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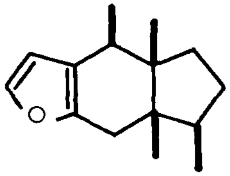
PTYCHANOLIDE, A SESQUITERPENOID WITH A NEW TYPE SKELETON FROM THE LIVERWORT *PTYCHANTHUS STRIATUS* (LEHM. ET LINDENB.) NEES

Reiji Takeda*, Hideo Naoki, Takashi Iwashita and Yoshio Hirose
Suntory Institute for Bioorganic Research
Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka 618, Japan

Abstract : The structure of ptychanolide, isolated from the liverwort *Ptychanthus striatus* , has been determined by spectroscopic analysis and chemical transformation.

Our investigation on the terpene constituents of the liverwort *Ptychanthus striatus* (LEHM. et LINDENB.) NEES has yielded, in addition to the known deoxopinguisone 1 [1)] and pinguisanene 2,[2)] a new compound "ptychanolide" 3 which has a unique carbon skeleton. In the following we wish to report the results of structural studies leading to structure 3.

Acetone extract of the semi-dry material (360 g) collected in Wakayama Prefecture, March 1980, was subjected to SiO_2 column chromatography using hexane and CH_2Cl_2 to give 1 (110 mg), 2 (140 mg) and ptychanolide (340 mg). Compounds 1 and 2 were identified with authentic samples.



