H, 9.19%, Calcd: C, 75.43; H, 9.50%); mp 183-189 °C (decomposition); $[\alpha]_D^{25}$ +397° (c 1, MeOH); m/e 318 (M^+)] in a yield of 8×10^{-7}% from dried leaves. Since the nmr spectrum[5] suggested that grayathol A has a modified grayanane skeleton, the structure was studied by X-ray analysis.

The crystal data of grayathol A are as follows: orthorhombic, space group $P2_12_12_1$, a = 15.171(6), b = 32.117(10), c = 7.304(4) Å, Z = 8, D_c = 1.189 g·cm^{-3}. Intensity data for $2\theta < 140°$ were collected on an automatic, four-circle diffractometer with LiF-monochromated CuKα radiation by using a θ-2θ scanning technique. 2629 independent structure factor amplitudes above 3σ(F) were selected for the structural study. The structure was solved by the Monte Carlo direct method[6] on the basis of 804 E-values above 1.30. The 30 strongest reflections were used as



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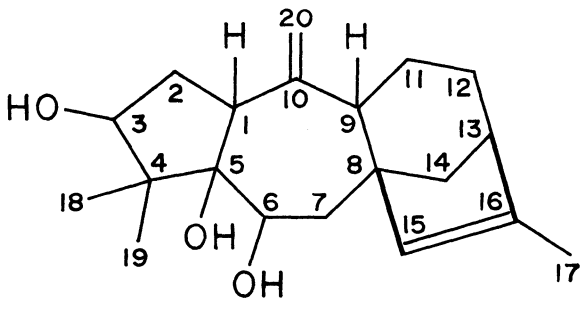

2

a starting set. The 309th random phase set which showed a low R_K-value of 32.5% ($R_K = \Sigma||E_o| - k|E_c||/\Sigma|E_o|$) gave a correct solution. An E-map computed with 731 phases yielded 43 out of the 46 independent non-hydrogen atoms. The remaining 3 atoms were located in a difference Fourier map. The structure thus obtained was refined by the block-diagonal least-squares method with anisotropic temperature factors. After 52 hydrogen atoms had been located in a second difference Fourier map, several cycles of the least-squares refinement were carried out including these hydrogen atoms. The final R-value was 8.3%. The molecular framework obtained is shown in Fig. 1. Thus, the structure of grayathol A has been established as 2 except for the absolute configuration.

Unlike the usual grayanoids, the new diterpene does not cause skin inflammation upon contact.

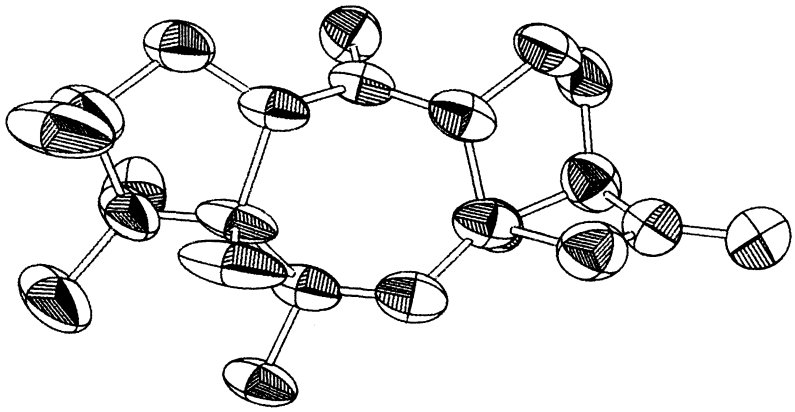

Fig. 1. A perspective view of one of the two independent molecules.

References and Notes

1) A. Furusaki, N. Hamanaka, H. Miyakoshi, T. Okuno, and T. Matsumoto, Chem. Lett., 1972, 783.
2) The compound can be an ent-1-epi-grayanoid. However, if the biogenetic relationship is taken into consideration, the 1-epi-grayanoid structure is highly probable.
3) The fraction consisting of "unknown compounds" described in the experimental section of ref. 4).
4) S. Gasa, R. Ikeda, N. Hamanaka, and T. Matsumoto, Bull. Chem. Soc. Jpn., 49, 935 (1976).
5) δ (pyridine d_5, 100 MHz) = 5.36 (1H, s), 5.26 (2H, br s), 4.07 (1H, br d, J=4 Hz, H_3), 4.00 (1H, d, J=10 Hz, H_6), 3.20 (1H, q, J=14 and 10 Hz, $H_{7\beta}$), 3.17 (1H, t, J=10 Hz, H_1), 1.68 (3H, s), 1.63 (3H, d, J=1.5 Hz), and 0.96 (3H, s).
6) A. Furusaki, Acta Crystallogr., Sect. A, 35, 220 (1979).

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