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A NEW DITERPENOID FROM LEUCOTHOE GRAYANA MAX.

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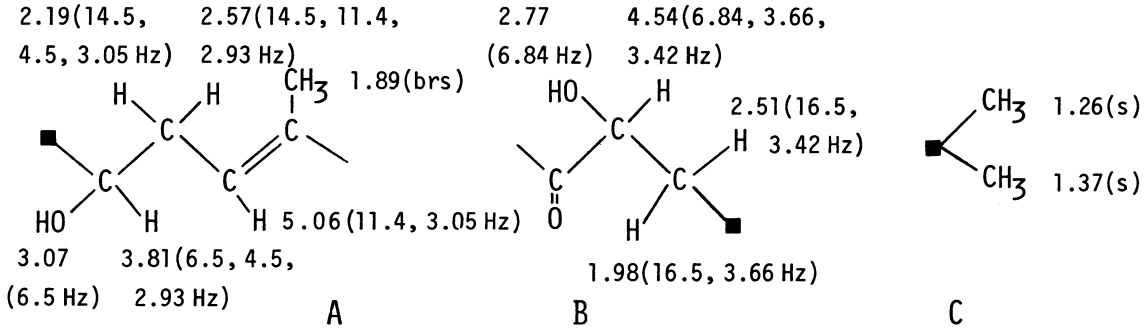
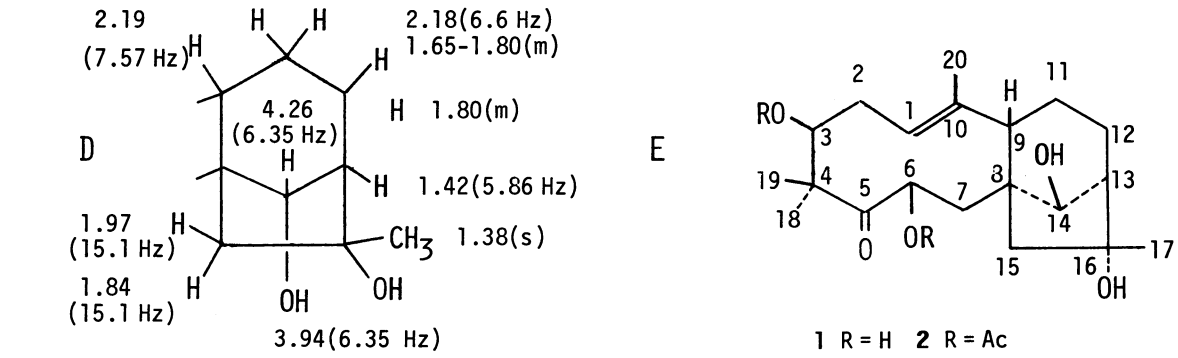
A new minor diterpenoid was isolated from the leaves of Leucothoe grayana Max., and its structure was characterized as a secograyanane derivative(1, 3(S), 6(R), 14(R), 16(R)-tetrahydroxy-5-oxo-5,10-seco-ent-kaur-1(10)-ene) by spectroscopic and chemical studies.

From the leaves of Leucothoe grayana Max., grayanol A and B(3)[1] have been isolated together with grayanotoxins(6-7),[2] leucothols,[3] and grayathol A.[4] Matsumoto et al.[5] have suggested that grayanols are the possible biogenetic precursor for grayathol and leucothols, even for grayanotoxins. In this paper, we wish to describe the isolation and the structural elucidation of a new minor diterpenoid from the same source.

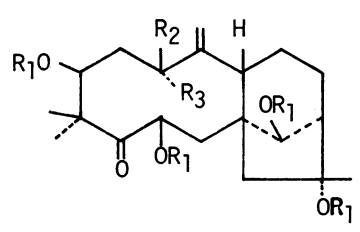
The methanol extract of the leaves of the title plant was extracted with ethyl acetate and BuOH. The BuOH extract was subjected to silica gel chromatography to afford crystals(1), mp 166-169°C, $[\alpha]_D^{27}$ -12°(c 0.1, EtOH). The formula, $C_{20}H_{32}O_5$, was given to 1 from elemental analysis and the mass spectrum(M^+ at m/z 352). The IR spectrum exhibited bands at 3550 cm^{-1}(OH), 1690 cm^{-1}(>C=O), and 1641 cm^{-1} and 874 cm^{-1}(-CH=C<). The ^1H NMR spectrum of 1 on a 400 MHz spectrometer showed signals of four tertiary methyls(each singlet δ1.26, 1.37, 1.38, and 1.89), three secondary carbinyl protons(δ3.81, 4.26, and 4.54) and one proton (double doublet δ5.06) due to a trisubstituted double bond in $CDCl_3$. These results suggest that 1 is a tricarbocyclic diterpenoid, such as grayanols. Detailed double resonance studies are consistent with the partial structures A, B, and C. The