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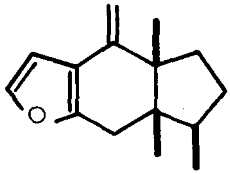

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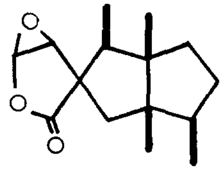

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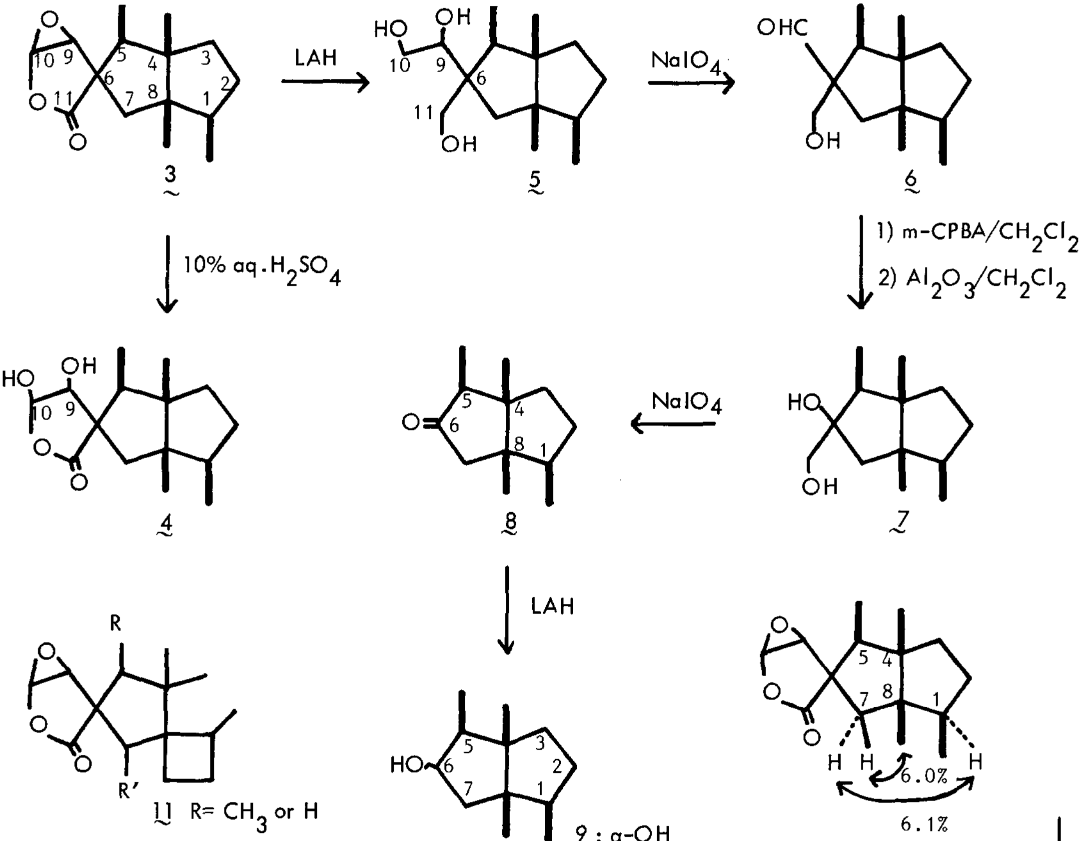
The physical constants of ptychanolide 3 are as follows ; $C_{15}H_{22}O_3$ (m/z 250, M^+) ; mp 143 ~ 4° (from EtOAc) ; $[\alpha]_D^{24}$ +23.2° (c = 0.47, $CHCl_3$) ; IR (KBr) : 1780 cm^{-1} (γ-lactone) ; ^1H-NMR (360 MHz, δ ppm, $CDCl_3$) : 0.79 and 0.93 (3H each, s, 4-Me and 8-Me), 0.84 (3H, d, J = 7.7 Hz, 1-Me), 0.98 (3H, d, J = 7.7 Hz, 5-Me), 1.3 ~ 1.4 (2H, m, 2-H_A and 3-H_A), 1.39 (1H, d, J = 13.6 Hz, 7-H_A), 1.71 (1H, m, 2-H_B), 1.87 (1H, m, 3-H_B), 1.99 (1H, d, J = 13.6 Hz, 7-H_B), 2.38 (1H, m, 1-H), 2.61 (1H, q, J = 7.7 Hz, 5-H), 3.55 (1H, d, J = 2.4 Hz, 9-H) and 5.52 (1H, d, J = 2.4 Hz, 10-H) ; ^{13}C-NMR (25.0 MHz, δ ppm, $CDCl_3$) : four CH_3's (10.7, 14.5, 16.7 and 18.4), three CH_2's (31.0, 35.5 and 44.6), two CH's (42.0 and 50.0), three quat-C's (54.4, 55.3 and 56.3), two HC-O's (57.5 and 76.1) and C=O (179.8).

