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MACULATOXANTHONE, A NEW PYRANOXANTHONE FROM HYPERICUM MACULATUM

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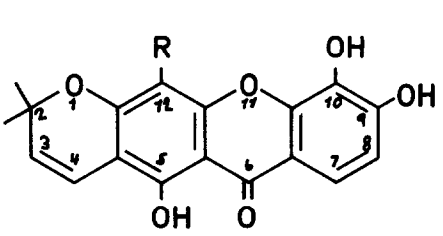
During a study on constituents of the sub-family Hypericoideae, fam.Guttiferae a new pyranoxanthone with a monoterpene side chain was isolated in 0.01 % yield (dry weight basis) from the roots of H.maculatum Crtz. The structure 5,9,10-trihydroxy-2,2-dimethyl-12-(5-methyl-2-isopropenylhex-4-enyl)-2H,6H-pyrano-[3,2-b]xanthene-6-one (Ia) is ascribed to the compound on the basis of spectroscopic evidence.

The compound was isolated from a methylene chloride extract of the plant material by chromatography on silicagel. Upon crystallisation from benzene-light petroleum (1:1) deep yellow plates, m.p.174-175° were obtained; $[\alpha]_D^{20}$ +18.7 (c 0.5, MeOH).

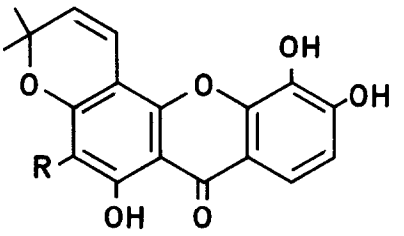
The high resolution mass spectrum of the compound showed a molecular ion peak of m/e 462.2020 corresponding to the formula $C_{28}H_{30}O_6$. The UV spectrum (see later) of the compound was suggestive of a xanthone, and this observation was confirmed by the presence in IR of a band at 1650 cm^{-1} (>C=O) (1). The molecular carbon content is thus compatible with a xanthone nucleus substituted with three C_5 units.

The NMR spectrum (100 MHz) of the compound (5 % in $CDCl_3$) showed three one-proton singlets at τ -3.15, 3.62, and 4.29, respectively, which disappeared upon deuteration with D_2O; the signals are ascribed to three phenolic protons, the chemical shift of the low field signal being characteristic for the strongly hydrogen bonded proton of a C-1 hydroxyl in a xanthone (2). A pair of one-proton doublets at τ 2.31 and 3.06, respectively, (J=9 cps) constitute an ortho-coupled aromatic AB system and are ascribed to the protons at C-8 and C-7 (3) of the xanthone nucleus.

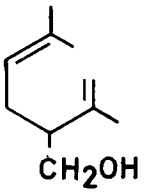
A second pair of doublets at τ 3.27 and 4.45 (J=10 cps) as well as a six-



I



II

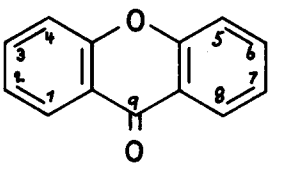


III

Ia, II R=5-methyl-2-isopropenylhex-4-enyl-

Ib R=H

Ic R=1,1-dimethylallyl-



IV

proton singlet at τ 8.51 are diagnostic of the olefinic and methyl protons, respectively, of a 2,2-dimethylchromene moiety (3).

A one-proton signal at τ 4.80 had the appearance of a triplet (J=6 cps) showing additional fine splitting and was found by spin-decoupling experiments to be coupling with two three-proton singlets, also showing fine splitting, at τ 8.27 and 8.39, as well as with a complex two-proton signal at approx. τ 7.8. The signals may be ascribed to the vinyl, methyl, and methylene protons, respectively, of a γ,γ-dimethylallyl grouping, the chemical shift of the methylene protons indicating a linking of this group to an aliphatic or alicyclic carbon.