presence of an α-ketol group was assumed by the observation that, in the ^{1}H NMR spectrum, the carbinyl hydrogen was considerably deshielded(δ4.54) and that **1** consumed the reagent on periodate oxidation. The $^{13}C\{^{1}H\}$ NMR spectrum of **1** in pyridine-d_5 showed twenty signals(at 22.5 MHz),[6] which could be assigned to one >C=O, one -CH=C- unit, one -COH, three -CHOH, two -C-, two -CH-, five $-CH_2-$, and four $-CH_3$. The carbon signals of **1** were assigned by comparisons of the spectrum

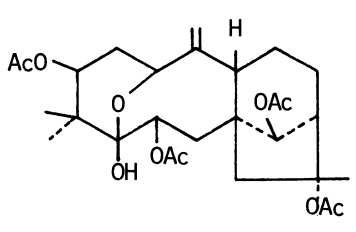




with those of the acetate(**2**)[7] of **1**, grayanol B(**3**),[1] 1-epi-grayanol B penta-acetate(**4**), the hemiketal(**5**)[5] derived from **4** and grayanotoxins.[8] The chemical shifts of the carbons on the six- and five-membered rings in the **1** were very similar to those of the analogs(**3**-**5** and grayanotoxin III(**6**)) having the bicyclo-[3.2.1]octane system. From this evidence and the ^{1}H NMR decoupling experiments, the partial structure D was deduced. The chemical shifts(δ1.26 and 1.37 due to



3 $R_1=R_2=H$ $R_3=OH$
4 $R_1=Ac$ $R_2=OAc$ $R_3=H$



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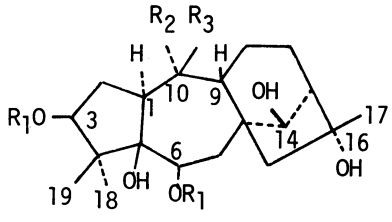

6 $R_1=H$ $R_2=OH$ $R_3=CH_3$
7 $R_1=H$ $R_2,R_3=CH_2$
8 $R_1=Ac$ $R_2,R_3=CH_2$

C-18 and C-19, respectively) of the methyls are considerably deshielded about ca. 0.10-0.15 ppm compared with those of 6(δ1.03 and 1.26) and grayanotoxin II(7, δ1.01 and 1.22). This led us to a conclusion that the geminal methyls(C) might be placed on the adjacent carbon of the carbonyl group in B. From these results and biogenetic ground, the partial structures A-D were expanded to E(1). This was confirmed by the conversion of 1 to the known compound, as described below. Acetylation of 1 with C_5D_5N-Ac_2O(1:1) at room temperature overnight afforded two diacetates(2 and 8, 7:3 ratio on silver nitrate-impregnated silica gel TLC). The former(2) was identified as 3,6-diacetate of 1 from the ^1H and ^{13}C NMR spectra.[7] The ^{13}C NMR spectrum of the latter(8) showed signals(δ149.0(s) and 114.2(t)) due to $>C=CH_2$ unit, but no signal due to carbonyl carbon. The rearrangement product 8 with the molecular formula $C_{24}H_{36}O_7$(m/z M^+ Found 436.2467, Calcd 436.2461) was considered to be produced by transannular cyclization of the 1,5-cyclodecenone ring, as seen in the report[9] on the stereospecific cyclization of preisocalamendiol to dehydrocalamendiol. In fact, the acetate 8 was identical with grayanotoxin II 3,6-diacetate by direct comparison of the IR, ^1H NMR, and ^{13}C NMR spectra. The acetate 2 in $CDCl_3$ was gradually changed into 8 at room temperature. Further, the transannular cyclization of 2 can be achieved by heating to reflux a solution of 2 in MeOH with silica gel for 30 min. Accordingly, the configurations at the C3-OH, C6-OH, C14-OH, and C16-OH in 2 and 1 were determined to be β(S), β(R), β(R), and α(R), respectively, and the junction of the ten- and six-membered rings in both compounds to be cis-orientation(C9-βH). In view of the predominant formation of the trans 1α(H),5β(OH)-product 8 and the easy cyclization[10] of 2 to 8, the conformation of the cyclodecenone ring in $CDCl_3$ solution was assumed to be similar to that(boat-chair) reported for 4[5] and the configuration around the 1(10) double bond was deduced to be E(trans). This was supported by the facts that the chemical shifts and the coupling constants of the C3-H and C6-H resonances of 2 were strikingly similar to those of 4. The signals for C20(δ18.4 in 2 and 20.3 in 1) and C9(δ56.6 and 57.0) were observed in a lower field compared with those of the major conformers of 3β-acetoxy-5,10-seco-1(10)-cholesten-5-one(C(10)-CH_3 at δ12.9)[11] and 7(C9 at δ53.0). They must be affected by 1,3-diaxial hydrogen-hydrogen interaction[12] between the 20-methyl C-H and the 9-βH bonds. As a consequence, the C(10)-CH_3 group in 2 and 1 must be located on the β-side of the ten-membered ring.