The spectral properties of 3 indicated the presence of a five-membered lactone and the absence of hydroxyl group. Hence the remaining oxygen atom was attributed to an ether linkage. Treatment of lactone 3 with 10% aq. H_2SO_4 in acetone afforded the diol lactone 4 ; IR ($CHCl_3$) : 3500, 1770 cm^{-1} (hydroxy and γ-lactone); ^1H-NMR ($CDCl_3$) : δ 4.13 ppm (1H, d, J = 2.4 Hz, 9-H) and 5.62 (1H, d, J = 2.4 Hz, 10-H). The formation of an α-glycol from an ether indicates that the diol is derived from an epoxy ring. Lactone 3 was



9 : α-OH

10 : β-OH

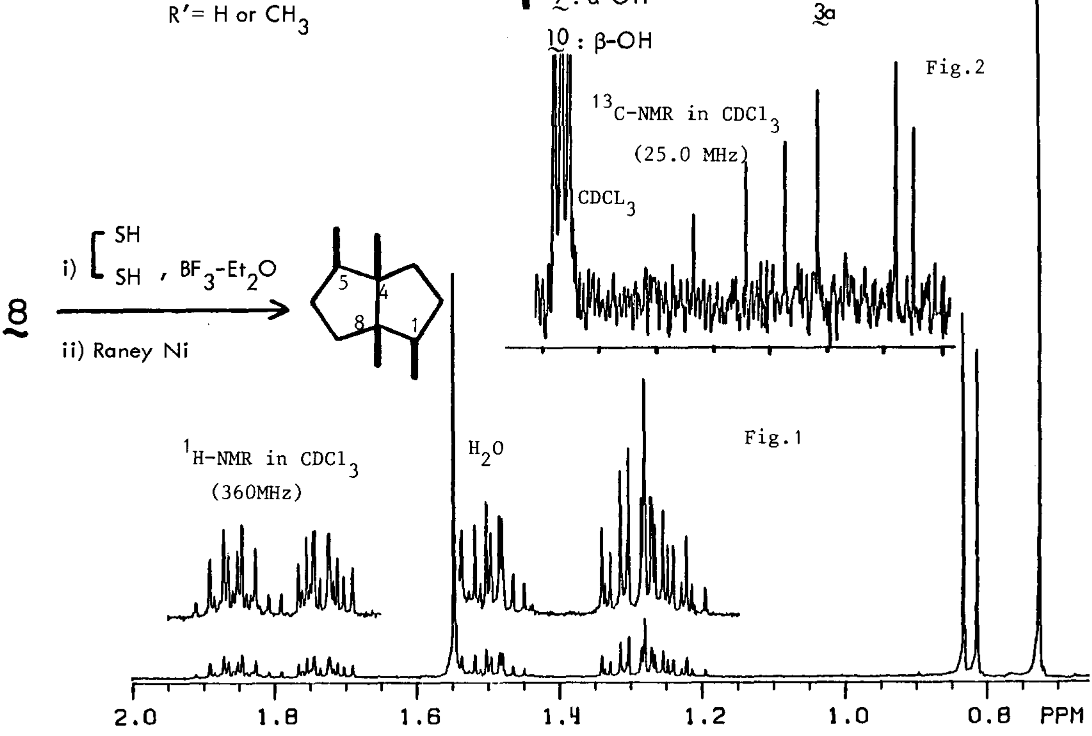


Fig.2

Fig.1

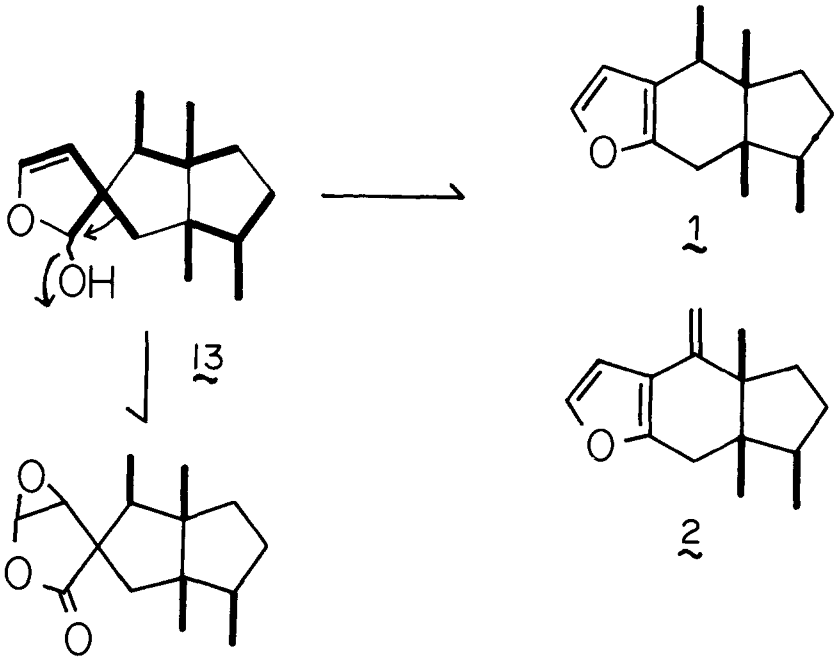
reduced with LAH in ether to triol 5: ^{1}H-NMR of triol 5 showed the presence of ■-CH_2OH (■ denotes quat. carbon; AB q, δ 3.64 and 3.84 ppm, J = 14.4 Hz) and ■-CH_AOH-$CH_{2(B,C)}OH$ (H_A, 3.92, dd, J = 4.0 and 7.2 Hz; H_B, 3.72, dd, J = 7.2 and 14.4 Hz; H_C, 3.76, dd, J = 14.4 and 4.0 Hz). Since the isolated hydroxymethyl group (C-11) and the 1,2-diol system (C-9,10) are attached to a quaternary carbon, it follows that the γ-lactone must form a spiro linkage at C-6 and that the epoxy ring is attached to the lactone ring.