A complex two-proton signal at τ 5.35 was found to decompose into a pair of AB doublets (J=2 cps) upon irradiation of a three-proton signal at τ 8.26. Furthermore a complex two-proton signal at τ 7.15 and a complex one-proton signal at τ 7.6 were observed from the spectrum. These eight protons can plausibely be arranged into a 3-methyl-but-3-enyl grouping substituted in the 1- or 2-position by the γ,γ-dimethylallyl grouping. Since the resulting ten-carbon skeleton should be substituted on to the xanthone nucleus, branching at the 2-posision is favoured, the two-proton signal at τ 7.15 being compatible with a methylene on an aromatic nucleus.

The ten-carbon skeleton is thus identical with that encountered in the naturally occuring monoterpene alcohol lavandulol (III). Its presence was con-

firmed by comparison of the pertinent signals in the NMR spectrum of the compound with that of lavandulol (4), the appearance and positions of the signals being almost identical except for the expected shift of the methylene signal at τ 7.15 in the compound to τ 6.45 in lavandulol.

High resolution mass spectral data were in accordance with the above observations. Thus a peak at m/e 447 is due to the loss of CH_3 from the dimethylchromene moiety. A peak at m/e 393 has the composition $C_{23}H_{21}O_6$ corresponding to allylic cleavage of the γ,γ-dimethylallyl chain from the molecular ion, while the base peak at m/e 339 with the composition $C_{19}H_{15}O_6$ is due to benzylic cleavage in the ten-carbon side chain.

The UV spectrum of the compound exhibited λ_{max}^{MeOH} (log ε) 240 (4.36), 283 (4.66), and 338 (4.32). On the basis of UV experimental data, the positioning of the two hydroxyl groups, the third being at C-1, may be deduced. Thus the identical bathochromic shifts (30 nm) of the high wavelength maximum produced by the addition of either NaOMe or NaOAc are indicative of a hydroxyl group para to the ring carbonyl (5). Furthermore, the strong bathochromic shifts of the high and medium wavelength bands (65 and 25 nm, respectively) produced by addition of $AlCl_3$, and the reduced bathochromic shifts (30 and 20 nm, repectively) upon further addition of HCl to the solution are indicative of the presence of both the chelating hydroxyl as well as an ortho situated dihydroxyl grouping (6). Bearing the NMR discussion in mind the possible hydroxylation patterns are 1,2,3-, 1,3,4, and 1,5,6. However, as the compound was stable in base the two former may be disregarded (5,6).

The remaing oxygen atom belonging to the dimethylpyran ring can be substituted on to the 3-position of the xanthone nucleus, since the UV spectrum of the compound is in excellent accordance with that of known 1,3,5,6-tetraoxygenated dimethylpyranoxanthones, namely jacarubin (Ib), λ_{max}^{EtOH} 240 (4.09), 279 (4.61), and 334 (4.26) (7), as well as macluraxanthone (Ic), λ_{max}^{EtOH} 242 (4.31), 283 (4.64), and 338 (4.28) (8).

The remaining question as to whether the dimethylpyran ring is linearly (Ia) or angularly (II) fused to the xanthone ring system has not been entirely solved. However, NMR measurements of chemical shifts for the compound in $CDCl_3$ and Py-d_5 at identical concentrations showed that the 4 -proton of the dimethylpyran ring is

deshielded by 0.29 ppm in Py-d_5 relative to in $CDCl_3$. The corresponding deshielding of the 3 -proton amounted to 0.04 ppm. Since it has been established (9), that protons situated in the vicinity of a phenolic hydroxyl exhibit pyridine-induced deshielding relative to $CDCl_3$ in a magnitude of 0.37-0.48 ppm for an ortho-H, 0.09-0.16 ppm for a meta-H, and 0.22-0.29 ppm for an ortho-CH_3, it is reasonable to favour the structure (Ia). In this the 4 -proton has a peri relationship to the hydroxyl at C-1 and thus may be expected to show a solvent shift intermediate between the values for an ortho- and a meta-H and in order of the values for an ortho-CH_3.

Maculatoxanthone is the first known example of a xanthone with an optically active side chain. Further work on the structure and the stereochemistry of the compound is in progress.

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