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FLEMICULOSIN, A NOVEL CHALCONE FROM FLEMENGIA FRUTICULOSA

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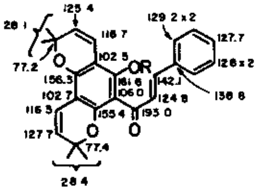
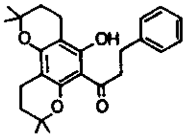
Abstract- Flemiculosin, a novel chalcone isolated from the leaves of Flemengia fruticulosa Wall, has been shown to possess an angular benzodipyran system, and its structure has been advanced as 1 on the basis of detailed spectroscopic evidence.

The genus Flemengia is notable for elaborating a variety of flavonoids, particularly chromenochalcones[1] and a number of Flemengia species have been chemically examined.[2] We report here the structure elucidation of flemiculosin, a novel chalcone with an angular benzodipyran system, isolated from the leaves of Flemengia fruticulosa wall. (Leguminosae). Chromatographic resolution of the petroleum ether extract of the leaves of F. fruticulosa yielded a crystalline red substance, flemiculosin, $C_{25}H_{24}O_4$ (M^+, at m/z 388), which was recognized as a chalcone from its color reactions and spectral data discussed in the sequel.

Flemiculosin (1), mp 98°C, which responds to tests for phenols with ferric chloride and phosphomolybdic acid reagents, gives negative Shinoda test under normal conditions, but responds positively and develops a pink coloration when the sample is boiled with ethanolic hydrochloric acid for several minutes prior to addition of zinc dust. This observation in conjunction with its uv (λ_{max} 210, 239sh, 255sh, 266sh, 278, 308, 360 nm; log ε, 3.08, 3.07, 3.14, 3.19, 3.24, 3.24, 3.15) and ir data (1632 and 3420 cm^{-1}) and ^1H nmr in $CDCl_3$ (δ 14.34, 1H, s) suggests that flemiculosin is a 2'-hydroxychalcone. 270 MHz ^1H nmr spectra of flemiculosin and its derivative in $CDCl_3$ were revealing and these clearly indicated it to be a chalcone with an unsubstituted B ring and a completely substituted A ring as a part of the benzodipyran system. The spectrum showed a pair of doublets (J=15.7 Hz) for trans-olefinic α- and β-hydrogens of the chalcone at δ 7.77 and 8.10, which, like typical 2'-hydroxy chalcones,[3] moved upfield to δ 7.43 and 7.52, respectively, in the spectrum of its monomethyl ether (1a), prepared by methylation of (1) with a large excess of diazomethane. The five aromatic hydrogens of the B ring appeared as two sets of multiplets at δ7.40 (2H, m) and 7.61 (3H, m) in the spectrum of flemiculosin and as a five-proton singlet in that of its hexahydro derivative (2), prepared by catalytic hydrogenation of (1). The presence of the benzodipyran system, like that of eriostemoic acid[4] (3) in flemiculosin, became evident from the display of twin peaks at δ 1.55 (6H, s) and 1.68 (6H, s) for two pairs of equivalent methyl groups and signals for four vinylic hydrogens as a pair of AB patterns with two equivalent A protons at δ 5.46 (2H, d, J=10.1 Hz) and non-equivalent B protons at δ 6.62 and 6.69 (1H, d each, J=10.1 Hz).



1: R = H
1a: R = Me.



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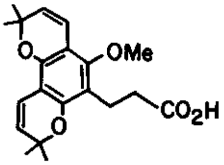
The oxygen substitution pattern of the A ring of flemiculosin was settled to be symmetrical in view of the similarity of ultraviolet absorption maxima of flemiculosin with rottlerone[5], a bis-chromenochalcone with unsubstituted B rings and fully substituted A rings with phloroglucinol-type oxygen substituents and of hexahydroflemiculosin (λ_{max} 283, 326 nm) with 5,7-dihydroxyflavanone[3]. A symmetrical oxygen substitution pattern for flemiculosin is also biogenetically consistent as prenyl substitutents in flavonoids and other related carboaromatic compounds are witnessed preponderently between two oxygen substituents, and therefore, two prenyl groups, necessary for giving rise to benzodipyran system by cyclization with ortho-hydroxyl groups, may best be available in 2',4',6'-trihydroxychalcone. Now, the formation of benzodipyran in such a system may take place in two possible ways; it may give rise to linear benzodipyran like eriostoic acid[6] (4) or angularly fused compounds like eriostemoic acid (3). The former type of fusion leads to symmetrical structure with phenolic hydroxyl para to the chalcone carbonyl. But such a structure for flemiculosin is ruled out on the grounds that uv maxima of flemiculosin does not suffer any bathochromic shift in the presence of sodium acetate.



