CHEMISTRY LETTERS, pp. 1679-1680, 1982.

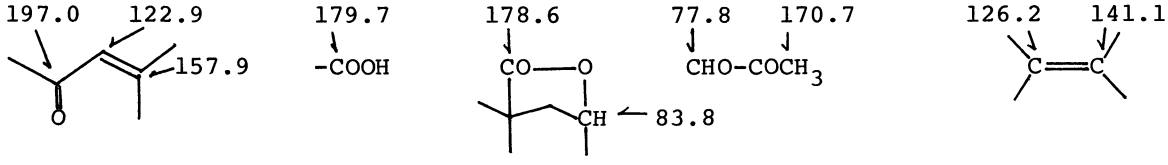
TRICHOLIDIC ACID, A NEW TRITERPENE LACTONIC ACID FROM TRICHOLOMA SPECIES

Shigeo NOZOE*, Akira TAKAHASHI, and Genjiro KUSANO
Pharmaceutical Institute, Tohoku University, Sendai 980
Akiko ITAI and Yoichi IITAKA
Faculty of Pharmaceutical Sciences, The University of Tokyo,
Hongo, Bunkyo-Ku, Tokyo 113

The structure of tricholidic acid, a new lanostane-type triterpene lactonic acid isolated from a toxic mushroom of Tricholoma species has been established by spectroscopic, chemical, and X-ray crystallographic analyses.

In the course of the investigation on biologically active substances obtained from toxic mushrooms, we have isolated a new triterpene lactonic acid from a toxic mushroom, Nagaeno-Matsushimeji, which is identified to a species of Tricholoma.[1] This paper deals with structural elucidation of this triterpene, tricholidic acid (1) on the basis of the chemical and spectroscopic properties as well as by X-ray crystallographic analysis. The methanol extract of the fresh mushroom collected at mountainous area of Miyagi prefecture was fractionated into ethyl acetate-, n-butanol- and water-soluble fractions. From the ethyl acetate and n-butanol fractions tricholidic acid (1) was obtained as a crystalline compound after repeated chromatography on silica gel and recrystallization from chloroform-methanol mixture.

Tricholidic acid (1), colorless needles, mp 213 - 215 °C, $[\alpha]_D^{22}$ -134.8 ° (c, 0.16, $CHCl_3$), CD: $[\theta]_{230}$ -7147 (c, 0.01, MeOH), Anal. Found: C, 70.87%; H, 8.32, Calcd. for $C_{32}H_{44}O_7$: C, 71.08; H, 8.20, showed mass fragment peaks at m/z 540 (M^+), 496 (M^+- COO), 436 (M^+- COO - AcOH), 83 (base peak, $COCH=CMe_2$), IR($CHCl_3$)cm^{-1}: 3050 (=C-H), 1760 (γ-lactone), 1720 (OAc), 1700 (COOH), 1680 (α,β-unsaturated ketone), 1617 (conjugated double bond), UVλ_{max}^{MeOH}nm (log ε): 235 (3.08). The ^1H NMR spectrum ($CDCl_3$,δ) of 1 displayed sharp singlets (0.89, 0.92, 0.95, 1.05, 3H × 4, 4 tertiary methyls), broadened singlets (1.92, 2.16, 3H × 2, two allylic methyls), a singlet (2.04, 3H, AcO-), an unsplitted signal (4.68, 1H, eq. H-C-OAc), a broadened singlet (5.12, 1H, lactone carbinyl H) and a broadened singlet (6.12, 1H, =C-H). The ^{13}C NMR spectrum of 1 showed thirty two signals, some of which could be assigned to the carbon atoms in the following partial structures. Taking into consideration of these results and molecular formular, tricholidic acid (1) must be a tetracyclic triterpene lactonic acid presumably with lano-



stane skeleton, since fungus produces many other lanostane-type metabolites.[2] Methylation of 1 with diazomethane gave a methyl ester (2), mp 267 - 269 °C, MS m/z: 554 (M^+ for $C_{33}H_{46}O_7$), 497, 479, 435, 83 (base peak), IR($CHCl_3$)cm^{-1}: 1760, 1720, 1685, 1620. ^1H NMR($CDCl_3$,δ): 3.67 (s, 3H). On treatment with 1% NaOH 1 afforded a desacetyl derivative (3) as sticky solid, IR($CHCl_3$)cm^{-1}: 3350, 1760, 1685, 1620.

The full structure of 1 was established by an X-ray crystallographic analysis. The crystal belongs to an orthorhombic space group $P2_12_12_1$. The cell parameters are a=16.085(5), b=27.165(8), c=7.155(2)Å, α=β=γ=90 ° with four tricholidic acid molecules and four methanol molecules in a unit cell. Intensity data were measured on a Philips PW1100 four-circle diffractometer using CuKα radiation monochromated by a graphite plate. A total of 2974, independent, non-zero reflection data were observed up to 2θ=156 ° using θ-2θ scanning technique. The structure was solved by the direct method using MULTAN program. An E-map gave the positions of 30 non-hydrogen atoms and the remaining 11 atoms were located on a subsequent difference Fourier map. Hydrogen atoms are also obtained from a difference map calculated after several cycles of least-squares refinement. The final refinement was made by the block-diagonal least-squares calculation assuming the anisotropic thermal motions for non-hydrogen atoms and isotropic ones for hydrogen atoms. The final R-factor was 0.049. The computer drawing of the molecule is shown in Fig.1. The negative sign of the CD curve of 1, which is attributed to the lactone ring, excluded a possibility of an antipode of lanostane-type triterpene for 1.

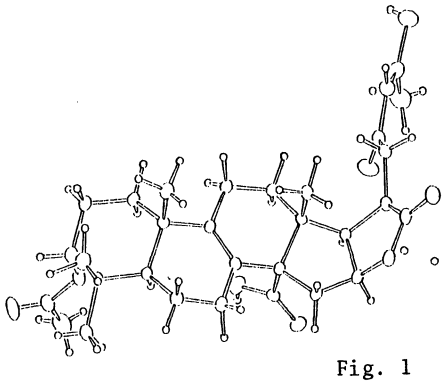
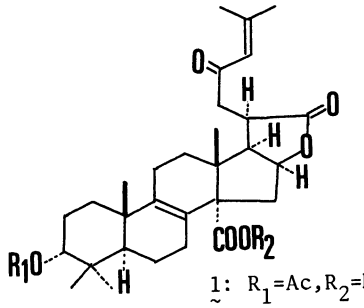


Fig. 1



1: R_1=Ac, R_2=H
2: R_1=Ac, R_2=Me
3: R_1=R_2=H

Tricholidic acid (1) has rather unique structure in the side chain moiety among lanostane group triterpene[3] with a partially similar case of kulolactone of a euphane-type triterpene.[4] This is a first isolation of an oxygenated lanostane type triterpene from Tricholoma species and biological activities of this compound are under examination.

References

1. Detailed classification of this fungus is under study.
2. Structures and chemistry of these metabolites should be reported elsewhere.
3. A. Kanematsu, S. Natori, K. Aoshima, Phytochemistry, 14, 487 (1975).
4. F. C. Chang and Chao-Kuo Chiang, Tetrahedron Lett., 1969, 891.

(Received August 13, 1982)