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ATOMARIC ACID, A NEW COMPONENT FROM TAONIA ATOMARIA[1]

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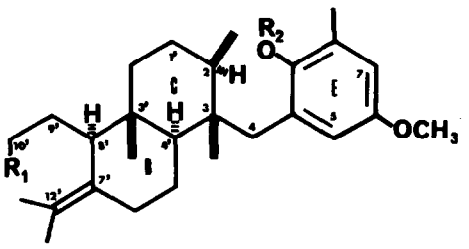
In preliminary papers we have reported the structure, chemical properties and synthesis of taondiol[2], a tocopherol-like compound isolated from the marine alga Taonia atomaria (Dyctiotaceae). From the same seaweed collected at the same time but in another place[3], we have isolated the acid I, designated as atomaric acid, as the only phenolic constituent. Its structure and stereochemistry was determined on the basis of the chemical and spectral evidence described below.

From the biogenetic point of view, the constitution of atomaric acid can be regarded as derived from taondiol methyl ether by cationic opening of the chroman ring, followed by an apparently concerted hydrogen-methyl shifts. Ring A of the terpenoid skeleton has been oxidatively cleaved between C-11′and C-12′ bond. The numbering and lettering systems in atomaric acid (I) follow directly from these biogenetic considerations and are the same as in taondiol[2].

Ether extraction of the air dried seaweed followed by column chromatographic purification on silica gel resulted in the isolation of I as an oil in ca. 0.09% yield (dry weight alga), $(\alpha)_D$ +49 (c, 0.42, $CHCl_3$). A composition of $C_{28}H_{42}O_4$ was indicated by the mass spectrum of I (M^+ at m/e 442) and confirmed by elemental analysis of its methyl ester derivative II (m.p. 112-115), obtained by methylation of the acid I with diazomethane. In the IR spectrum compound II shows bands at 3620, 1740, 1620, 1490 and 860 cm^{-1}, and in the UV at 293 nm (ε, 3,270). Upon methylation with Me_2SO_4, compound II afforded the methoxy derivative V, $C_{30}H_{46}O_4$ (M^+ at m/e 470), which confirms the phenolic nature of I.

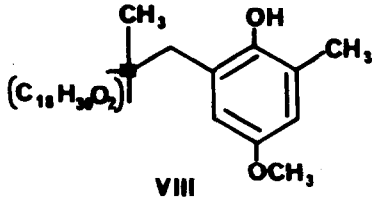


I;	R_1 : COOH	R_2 : H
II;	R_1 : $COOCH_3$	R_2 : H
III;	R_1 : $COOCH_3$	R_2 : Ac
IV;	R_1 : $COOCH_3$	R_2 : Bz
V;	R_1 : $COOCH_3$	R_2 : CH_3
VI;	R_1 : CH_2OH	R_2 : CH_3
VII;	R_1 : CH_2OAc	R_2 : CH_3

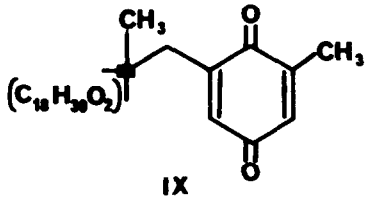
The NMR spectrum of II (100 MHz, $CDCl_3$, τ-scale) displayed signals due to two meta-coupled protons at 3.32 and 3.51 (2d, 1H each, J=3 Hz); a broad peak at 5.66 (1H, exchangeable with D_2O) assigned to the phenolic hydroxyl proton; one methoxy group at 6.28 (3H, s); one methyl ester group at 6.36 (3H, s); two benzylic protons with restricted rotation and no protons on adjacent carbon atom at 7.14 and 7.75 (2d, 1H each, J=14 Hz); one aromatic methyl group at 7.78 (3H, s), and two olefinic methyl groups at 8.30 and 8.32 (s, 3H each). In the upfield region appear signals for one secondary methyl group at 8.84 (3H, d, J=7 Hz) and two tertiary methyl groups at 8.96 and 9.04 (s, 3H each). Examination of the mass spectra of II and V lends support to the prenyl-phenolic nature of the compound: the base peak at m/e 151 ($C_9H_{11}O_2$) in II (base peak at m/e 165 in V) arises by cleavage of the aromatic ring[4]. Further peaks at m/e 305 ($C_{20}H_{33}O_2$) and 218 ($C_{16}H_{26}$) in the mass spectrum of II, shown also in that of V, are due to the diterpene entity of the molecule.

