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STRUCTURE OF MURRALONGIN, A NOVEL MONOMERIC COUMARIN FROM MURRAYA ELONGATA : STEREOCHEMISTRY AND PREFERRED CONFORMATION OF ITS UNIQUE SIDE CHAIN

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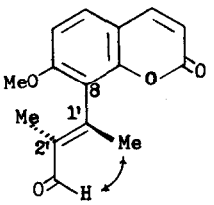
The structure and stereochemistry of murrangatin[1], a new monomeric coumarin isolated from the leaves of Murraya elongata Alph. DC (Rutaceae) has been reported by us recently. We now present the chemical and spectral evidence leading to the structure and stereochemistry of another new coumarin, murralongin (I), isolated from the same plant in much lower yield. The N.O.E. evidence for the trans double bond and the preferred conformation of its unique 5 carbon side chain and its probable biogenesis have also been presented.

The petrol (b.p. 60-80°) extract of the leaves upon repeated chromatography over silica gel afforded from the petrol-benzene (1:1) and benzene eluates murralongin* (I) crystallising from ether as colourless heavy needles, m.p. 135° (t.l.c. - silica gel G, R_f 0.74, chloroform-methanol 93:7), $C_{15}H_{14}O_4$ (M^+ 258). It displayed the following spectral characteristics: λ_{max} (EtOH) 320 nm (log ϵ, 4.16), 236 (4.17); λ_{min} 270 (3.69) and 228 (4.15) - unaffected by alkali; ν_{max} (KBr) 1725 (coumarin CO), 1665 (conjugated CO), 1605 and 1500 (aromatic) and 1575 cm^{-1} (α-pyrone double bond); 100 MHz ^1H n.m.r. ($CDCl_3$, δ) : 6.20 and 7.64 (1H, d each, H-3 and H-4, J 9.5 Hz), 7.44 and 6.88 (1H, d each, H-5 and H-6, J 8.5 Hz), 3.81 (3H, s, 7-OMe), 2.42 (3H, s, 1'-Me), 1.78 (3H, s, vinylic Me at C-2') and 10.24 ppm (1H, s, not exchangeable with D_2O, 2'-CHO).

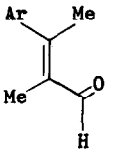
The $NaBH_4$ reduction of (I) followed by acetylation yielded murralonginol acetate (II), $C_{17}H_{18}O_5$, m.p. 110°; λ_{max} (EtOH) 318 nm (log ϵ, 4.18) and 257 (3.67); λ_{min} 270 (3.59) and 243 (3.55) - characteristic of 7-methoxy-8-alkyl coumarins[2]. The u.v. subtraction curve of (I) and (II), λ_{max} 242 nm (log ϵ, 4.02), resembled the u.v. spectrum of an α,β-unsaturated aldehyde. This supported the expected nonplanarity of the unsaturated aldehyde moiety and hence the lack of resonance with the aromatic ring due to steric hindrance.

*All new compounds showed reasonable i.r., u.v., ^1H n.m.r. and mass spectra.

Consistent with the completely aromatic structure with a conjugated side chain the mass spectrum of (I) (at 70 eV) exhibited the stable M^+ (258) as the base peak. The mass spectrum of (II) showed M^+ 302 (27%) and the base peak at m/e 242 due to the ion a generated as shown. Dihydromurralongin (III), m.p. 120° (M^+ 260, 0.2%), obtained in poor yield by hydrogenation of (I), showed the base peak at m/e 203, attributable to the ion b arising out of the extremely facile benzylic cleavage, thus confirming the presence of a methyl group at C-1'.

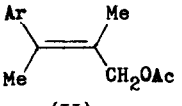


(I) s-trans

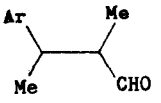


(Ia) s-cis

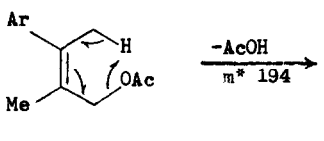
Ar = 7-methoxycoumarin-8-yl



(II)

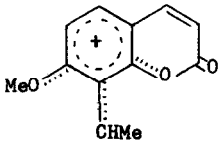


(III)



(II)

a, m/e 242



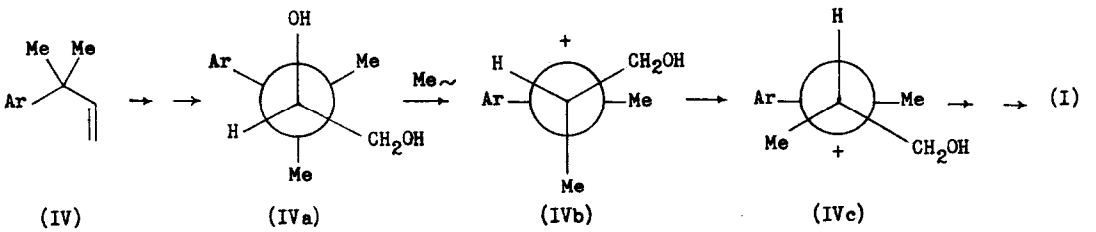
b, m/e 203

The stereochemistry of the double bond in the side chain of (I) has been established by N.O.E.[3] studies. Considerable N.O.E.[+] was observed for $\angle$1'-CH_3 $\rfloor \rightarrow$ C<u>H</u>O (25-30%) but none for $\angle$2'-CH_3 $\rfloor \rightarrow$ CHO leading to the conclusion that a) the 1'-CH_3 protons contributed more to the relaxation of C<u>H</u>O proton and hence must be in close nuclear proximity to the CHO proton necessititating the <u>trans</u> stereochemistry of the double bond and the preferred s-<u>trans</u> conformation (I) or its mirror image for the side chain in murralongin and b) the s-<u>cis</u> conformation (Ia), in which the protons of 2'-CH_3 and C<u>H</u>O being located in each other's vicinity are expected to display N.O.E. between them, must have too little residence time at room temperature for N.O.E. to be observed. However, the occurrence of N.O.E. in such a conformationally mobile system is not sufficient evidence for the time-independent proximity of 1'-CH_3 and C<u>H</u>O protons and the effect will definitely vary with temperature. The absence of any N.O.E. for $\angle$1'-CH_3 $\rfloor \rightarrow$ 7-OCH_3 and $\angle$2'-CH_3 $\rfloor \rightarrow$ 7-OCH_3 definitely shows that both CH_3's lie too far apart from the

[+]Proton signals saturated are shown in square brackets and the enhancement of the intensity in parentheses.

7-OCH_3 proving the nonplanarity of the α,β-unsaturated aldehyde system with the aromatic ring in the preferred conformation (I') (cf. u.v. data) and that the residence time of the high energy* planar conformation is far too short for any occurrence of N.O.E.

The novel 2-methylcrotonaldehyde side chain has so far not been found to occur in any coumarin or natural product. An attractive possibility of the biogenesis of (I) incorporating the unique side chain, outlined in Scheme I, would be through the intermediacy of (IV) having the α,α-dimethyl allyl side chain, as found in a number of coumarins reported from Rutaceae plants recently[4]. The diol (IVa) in its preferred conformation will form the open carbonium ion (IVb) and then (IVc) in which H-2' immediately finds itself in the plane of the vacant p orbital of (IVc) and thus would produce the trans isomer preferentially as outlined in Scheme I.



SCHEME I

Further studies on the chemistry and synthesis of murralongin are currently in progress.

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*Due to the severe steric interaction of the 1'-CH_3 and 2'-CH_3 with the 7-OCH_3 and coumarin lactonic oxygen - as is clearly seen by a scale model.

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