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MAINGAYIC ACID, A PISCICIDAL CONSTITUENT OF *CALLICARPA MAINGAYI*

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Continuation of our studies on piscicidal constituents of plants of the *Callicarpa* genus[1,2] had led us to isolate an acid as a piscicidal constituent from the leaves of *Callicarpa maingayi* King *et* Gamble, a tropical tall tree found throughout Southeast Asia.

The acid (I) (2.9 g), $[\alpha]_D^{20°}$ -252° (*c* 3.0, chloroform), ir bands (Nujol): 2800-2400 and 1690 cm^{-1}, was isolated from the hexane soluble portion of the methanol extract of the dried leaves (5.2 kg) by silicic acid and Florisil chromatography (solvent system: benzene-ethyl acetate).

The acid (I) which was named maingayic acid exhibited about 15 % toxicity of pentachlorophenol.

The molecular formula, $C_{20}H_{28}O_3$, was assigned to I from the elemental analysis and the M^+ peak (*m/e* 316) in the mass spectrum.

The Ehrlich's color test and the uv (ethanol) (no maximum above 210 nm), ir (Nujol) (1560, 1505, 1035, 878 cm^{-1}), nmr** (6.28, 1H, m.; 7.20, 1H, m.; 7.34 ppm, 1H, t.) and mass spectrum (*m/e* 81) of I indicated the presence of a β-substituted furan ring. The prominent peaks at *m/e* 95 and 221 (M-95) suggested the furan ring exists as furylethyl group.

The nmr spectrum of I in benzene clearly revealed the presence of one tertiary methyl (0.80 ppm, 3H, s.), one secondary methyl (0.74 ppm, 3H, d., *J*=6.7 Hz), one vinyl methyl (1.65 ppm, 3H, s.) and one olefinic proton (5.45 ppm, 1H, m.).

The presence of the group, $-C(CH_3)=CH-CH_2-$, was deduced from the collapse of the multiplet at 5.45 ppm (olefinic proton) to a quartet (*J*=4.5 and 2.5 Hz) by the irradiation at 1.65 ppm.

Hydrogenation of its methyl ester (II) (3.65 ppm, 3H, s., $-OCH_3$) in acetic acid gave methyl hexahydromaingayate (III). Its nmr spectrum showed a doublet (*J*=5.5 Hz) at 0.75 ppm ascribable

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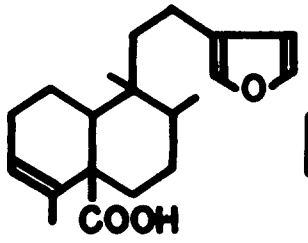
** Unless otherwise stated, the spectra were taken in deuteriochloroform at 60 MHz.

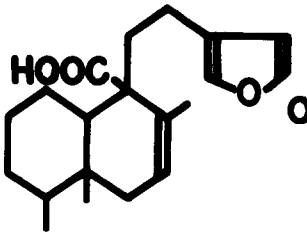
to a newly generated secondary methyl instead of signals ascribed to vinyl methyl and olefinic proton.

The findings above suggested that maingayic acid (I) is a furanoid diterpene possessing a rearranged labdane skeleton. This was verified by the formation of 1,2,5-trimethylnaphthalene on dehydrogenation of II with selenium.

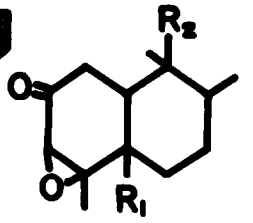
The resistance of II to alkaline hydrolysis and an AB-type signal (3.55 and 4.06 ppm, J =11.5 Hz) ascribed to $-CH_2OH$ group of the derived alcohol (IV) ($LiAlH_4$ reduction product)