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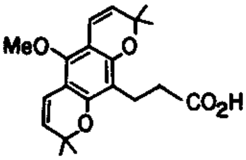

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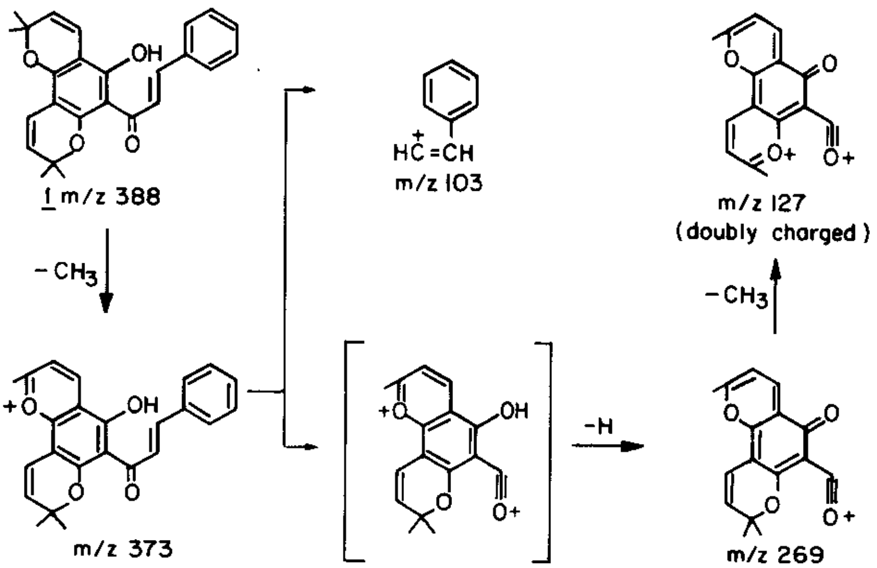
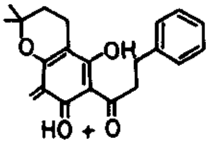
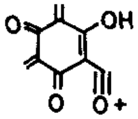
The ^1H nmr ($CDCl_3$) data of flemiculosin and particularly those of its hexahydro derivative (2) also spoke against a symmetrical structure and suggested the structure (1) for flemiculosin. 270 MHz ^1H nmr spectrum of hexahydroflemiculosin (2), $C_{25}H_{30}O_4$, mp 81°C, showed in addition to signals for four quaternary methyls and five aromatic hydrogens, six sets of signals for three isolated $-CH_2-CH_2-$ systems. One of these three pairs of adjacent methylene groups appeared as triplets at δ3.02 and 3.40 which were attributed to the methylenes of dihydrochalcone ($-CO-CH_2-CH_2-Ar$). The remaining two pairs of methylenes showed deceptively simple triplets at δ 1.74, 1.77, 2.53 and 2.62 for two pairs of non-equivalent methylenes for the two dimethyldihydropyran systems. ^{13}C nmr data ($CDCl_3$) also disclosed the absence of any symmetry element in ring A of flemiculosin and confirmed its structure as 6-cinnamoyl-5-hydroxy-2,2,8,8-tetramethyl-2H,8H-benzo[1,2-b:3,4-b']dipryan (1). Mass spectrum of flemiculosin showed, in addition to the molecular ion peak at m/z 388 (73%), other important ion peaks at m/z 373 (base peak), 269 (82%), 241 (15%), 131 (8%), 127 (12%), 103 (14%) and 77 (11%) in support of the structure (1). The genesis of these fragment ions from the molecule is shown below:



The fragmentation mode of hexahydroflemiculosin is dominated by retro Diels-Alder cleavage of the dihydropyran moieties, and as a result, abundant fragment ions at m/z 339(a) and 117(b), in addition to the expected base peak at m/z 91, due to the tropylium cation, are discernible in its mass spectrum. The ions, a and b, adduce additional evidence to the presence of benzodipyran system in flemiculosin.



(a)



(b)

Flemiculosin is unique in the group of chalcones and it is the first member in the flavonoid class of compounds to have a benzodipyran system.

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