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LEUCOTHOL B AND C, FURTHER EXAMPLES OF ANTHRADITERPENOIDS FROM LEUCOTHOE GRAYANA MAX.

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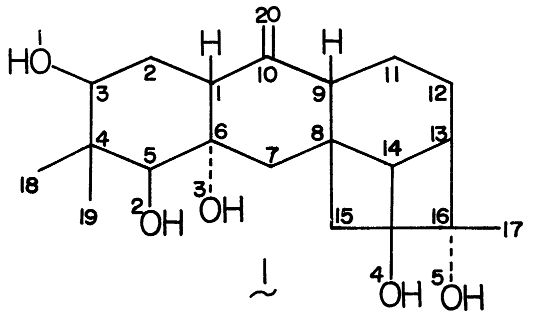
The structure of leucothol B, a new diterpenoid from Leucothoe grayana Max., has been determined as 1 by X-ray crystallographic analysis. Leucothol C has been characterized as 2 by spectroscopic and chemical means.

We wish to report on the isolation and structural elucidation of novel anthraditerpenoids[1)] leucothol B (1) and C (2) from Leucothoe grayana Max..

Leucothol B, $C_{20}H_{32}O_5$[2)], mp 241-242°, $[\alpha]_D$ +1.6° (MeOH, c = 1.0), ν (nujol) 3420, 3340, 3200 (OH), 1650, 880 ($C{=}CH_2$) cm^{-1}, is isomeric with grayanotoxin II and was separated from it by careful chromatography on silica



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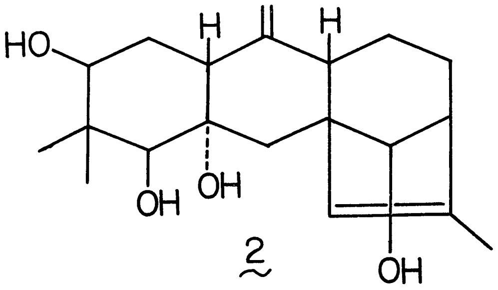

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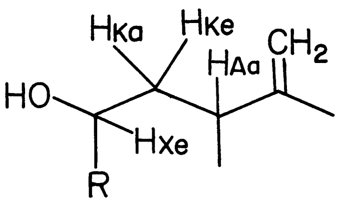

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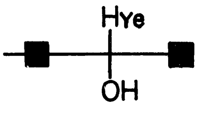

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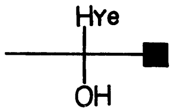

■ denotes a quarternary carbon atom.

gel in 10^{-3}% yield from dried leaves³⁾. The NMR spectrum (100 MHz, pyridine-d_5) was however considerably different from that of grayanotoxin II except for the peaks due to an exo-methylene (δ 5.04 and 4.95, each 1H, b.s), a hydroxymethine at C-14 (δ 4.50, 1H, s)⁴⁾ and three methyls (δ 1.48, 1.47, 1.40, each 3H, s). Characteristic for leucothol B were two sets of AB quartet (δ 2.63 and 2.29, J = 15 Hz; 2.14 and 1.92, J = 15 Hz) and signals⁵⁾ which suggested presence of either the partial structure **3** or **4**. Namely, the broad doublet (1H, J = 13 Hz, W_H of each peak 7 Hz) centered at δ 3.07, ascribable to an allylic methine H_{Aa} of **3**, couples with H_{Ka} (δ 2.41, $J_{Aa,Ka}$ = 13 Hz) and with H_{Ke} (δ 1.94, $J_{Aa,Ke}$ = 3.5 Hz), both of which in turn split by H_{Xe} (δ 3.93) with $J_{Ka,Xe}$ = 3.5 Hz and $J_{Ke,Xe}$ = 3.5 Hz. The signal due to H_{Xe} further couples (J = 2.0 Hz) with H_{Ye} (δ 3.46, d). All these data are best explained by assuming a structure related to leucothol A such as **1** for leucothol B. However, since only a small amount of the material was available, structure determination by interrelating leucothol A and B was abandoned.

Unequivocal proof of the structure **1** was achieved by X-ray crystallographic analysis of leucothol B monohydrate. Crystal data are summarized in Table 1. Intensities of 1948 unique reflections with 2θ values up to 140° were collected on a Rigaku automatic four-circle diffractometer at this university with monochromatized Cu $K\alpha$ radiation.

The structure was solved by the symbolic addition method on the basis of 371 $|E|$ values above 1.30.⁶⁾ The first E-map calculated with 341 phases yielded only 13 atoms. Two more cyclic processes of phase calculation and E-Fourier synthesis were carried out until all the 25 atoms in a leucothol B molecule and an oxygen atom of water of crystallization were found. The assignment of oxygen

Table 1. The crystal data.

Crystal system	Monoclinic
Space group	$P2_1$
a	11.797 Å
b	7.560
c	11.469
β	96.67°
Z	2

atoms was made by taking into consideration the isotropic temperature factors as well as the atomic arrangement. The positions of 34 hydrogen atoms were also found from a difference map. The atomic parameters thus obtained were refined by the block-diagonal-matrix least-squares method. The final R factor is 4.2%. The molecular framework of leucothol B found in the crystal is shown in Fig. 1 and the final atomic coordinates are listed in Table 2.