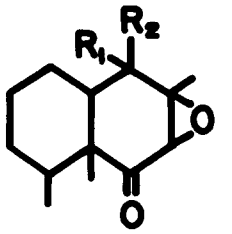
Ia



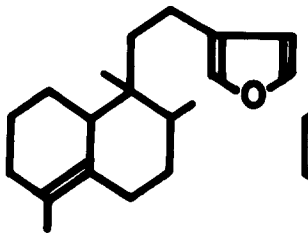
Ib



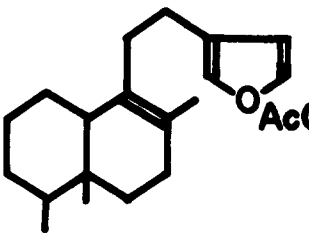
VIIIa



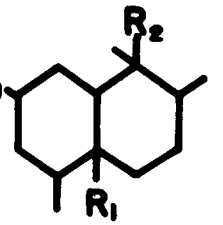
VIIIb



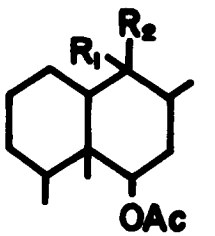
Va



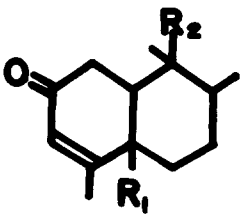
Vb



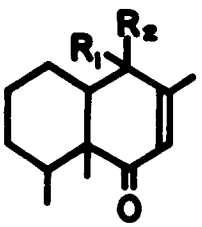
Xa



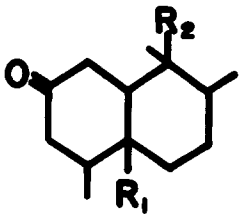
Xb



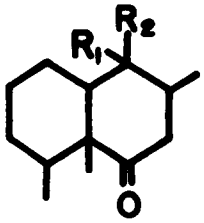
VIIa



VIIb



XIa



XIb

$R_1 = COOCH_3$ $R_2 = CH_2CH_2$  $Ac = COCH_3$

indicated the carboxyl group of I is tertiary and axial. The pK_{MCS}[3] value (8.35) of I is compatible with the above assignment.

Narayanan *et al*[4] found that in the nmr spectra of some diterpene acids in pyridine the methyl group which is in 1,3-diaxial relation with the carboxyl group resonates downfield by ca. 17 Hz, as compared with that of the corresponding methyl esters. The tertiary methyl signal of I in pyridine was observed at a lower field by 17.7 Hz than that of II. This indicates the tertiary methyl is in 1,3-diaxial relation with the carboxyl group in I.

Maingayic acid (I) was heated at 280-290°/1 mmHg to afford a compound (V), which showed no absorptions ascribed to carboxyl and diene in the ir and uv spectrum. The nmr spectrum of V exhibited no olefinic proton signal, but vinyl methyl proton signal at 1.65 ppm. Therefore, the compound (V) was inferred to have a tetrasubstituted double bond, which was formed by migration of the β,γ-double bond on decarboxylation of I. The M^+ peak was observed at *m/e* 272 in the mass spectrum of V.

From all the data described above the structure Ia or Ib can be formulated for maingayic acid (I).

Hydrogenation of II in ethanol afforded methyl tetrahydromaingayate (VI), with nmr signals ascribed to tetrahydrofuran ring protons at 3.30 (1H) and 3.64-4.08 ppm (3H). Oxidation of VI with chromium trioxide in acetic acid gave an enone (VII), m.p.70-72°; λ_{max}^{EtOH} 244 nm (ε 5,710), whose nmr spectrum showed a three-proton singlet at 0.63, a three-proton doublet (J=1.5 Hz) at 1.87 and a one-proton doublet (J=1.5 Hz) at 5.95 ppm. The enone (VII) was converted into an epoxy ketone (VIII) on treatment with alkaline hydrogen peroxide in methanol. In the nmr spectrum of VIII, two tertiary methyl and one epoxide proton signals were observed as singlets at 0.53, 1.28 and 3.17 ppm, respectively, and one methylene proton signal at 2.35 ppm as a nearly doublet. Hydrogenation of VII in acetic acid yielded a secondary alcohol (IX), ir (CCl_4): 3410 cm^{-1}, nmr: 0.78 ppm, 3H, d., J=5.0 Hz (newly generated secondary methyl), which formed an acetate (X), m.p.120-123°, nmr: 2.05, 3H, s. and 4.75 ppm, 1H, m. ($CH_3COO\overset{|}{C}H$). A ketone (XI), λ_{max}^{EtOH} 280 nm (ε 31); ir (CCl_4): 1710 cm^{-1}, nmr: 0.58 ppm, 3H, s., was obtained from IX on oxidation with the Jones reagent.

The following observations in the nmr spectra of the compounds (VII-XI) lead to exclude the formulation of the b-series; 1) the proton on the carbon atom bearing the acetoxyl group in X displayed a hardly resolved multiplet at 4.75 ppm, 2) the tertiary methyl protons of VII, VIII and XI resonated at higher fields (0.53-0.63 ppm) than tertiary methyl protons situated

on the β position to a carbonyl group and 3) a two-proton signal ascribed to methylene adjacent to the keto group in VIII was discernible at 2.35 ppm. Therefore, we propose the structure Ia for maingayic acid (I).

The maximum number of 1,3-diaxial interaction[3] with the carboxyl group counted is 2 in Ib while 3 in Ia. The latter coincides with the number of the interaction calculated from the pK_{MCS} value (8.35) of I. It supports the structure Ia.

Anthonsen *et al*[5] had isolated solidagoic acid A from the roots of *Solidago serotina* and tentatively assigned this compound the structure Ia, but it was confirmed that this compound is different from maingayic acid in the nmr spectrum.

We suppose solidagoic acid A may be one of the stereoisomers of maingayic acid (I).

Acknowledgements

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