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AURAPTENOL, A COUMARIN COMPOUND IN BITTER (SEVILLE) ORANGE OIL

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Abstract—7-Methoxy-8-(2-hydroxy-3-methyl-3-butenyl)-coumarin has been isolated from bitter orange oil and named auraptenol. NMR spectra together with IR spectra and analytical data are presented as evidence of its constitution.

IN A survey of the coumarin and psoralen compounds in citrus oils, a compound (I) was isolated by silicic acid column chromatography[1] from bitter orange (*Citrus aurantium* Linn., subspecies *amara* Linn.) oil. The UV absorption spectrum of this compound is virtually identical with that of osthol (II)[2,3,4] (Fig. 1), and it is not affected by the addition of base, indicating the absence a free phenolic hydroxyl group. It gives a negative magnesium–hydrochloric acid test for flavonoid compounds The elemental analysis of I agrees with a molecular formula of $C_{15}H_{16}O_4$. The m.p. is 109–110° and $[\alpha]_D^{26} = 14°$. The IR absorption spectrum of I has a broad peak at 3500 cm^{-1} indicating the presence of a hydroxyl group, a peak at 1725 cm^{-1} characteristic of the coumarin lactone ring and at 1615 cm^{-1} characteristic of an aromatic ring. The broad peak at 900 cm^{-1} is presumed to be that of a terminal methylene group.

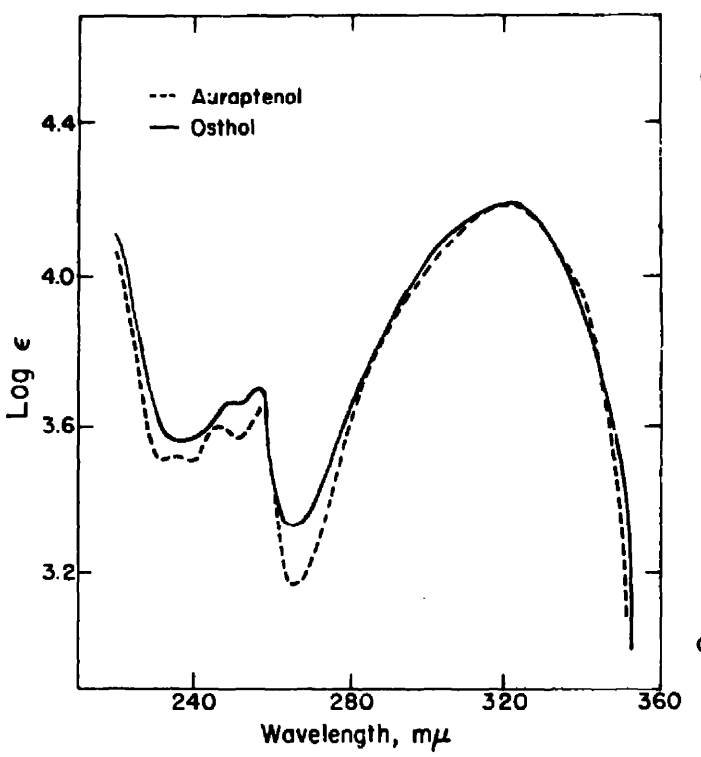
From the analytical and spectral data, I appears to be a derivative of herniarin (7-methoxycoumarin) having a 5-carbon side chain containing a hydroxyl and terminal methylene group attached at the 8-position of coumarin. Additional evidence from NMR analysis confirms this and determines the constitution as 7-methoxy-8-(2-hydroxy-3-methyl-3-butenyl)-coumarin for which the name "auraptenol" has been chosen. The following observations and argument support the proposed structure.

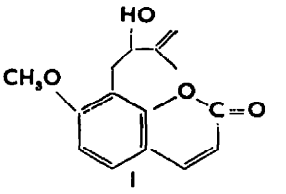
In the discussion the 16 protons in auraptenol are identified with capital letters as indicated in Fig. 2. The NMR spectrum of auraptenol shows the presence of two methyl groups. One of the methyl groups, the 7-methoxyl (H_E), occurs at 6·12τ, the other, H_J, at 8·17. The assignment of the position of the latter group is justified by both anisotropic and electron-removing effects of the neighboring vinyl and hydroxyl groups.

The two olefinic protons, H_A and H_B, appear at 3·84 and 2·44τ ($J = 9·5$ c/s), as expected of coumarin compounds.[5] The two *ortho* protons, H_C and H_D, absorb at

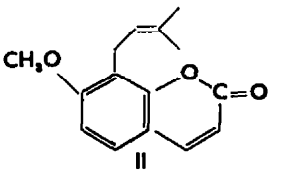
* A laboratory of the Western Utilization Research and Development Division, Agricultural Research Service, U.S. Department of Agriculture.