Leucothol C, $C_{20}H_{30}O_4$$^{2)}$, mp 205-208° (dec.), ν(nujol) 3320-3460 (OH), 1650 ($C=CH_2$) cm^{-1}, $[\alpha]_D$ +25° (MeOH, c = 0.45) was obtained in 10^{-5}% yield from dried leaves. The NMR spectrum (100 MHz, pyridine-d_5 containing a small amount of D_2O) indicated presence of two tertiary methyls (δ 1.32, 1.42), an olefinic methyl (δ 1.65, d, J = 2 Hz), a methylene lying between two quarternary carbon atoms (δ 2.68 and 2.46, J = 15 Hz), an allylic methine (δ 2.98, b.d, J = 12 Hz), three secondary hydroxymethines (δ 3.36, 1H, d, J = 2 Hz; 3.92, 1H, m, W_H 7 Hz; 4.41, 1H, s), a vinylidene group (δ 5.04, 2H, b.s) and an olefinic hydrogen (δ 5.15, 1H, q, J = 2 Hz). Comparison of these data with those of leucothol B suggested that leucothol C would be anhydroleucothol B of the structure **2**. The reasoning was proved correct by dehydrating leucothol B under acidic conditions (acetone, $HClO_4$, rt). The product $C_{20}H_{30}O_4$, obtained in 40% yield, was identical in all respects with leucothol C from natural source.

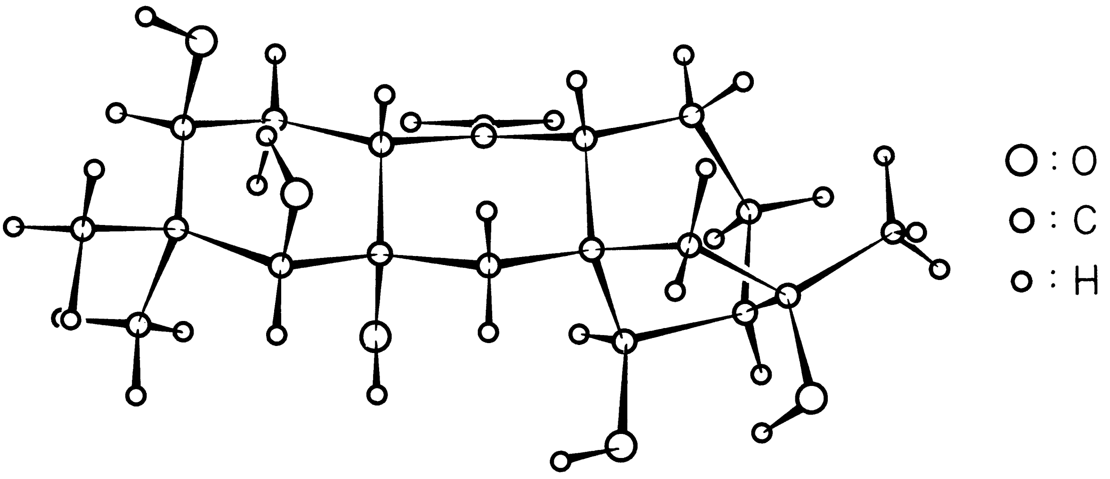

Fig. 1

Table 2. The final atomic coordinates.

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
O(1)	0.7224	0.3288	0.8532	C(8)	0.7085	0.2735	0.3740
O(2)	0.8123	0.5420	0.6913	C(9)	0.6121	0.1699	0.4270
O(3)	0.9011	0.1367	0.5509	C(10)	0.6618	0.0566	0.5290
O(4)	0.8727	0.2329	0.2619	C(11)	0.5328	0.0752	0.3303
O(5)	0.7312	0.3836	0.0896	C(12)	0.5942	-0.0060	0.2333
O(W)	0.0662	0.2815	0.4323	C(13)	0.6877	0.1146	0.1951
C(1)	0.7219	0.1676	0.6268	C(14)	0.7761	0.1476	0.3021
C(2)	0.7592	0.0729	0.7428	C(15)	0.6526	0.4015	0.2777
C(3)	0.8102	0.2032	0.8355	C(16)	0.6496	0.3018	0.1585
C(4)	0.9160	0.2989	0.7994	C(17)	0.5362	0.3183	0.0814
C(5)	0.8826	0.3898	0.6784	C(18)	0.9573	0.4410	0.8914
C(6)	0.8216	0.2680	0.5817	C(19)	1.0148	0.1691	0.7947
C(7)	0.7784	0.3768	0.4722	C(20)	0.6546	-0.1187	0.5337

References and Notes

1) For the first example of anthraditerpenoid leucothol A; A. Furusaki, N. Hamanaka, H. Miyakoshi, T. Okuno and T. Matsumoto, preceding paper.

2) Elemental formulas were confirmed by concordant elemental analyses.

3) Professors Hikino and Takemoto also isolated leucothol B from the same plant (H. Hikino, private communication).

4) T. Okuno, N. Hamanaka, H. Miyakoshi and T. Matsumoto, Tetrahedron, 26, 4765 (1970).

5) Assignments were deduced by extensive spin decoupling experiments.

6) The calculations necessary for the present study were carried out on a FACOM 230-60 computer at the Computer Center of Hokkaido University using our programs.

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