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STRUCTURES OF XANTHOLIDES A AND B, TWO NEW GUAIANOLIDES FROM XANTHIUM CANADENSE MILL.

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Abstract The structures of xantholides A and B were deduced on the basis of IR and NMR spectra, and confirmed by X-ray analysis. Xantholide A inhibited the larval growth of Drosophila melanogaster.

In the course of our search of biologically active substances, we have found remarkable larval growth inhibition (Drosophila test[1]) in Xanthium canadense Mill.[2] The subsequent investigation resulted in the isolation of its active principle, xantholide A and its dihydro derivative, xantholide B.

These compounds were isolated from the air-dried root by steam distillation, SiO_2 column chromatography (hexane-EtOAc (9:1)) and further preparative GLC (5% OV 17, 220°).

Xantholide A $\underset{\sim}{1}$, $C_{15}H_{18}O_2$, m.p. 71-72°, $[\alpha]_D$+170.5°, m/e 230 (M^+), 202 (base peak), exhibits the following absorptions: λ_{max}^{MeOH} 204.5 nm (ϵ 9900), ν^{KBr} 1749, 1653, 924 cm^{-1}. The detailed NMR analysis ($CDCl_3$) applying double resonance technique and LIS reagents revealed the arrangement of protons shown in Fig. 1. The chemical shifts of H_1, H_5, H_{9a} and H_{9b} suggested these hydrogens to be allylic in nature. Therefore, C_1 and C_{10}, C_4 and C_5, and C_9 and C_{10} were reasonably connected each other, respectively, to culminate in the planer structure $\underset{\sim}{1}$.

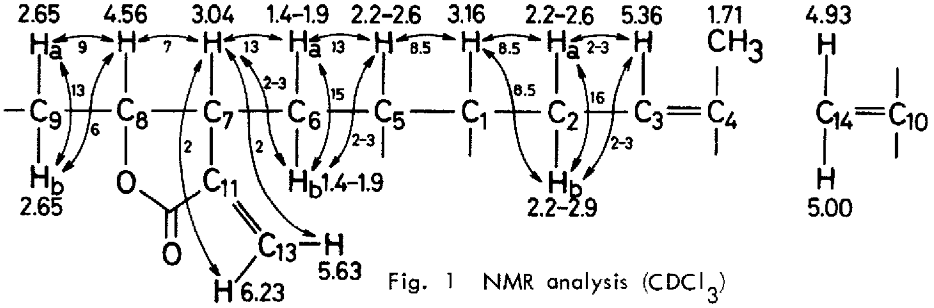


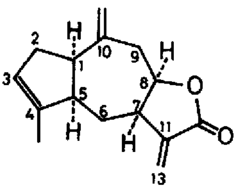
Fig. 1 NMR analysis ($CDCl_3$)

Small coupling constants between H_7 and both H_{13} indicated cis-fusion[3] of the lactone ring which must have β-configuration because $\underset{\sim}{1}$ showed negative CD spectrum ($[\theta]_{265}^{MeOH}$ -3740)[4]. Cis-relationship of H_5 and H_7 was derived from the large coupling constants (axial-axial) between these two protons and H_{6a}.

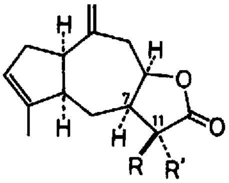
H_1 and H_5 on the 5-membered ring are in cis-orientation because they have relatively small mutual coupling constant[5].

NMR spectrum ($CDCl_3$) of xantholide B **2**, $C_{15}H_{20}O_2$, m.p. 76-77°, m/e 232, ν^{KBr} 1761, 886 cm^{-1}, is very similar to that of **1** except the presence of a methyl doublet at 1.31 ppm (J=7 Hz) in place of the two signals due to H_{13} of **1**. **2** was thus suggested to be a dihydro derivative of **1**. The small coupling constant (J=3.5 Hz) between H_7 and H_{11} in **2** indicated trans-disposition of these hydrogens and therefore α-configuration of the methyl group. For the chemical correlation, **1** was reduced with $NaBH_4$ to give a dihydro derivative **3**, m.p. 71.5°, which was not identical with **2**. However, treatment of **2** with NaOMe (60°, 13 hrs) afforded a 5:2 mixture of **2** and **3**.

For the final proof of the structure, X-ray crystallographic analysis of **2** was carried out. Single crystal, a colorless prism, belongs to orthorhombic system, space group $P2_12_12_1$, with four molecules in a unit cell ($\underline{a}=13.411_2$Å, $\underline{b}=15.058_3$Å, $\underline{c}=6.543_5$Å). Three-dimensional intensity data were collected using MoKα radiation. A total of 1216 independent non-zero structure factors was evaluated for analysis. The structure was solved by direct method (MULTAN) and refined by block-diagonal least squares calculation. Although the R value remained at 16.3%, it was sufficient to deduce the structure[6]. The perspective molecular view along the c-axis of the crystal is shown in Fig. 2.



1



2 R=H, R'=Me

3 R=Me, R'=H

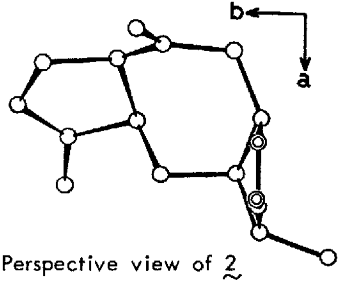


Fig. 2 Perspective view of **2**

Compound **1** inhibits the larval growth of Drosophila melanogaster completely at 5mg/2g concentration and is active with 1.3mg/2g[1]. However, **2** is essentially inactive for the test.

References and Notes

1) K. Kawazu, M. Arima and Y. Kii, Agric. Biol. Chem., 41, 223 (1977).

2) Elemophilanolides have been isolated from the roots. N. Tanaka, T. Yazawa, K. Aoyama and T. Murakami, Chem. Pharm. Bull., 24, 1419 (1976).

3) Z. Samek, Tetrahedron Letters, 671 (1970); Idem, Coll. Czech. Chem. Comm., 43, 3210 (1978).

4) W. Stöcklin, T. G. Waddell and T. A. Geissman, Tetrahedron, 26, 2397 (1970).

5) Coupling constant of cis compounds is less than 10 Hz while that of trans compounds is around 13 Hz. For example, see, M. Holub, Z. Samek, S. Vasickora and M. Masojidkova, Coll. Czech. Chem. Comm., 43, 2444 (1978); T. A. Dullforce, G. A. Sim, D. N. J. White, J. E. Kelsey and S. M. Kupchan, Tetrahedron Letters, 973 (1969); W. Herz, R. Murai and J. F. Blount, J. Org. Chem., 44, 1873 (1979); M. Katayama and S. Marumo, Tetrahedron Letters, 1773 (1979).

6) At this stage, no peak attributed to non-hydrogen atom was observed on the electron density difference map, though not all the hydrogen atoms were located. The large R value seems to be due mainly to slight decomposition of the molecule during recrystallization.

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