[1] W. L. Stanley and S. H. Vannier, *J. Amer. Chem. Soc.* **79**, 3488 (1957).
[2] H. Böhme, *Arch. Pharm.* **277**, 61 (1939).
[3] G. A. Kuznetsova, Trudy Botan. Inst. im V. L. Komarova *Akad. Nauk SSSR* 5(5), 21 (1959).
[4] Y. D. Mao and L. M. Parks, *J. Amer. Pharm. Assoc.* **39**, 107 (1950).
[5] High Resolution NMR Spectra Catalog, Varian Associates, Palo Alto, California (1962).





I

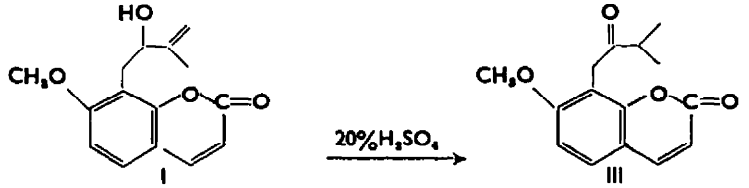


II

FIG. 1. UV absorption spectra of auraptenol and osthol.

2·72 and 3·20τ (J = 9·0 c/s), respectively. The terminal vinyl protons, H_I, appear at 5·20τ and show a barely visible long range coupling to H_G and the methyl group at H_J. The tertiary hydrogen, H_G, occurs as the X portion of an ABX system at 5·70τ. The benzylic protons, H_F, appear at 6·90τ showing the expected AB pattern of an ABX system. The 8·08τ peak was assigned to the hydroxyl group since it disappeared on the addition of deuterium oxide to the solution. Electronic integration of the spectrum completely confirmed the assignment.

Auraptenol may be converted to isoaurapten (III) by heating with 20% sulfuric acid. Although the isoaurapten thus formed failed to crystallize (reported m.p. 66°),[6] its oxime derivative was prepared and obtained crystalline, m.p. 163–166° (lit. 166–167°). IR and NMR spectra (Fig. 3) fully support the identity of isoaurapten..



I III

In the IR spectrum of isoaurapten the peaks for hydroxy and terminal methylene absorptions found in auraptenol are missing. The carbonyl band at 1725 cm^{-1} is considerably enhanced. A 5·95τ singlet peak in the NMR spectrum of isoaurapten

[6] H. Bohme and G. Pietsch, *Ber. Dtsch. Chem. Ges.* 72, 773 (1939).

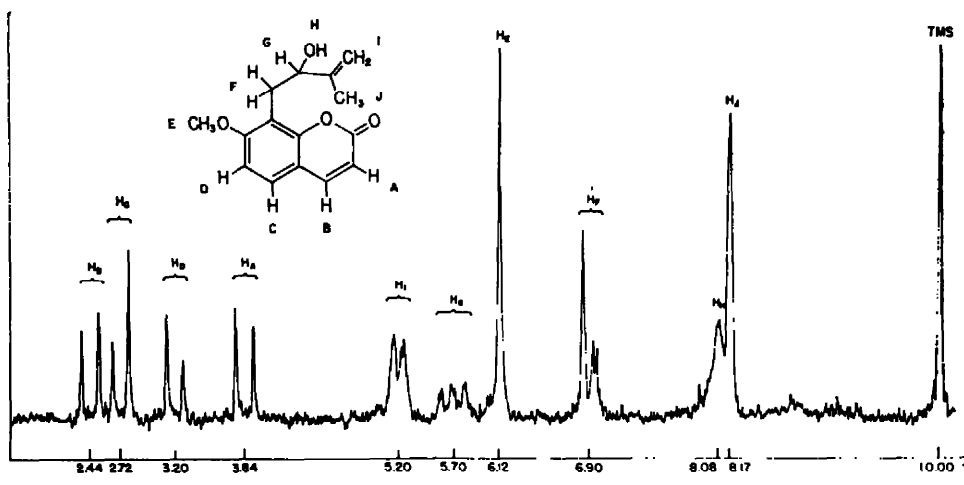


FIG. 2. 60-megacycle NMR spectrum of auraptenol in deuterochloroform.