References

1) S. Fushiya, H. Hikino, and T. Takemoto, Tetrahedron Lett., 1974, 783.

2) A. Furusaki, S. Gasa, R. Ikeda, T. Matsumoto, N. Yasuoka, and Y. Matsuura, Bull Chem. Soc. Jpn., 54, 1622(1981).

3) A. Furusaki, N. Hamanaka, H. Miyakoshi, T. Okuno, and T. Matsumoto, Chem. Lett., 1972, 783; H. Hikino, S. Koriyama, and T. Takemoto, Tetrahedron, 29, 773(1973).

4) A. Furusaki, S. Gasa, N. Hamanaka, R. Ikeda, and T. Matsumoto, Chem. Lett., 1979, 665.

5) T. Terai, H. Meguri, N. Hamanaka, T. Matsuzaki, A. Furusaki, T. Kato, and T. Matsumoto, Chem. Lett., 1980, 1111.

6) ^{13}C NMR(22.5 MHz, C_5D_5N):δ16.3(18), 20.3(20), 23.9(17), 24.3(19), 22.1(11), 26.9(12), 33.5(2), 44.1(7), 52.4(8), 54.0(13), 55.3(4), 57.0(9), 57.3(15), 70.0(6), 77.1(3), 77.9(16), 80.0(14), 125.5(1), 142.2(10), 214.4(5).

7) ^{1}H NMR(90 MHz, $CDCl_3$):δ1.08, 1.19, 1.33, 2.03(each 3H, s), 2.06, 2.11($COCH_3$), 4.43(1H, d, J=4.6 Hz), 4.80(1H, t, J=7.6 Hz), 5.13(1H, dd, J=4.0, 9.7 Hz), 5.50(1H, d, J=6.5 Hz). ^{13}C NMR(22.5 MHz, C_5D_5N):δ16.4(18), 18.4(20), 23.5(19), 23.8(17), 22.1(11), 26.7(12), 29.3(2), 40.1(7), 51.5(4), 54.4(13), 56.6(9), 57.4(15), 69.5(6), 76.3(3), 78.5(16), 121.6(1), 147.0(10), 207.3(5), 20.9, 21.1 ($CO\underline{C}H_3$), 170.3($\underline{C}OCH_3$ x 2).

8) T. Ohta and H. Hikino, Org. Magn. Reson., 12, 445(1979); T. Masutani, K. Kawazu, K. Uneyama, S. Torii, and J. Iwasa, Agric. Biol. Chem., 43, 631 (1979); N. Shirai, H. Nakata, and J. Sakakibara, Chem. Pharm. Bull., 28, 365 (1980).

9) Y. Terada and S. Yamamura, Tetrahedron Lett., 1979, 1623.

10) M. Lj. Mihailović, Lj. Lorenc, M. Gasić, M. Rogic, A. Melera, and M. Stefanović, Tetrahedron, 22, 2345(1966); M. Niwa, M. Iguchi, and S. Yamamura, Bull. Chem. Soc. Jpn., 49, 3148(1976).

11) Hans-Christian Mez, G. Rist, O. Ermer, Lj. Lorenc, J. Kalvoda, and M. Lj. Mihailović, Helv. Chim. Acta, 59, 1273(1976).

12) H. Beierbeck, J. K. Saunders, and J. W. ApSimon, Can. J. Chem., 55, 2813(1977).

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