The relative position of the substituents on the aromatic ring was determined by the following reactions. Chromic acid oxidation of II gave the prenyl quinone IX: UV, 255 nm (changing to 290 nm after $NaBH_4$ treatment); IR, 1645 cm^{-1}; NMR, τ 3.34 (1H, d, J=3 Hz), 3.47 (1H, dd, J=3 and 1.5 Hz) and 7.97 (3H, d, J=1.5 Hz), which was characterized as a 2-methyl-6-prenyl-1,4-benzoquinone[4]. The NMR spectra of the acetate (III) and benzoate (IV) shown an upfield shift of the aromatic methyl group (0.15 ppm) and benzylic protons (0.20), whereas the aromatic protons remain almost unchanged. This provides good evidence for the 2-methyl-4-methoxy-6-prenylphenol nature of the chromophore. Therefore, the partial

structure VIII is involved in I.



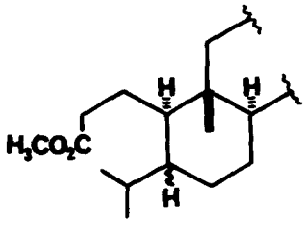
VIII



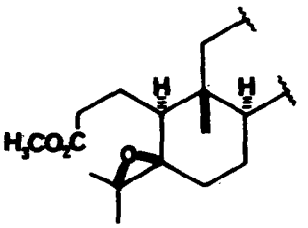
IX

On treatment with $LiAlH_4$ in THF, V afforded a primary alcohol (VI); IR, 3420 cm^{-1}; NMR spectrum showed a two-proton broad singlet at τ6.50 attributable to methylene protons of R-$C\underline{H}_2$-OH, which in the acetate (VII) are shifted to τ6.10. Compound II consumed one mol of H_2 over PtO_2 in ethanol to give the dihydro-compound X, $C_{29}H_{46}O_4$ (M^+ at $\underline{m/e}$ 458), together with the major fragment ions at $\underline{m/e}$ 307, 220 and 151; the NMR spectrum exhibits methyl signals at τ8.85 (3H, d, J=7 Hz), 9.18 (6H, s) and 9.24 (6H, s), while the original signals due to olefinic methyl protons disappeared. Oxidation of III with peroxybenzoic acid in chloroform resulted in the formation of a 32:68 mixture of two epoxides which were separated by column chromatography: XIa, NMR, τ 8.73 (s, 3H, C-5'Me) and 8.84 (s, 6H, C-12'Me); XIb, τ 8.73 and 8.77 (s, 3H each, C-12'Me) and 8.98 (s, 3H, C-5'Me). Because of the presence of the β-Me group at C-3' the α oxide is formed preferentially to the β one (XIa).

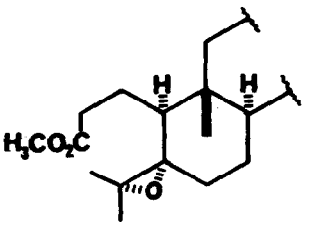
The molecular formula of stomaric acid, when coupled with knowledge of the functional groups, requires that the terpenoid entity of the molecule be bicarbocyclic. Ozonolysis of the acetate III led to the formation of acetone and a six-membered cyclic ketone XII, $C_{28}H_{40}O_6$ (M^+ at $\underline{m/e}$ 472); IR, 1700 cm^{-1}; NMR, methyl signals at τ8.80 (3H, d, J=6 Hz), 9.10 and 9.18 (s, 3H each). Treatment of XII with $NaBH_4$ afforded the alcohol XIII. The configuration of the C-7' OH group in XIII was determined as β-axial from its NMR spectrum, which contained a methine signal at τ 6.30 ($W\frac{1}{2}$=6 Hz) attributed to the α-equatorial C-7' proton, a tert methyl signal at τ 8.92 was assigned to the C-3' methyl group, shifted downfield by 0.26 ppm relative to the corresponding signal of XII[5]. Dehydration of XIII proceeded readily with $POCl_3$/py to give the olefine XIV; NMR, τ 4.90 (1H, bs, $W\frac{1}{2}$=10 Hz). This reaction sequence did not establish the stereochemistry at C-8' in stomaric acid, but the easy dehydration of XIII to XIV supported the α-axial



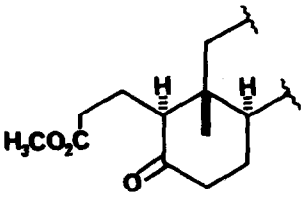
X



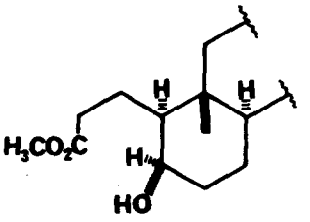
XIa



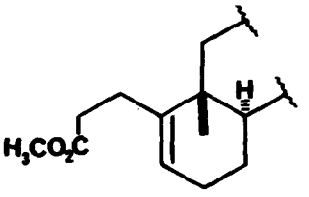
XIb



XII



XIII



XIV

configuration assigned in I to the C-8′ proton.

From the chemical and spectroscopic data mentioned above, the structure of atomaric acid would be reasonably assigned as I.

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