(Fig. 3) can be appropriately assigned to the benzylic protons because of the combined diamagnetic effects of the aromatic nucleus and carbonyl group. As expected, the terminal methyl groups are shifted upfield to 8·99τ, as a doublet (J = 7 c/s) whereas the tertiary hydrogen appears as an incompletely resolved septet at 7·10τ. Again, this assignment was confirmed by integration of the spectrum.

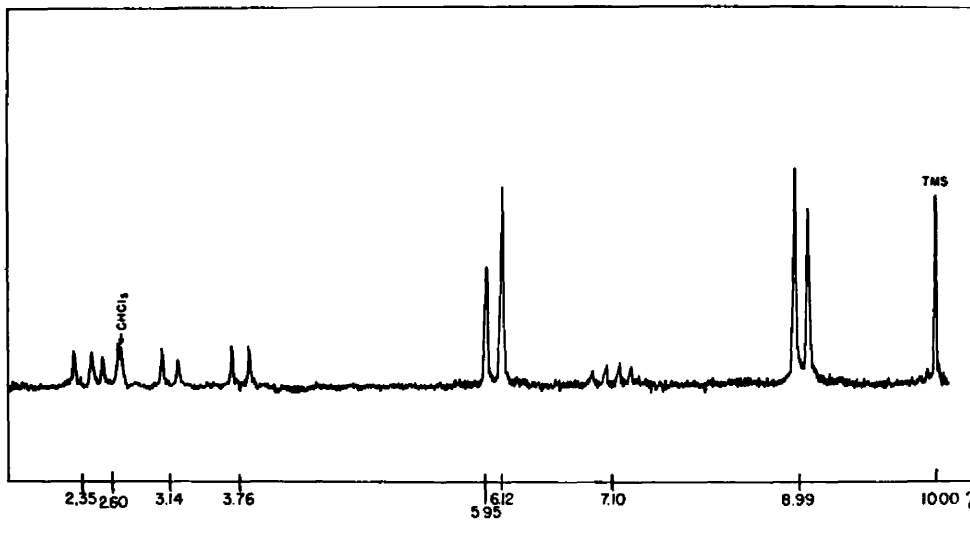


FIG. 3. 60-megacycle NMR spectrum of isoaurapten in deuterochloroform.

EXPERIMENTAL

Isolation of auraptenol (I). A 400-g portion of commercial oil of bitter orange was applied to a column of powdered silicic acid 3-1/2″ in diameter and 12″ long prepared from a hexane slurry.[7] The column was developed with hexane followed by successive increments of hexane containing

[7] J. M. Miller and J. G. Kirchner, *Analyt. Chem.* **24**, 1480 (1952).

increasing amounts of ethyl acetate. Eluted fractions were collected in a timeractuated fraction collector and were tested for eluted components by analysis with thin layer chromatography as described earlier.[1] A fraction showing strong blue fluorescence under UV was evaporated under a stream of N_2 to yield 187 mg crude auraptenol which on recrystallization from ethanol yielded 105 mg needles, m.p. 109–110°, λ_{max}^{EtOH}322 mμ log ϵ 4·17, $\nu_{max}^{CHCl_3}$3500, 1725, 1615, and 900 cm^{-1}, $[\alpha]_D^{25°} = 14°$ (ethanol, $c = 1$). The NMR spectrum (Fig. 2)[5] is remarkably good considering that it is taken from a 10 mg sample. (Found: C, 69·3; H, 6·22; MeO-, 12·5. $C_{15}H_{16}O_4$ requires: C, 69·21; H, 6·20; 1 MeO-, 11·9).

Isoaurapten (III). Auraptenol, 10 mg, was refluxed gently in 2 ml of 20% H_2SO_4 for 4 hr. The product was extracted with chloroform and the extract was washed with 5% $NaHCO_3$ aq and water and was then dried (Na_2SO_4). The slightly colored oil obtained after removal of solvent was chromatographed through 2 g of silicic acid. Isoaurapten was eluted from the column with a 50:50 v/v mixture of ether and benzene. Six mg of oil was recovered. Repeated attempts to crystallize the isoaurapten failed. The NMR[5] (Fig. 3) and IR ($\nu_{max}^{CHCl_3}$ 1725, 1615 cm^{-1}) spectra were taken on this oil. The crystalline oxime of isoaurapten was prepared according to the procedure of Böhme and Pietsche[6] m.p. 163–166° (lit. m.p. 166–167°).

Reference to a company or product name does not imply approval or recommendation of the product by the U.S. Department of Agriculture to the exclusion of others that may be suitable.

[5] The NMR spectra were taken in deutero-chloroform with tetramethylsilane as internal reference using the Varian A-60 Spectrometer.