Oxidation of triol 5 with $NaIO_4$ gave aldehyde 6, which was further oxidized with *m* -CPBA and hydrolyzed with Al_2O_3 to yield diol 7. The diol was oxidized further with $NaIO_4$ to the corresponding ketone 8; IR (film): 1740 cm^{-1} (cyclopentanone). These results establish that ptychanolide 3 has a spiro-lactone moiety at C-6. Reduction of ketone 8 with LAH in ether afforded alcohols 9 and 10, the ^{1}H-NMR data of which showed that the *sec* -OH function was flanked by a methylene group and *sec* -Me; 9: 6-H (δ 4.20 ppm, dt, J = 5.4 and 7.2 Hz), 7-H_A (1.42, dd, J = 5.4 and 13.6 Hz), 7-H_B (1.95, dd, J = 7.2 and 13.6 Hz), 5-H (1.87, dq, J = 7.2 and 7.7 Hz); and 10 : 6-H (3.77, dt, J = 9.4 and 7.7 Hz), 7-H_A (1.49, dd, J = 7.7 and 13.6 Hz), 7-H_B (1.79, dd, J = 7.7 and 13.6 Hz), 5-H (1.74, dq, J = 9.4 and 7.7 Hz). The 360 MHz tilted 2DJ spectra$^{3)}$ completely resolved and separated the five proton resonances at C-1/C-2/C-3 of 9, thus enabling full assignments of δ and J values. These results together with spin decoupling experiments of 3 indicated that ptychanolide 3 had a ■-$CH(CH_3)$-CH_2-CH_2-■ moiety. These results lead to two possible structures 3 or 11 for ptychanolide.

We have established that ptychanolide is represented by formula 3 in the following manner. Ketone 8 (10 mg) was treated with ethanedithiol to give the corresponding thioketal which was refluxed with Raney Ni in EtOH ; the catalyst was filtered, the filtrate was treated with water and extracted with pentane to give the volatile hydrocarbon 12 (4 mg). The ^{1}H-NMR spectrum (Fig. 1) showed only two methyl groups (δ 0.78 and 0.82 ppm) and five protons [1.18~1.35 (2H), 1.50, 1.73 and 1.86] while the ^{13}C-NMR spectrum (Fig. 2) showed only six carbon peaks (15.0, 18.0, 31.7, 37.5, 44.4 and 53.7). Hydrocarbon 12, therefore, has the symmetric bicyclo[3.3.0] octane skeleton in which the four methyl groups are all β (or α), or α (or β) at C-1/C-5 and β (or α) at C-4/C-8.

In the NOE experiments with ptychanolide 3 (see 3a), a 6.0% NOE$^{4)}$ was observed on 7β-H (δ 1.39 ppm) upon irradiation of 8β-Me (δ 0.79), and a 6.1% NOE was observed on 7α-H (δ 1.99) upon irradiation of 1α-H (δ 2.38), *i.e.*, the 8- and 1-Me groups have a *cis* -relation. Therefore, the configuration of the four methyl groups are either all α or β. Ketone 8 exhibited a positive CD Cotton effect at 295 nm (MeOH) Δε + 2.6; although application of the octant rule$^{5)}$ requires precaution,$^{6)}$ it would be safe to use it in the present case since the 5-Me, and not the remote 1-Me would be making the dominant contribution to the CD of this ketone having a symmetric skeleton. This leads to the absolute configuration shown for 8 which is corroborated by the established configuration of congeners 1$^{1,7)}$ and 2.$^{2)}$ The structure of ptychanolide is thus represented by 3; configuration at chiral centers 6, 9 and 10 remain to be determined.

The biogenesis of the pinguisone type sesquiterpenoids represented by deoxopinguisone 1 and pinguisanene 2 is as yet not clear. However, the isolation of ptychanolide 3 from the same liverwort suggests that they are derived from an intermediate such as 13.



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Acknowledgment.

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