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TWO NEW ANTIFUNGAL COMPOUNDS FROM DENDROPANAX TRIFIDUS

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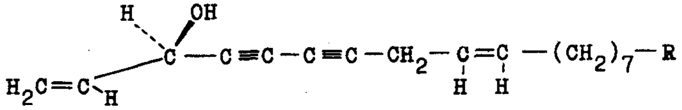
As part of a study on antifungal constituents of higher plants, we have isolated two new antifungal compounds (I and II) from the fresh leaves of Dendropanax trifidus Makino (Araliaceae), which have been used as an antiseptic.

Both compounds (I and II) were isolated by silica gel adsorption and partition chromatography of the ethyl acetate extract as colorless oils in yields of 0.034 % and 0.23 %, respectively, of the fresh leaves.

The compound (I), $[\alpha]_D$ -2.1° ($\underline{c}$ 1.9, $CHCl_3$) showed ir absorption bands$^{1)}$ ascribed to disubstituted acetylenic (2260), cis disubstituted olefinic (1655, 700), vinyl (1648, 1410, 985, 935), and hydroxyl groups (3605, 3500-3200 cm^{-1}). Its uv absorption bands [231(ε 1048), 243(953), 256(782), 269(664), 285 nm(540)] suggest that the acetylenic group is a conjugated diyne which is not in conjugation with the other unsaturated groups. Its pmr spectrum showed signals ascribed to $H_2C{=}C\underline{\underline{H}}-\overset{|}{\underset{|}{C}}H$ (5.64-6.20, m, J= 17, 9, 5 Hz), $H-\overset{|}{\underset{|}{C}}-C\underline{\underline{H}}(OH)-C<$ (4.87, d, J= 5 Hz), $>C-C\underline{\underline{H}}_2-CH=$ (3.00, d, J= 6 Hz), methylene groups (1.34, 12H) and $CH_2-C\underline{\underline{H}}_2-OH$ (3.58, t, J= 6 Hz). Signals (4H) at 5.05-5.55 were assignable to the terminal methylene protons and the cis olefinic protons.

Acetylation of I with acetic anhydride-pyridine gave a diacetate (III), whose pmr spectrum exhibited the signals due to two acetoxyl groups (2.05, 2.09, 3H each). On hydrogenation over Adams catalyst, I absorbed 6 molar equivalents of hydrogen to yield a dodecahydro derivative (IV), $C_{18}H_{38}O_2$, mp. 77-78.5° C, $[\alpha]_D$ -0.2° ($\underline{c}$ 1.0, ethanol), ir (KBr, 3350, 733, 722 cm^{-1}), pmr(pyridine-d_5, 1.05, 3H; 3.82, 3H). These data showed that I is an unsaturated diol of C_{18} straight chain having a primary hydroxyl group and a vinyl group at both termini. Combination of the partial structures described above by more close interpretation of the pmr data and the results of double resonance experiments led us to the structure, cis-9,17-octadecadiene-12,14-diyne-1,16-diol. The dodecahydro derivative (IV) which proved to be (-)-octadecane-1,16-diol should have the R-configuration according to Brewster's rule.[2] Therefore, it is obvious that I possesses the R-configuration.



I, R= CH_2OH
II, R= COOH

The compound (II), $[\alpha]_D$ -0.3° (c 2.0, CCl_4) showed uv absorption bands [231(ε 1140), 243(987), 256(597), 274(261), 291 nm(202)] similar to those of I. The ir spectrum of II exhibited the presence of a carboxyl group (2800-2400, 1710 cm^{-1}) in addition to the functional groups present in I. The pmr spectra of I and II were the same except the chemical shifts of the methylene protons adjacent to the carboxyl or the hydroxyl group. Methylation of II with diazomethane gave a monomethyl ester (V) [ir 1740 cm^{-1}; pmr 3.66 (3H, s)] which was acetylated to a monoacetyl monomethyl ester (VI) [ir 1755, 1215 cm^{-1}; pmr 2.07 (3H, s)]. On hydrogenation over Adams catalyst, VI gave methyl stearate. These results indicate that II is the corresponding carboxylic acid of I. Identification of the $LiAlH_4$ reduction product of the dodecahydro derivative of V with IV in respects of mixed mp., ir, pmr and specific rotation confirms that II is R-(-)-16-hydroxy-cis-9,17-octadecadiene-12,14-diynoic acid.

Perfect inhibition against conidium germination of Cochliobolus miyabeanus was observed at concentrations of 12.5 μg/ml of I and 50.0 μg/ml of II.

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Reference and Footnote

1) Unless otherwise stated, the ir spectra were taken in carbon tetrachloride, uv spectra in ethanol, and pmr spectra in deuteriochloroform containing tetramethylsilane as internal standard.

2) J. H. Brewster, J. Amer. Chem. Soc., 81, 5475 (1959).