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ATHEROLINE, A YELLOW PHENOLIC ALKALOID FROM ATHEROSPERMA MOSCHATUM LABILL.

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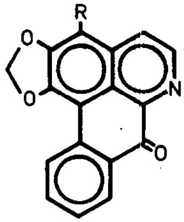
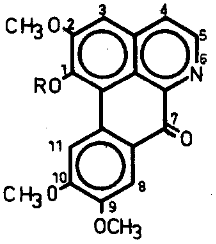
The presence of two yellow, non-phenolic alkaloids, spermatheridine (I) and atherospermidine (II), in the bark of *Atherosperma moschatum* Labill. has already been reported (1), and they have been shown to belong to the small class of alkaloids which possess a 7-oxo-dibenzo(de,g) quinoline skeleton (2). An examination of the phenolic alkaloids of *A. moschatum* has resulted in the isolation of small quantities of a further yellow base, atheroline, m.p. 250–260° (decomp). Its i.r. spectrum had a carbonyl peak at 1639 cm^{-1}, and its u.v. and visible light absorption spectra showed that it also belonged to the above-mentioned class of alkaloids (2).

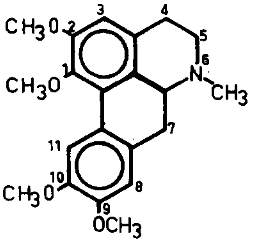
A positive ferric chloride test and an absorption band at 3250 cm^{-1} in its i.r. spectrum indicated the presence of a phenolic hydroxy group. Treatment of atheroline with acetic anhydride in pyridine yielded O-acetylatheroline which crystallised from pyridine as yellow needles, m.p. 190–195° and analysed for $C_{21}H_{17}O_6N$ with three methoxy groups. In the aromatic proton region, the n.m.r. spectrum of O-acetylatheroline showed three one-proton singlets at δ7.11, 8.20 and 8.80 ppm, and two one-proton doublets (J=6 cps) centred at δ7.64 and 8.80 ppm respectively. These features are compatible with structure (III), which has oxy substituents at positions 1,2,9 and 10. The singlet at high field may be assigned to H_3 (3), that at δ8.20 ppm to H_8 and that at δ8.80 ppm to H_{11} (3). The doublets form an AB quartet arising from H_4 and H_5; by comparison with pyridine (4), H_5 would be expected at lower field than H_4, which is thus assigned the doublet around δ8.80 ppm. The conversion of atheroline into the known alkaloid 1,2,9,10-tetramethoxy-7-oxo-dibenzo-(de,g)-quinoline (5) (IV) by methylation with methyl iodide and methanolid sodium methoxide confirmed the skeleton of atheroline and the location of oxy substituents at position 1,2,9 and 10.



I.(R=H).
II.(R=OCH$_3$).



III.(R=Ac).
IV.(R=CH$_3$).
VI.(R=H).



V.

TABLE 1.

U.V. and Visible Light Absorption Spectra of Atheroline.

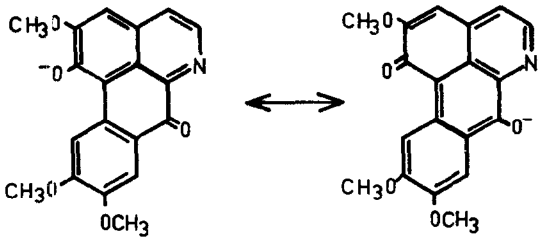
in EtOH		in 0.05N HCl (EtOH/H_2O)		in 0.05N NaOH (EtOH/H_2O)	
λ_{max}, mμ	$\log\epsilon_{max}$	λ_{max}, mμ	$\log\epsilon_{max}$	λ_{max}, mμ	$\log\epsilon_{max}$
244	4.09	257	4.12	252	4.04
273	4.17	282	4.12	294	3.99
292 (sh.)	3.96			320	3.98
355	3.90				
380 (sh.)	3.83	385	4.05	390	3.74
435	3.62	500	3.38	535	3.46

In the n.m.r. spectrum of O-acetylatheroline, a peak of intensity six protons occurred at δ4.01 ppm and one of intensity three protons at δ4.03 ppm. All three methoxyls thus give almost indistinguishable proton absorptions; with O-methylatheroline and glaucine (3) (V), however, three of the methoxyls absorb at the same field, while the fourth absorbs at distinctly higher field. In the case of glaucine, the latter absorption (at δ3.75 ppm) has been assigned (3) to the methoxyl at position 1, and the former (at δ3.95 ppm) to the remaining three methoxyls, the difference being ascribed to the crowding around position 1 which forces the attached methoxyl slightly out of the plane. The same consideration should hold good for O-methylatheroline (IV), and thus the three proton peak at δ3.95 ppm can be assigned to the methoxyl at position 1, and the nine-proton peak at δ4.03 ppm to the remaining three methoxyls. The absence of a peak around δ3.95 ppm in the spectrum of O-acetylatheroline indicates that this base has its acetoxy group located at position 1 and that it may be represented by (III), while atheroline is represented by (VI).

Support for this proposal was furnished by the u.v. and visible light absorption spectra of atheroline in aqueous ethanolic alkali. A considerable bathochromic shift of the absorption bands from those observed in neutral solution resulted, particularly in the visible region (see Table 1.). This shift can be ascribed to mesomerism of the anion (VII) formed by ionisation of the phenolic group. The contributing form, (VIII), to the resonance hybrid contains three aromatic rings as for (VII) and should have comparable energy to the latter form. This fact, together with the distribution of charge between the two canonical forms, would be expected to produce a considerable deepening of colour of the anion as compared to the neutral molecule (6), greater than if the hydroxyl was located in any of the alternative positions, 2, 9 or 10, since none of these locations for the hydroxyl would result in anions with contributing forms of so nearly equal energy.

As a result of the mesomeric stabilisation of the anion, atheroline has well-marked acidic properties and dissolves in aqueous sodium carbonate to produce a blue salt; it is in fact a vinologous carboxylic acid.

Synthetic experiments are in hand to confirm the proposed structure of atheroline.



VII. VIII.

Acknowledgments

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