GALANGUSTIN, A NEW FLAVONE FROM GALEOPSIS ANGUSTIFOLIA

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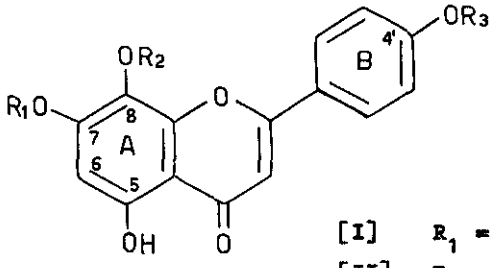
Abstract - Galangustin has the structure of 5,7-dihydroxy-8,4'-dimethoxyflavone.

During the examination[1] of the acetone extract of the aereal part of a sample of Galeopsis angustifolia Ehrh. ex Hoffm. (family Labiatae) collected in Northern Italy, we isolated a flavone amongst other products. As the substance seems to be new, we discuss its structure here and propose for it the name galangustin.

Galangustin has m.p. 225°C (from MeOH) and formula $C_{17}H_{14}O_6$ (MS, M^+ 314). Its MS shows peaks at m/z 314 (68%), 299 (100), 271 (22), 167 (10), 139 (18), 135 (7), 133 (6), 132 (18), 121 (4), 118 (20), 111 (11). The NMR spectrum (60 MHz, DMSO-d_6) has a singlet at δ 3.81 for two OCH_3 groups, a singlet at 6.28 (one proton), a singlet at 6.83 (one proton), an A_2B_2 quartet at 7.12 and 8.01 with J 9 Hz, and a singlet at 12.59 for a phenolic chelated OH.

The above data indicate that: ring B is substituted only at position 4' and probably with an OCH_3 group (NMR: A_2B_2 system; MS: peaks 135, 132, 121, 118); the chelated OH group is on position 5; the second OCH_3 group and the second OH group should be on ring A (NMR: singlets at δ 6.28 and 6.83, no coupling; MS: peaks 167, 139, 111). The base peak at 299 is consistent[2] with the very easy loss of CH_3 from an OCH_3 group at positions 6 or 8.

The UV spectrum (abs. EtOH) shows maxima at nm 275 (log ε 4.09), 297 (4.04), 315 (sh, 4.00); addition of NaOAc promotes a small bathochromic shift from nm 275 to 280 (4.12), whereas the maximum at 297 changes into a sh and the sh at 315 shifts at 350 (3.66); addition of EtO^- gives a shift from 275 to 285 (4.30) and from 315 to 385 (3.64), whereas the maximum at nm 297 disappears. This behaviour rules out[3] the possibility of a 4'-OH substituent and favours position 7 as the site of the second OH group; the strong decreasing of the absorbance of the sh at 315 after addition of NaOAc is typical[4] of a 7-OH group when no other OH occurs



[I] $R_1 = CH_3$ $R_2 = CH_3$ $R_3 = CH_3$
[II] $R_1 = H$ $R_2 = CH_3$ $R_3 = CH_3$
[III] $R_1 = CH_3$ $R_2 = H$ $R_3 = CH_3$
[IV] $R_1 = CH_3$ $R_2 = CH_3$ $R_3 = H$

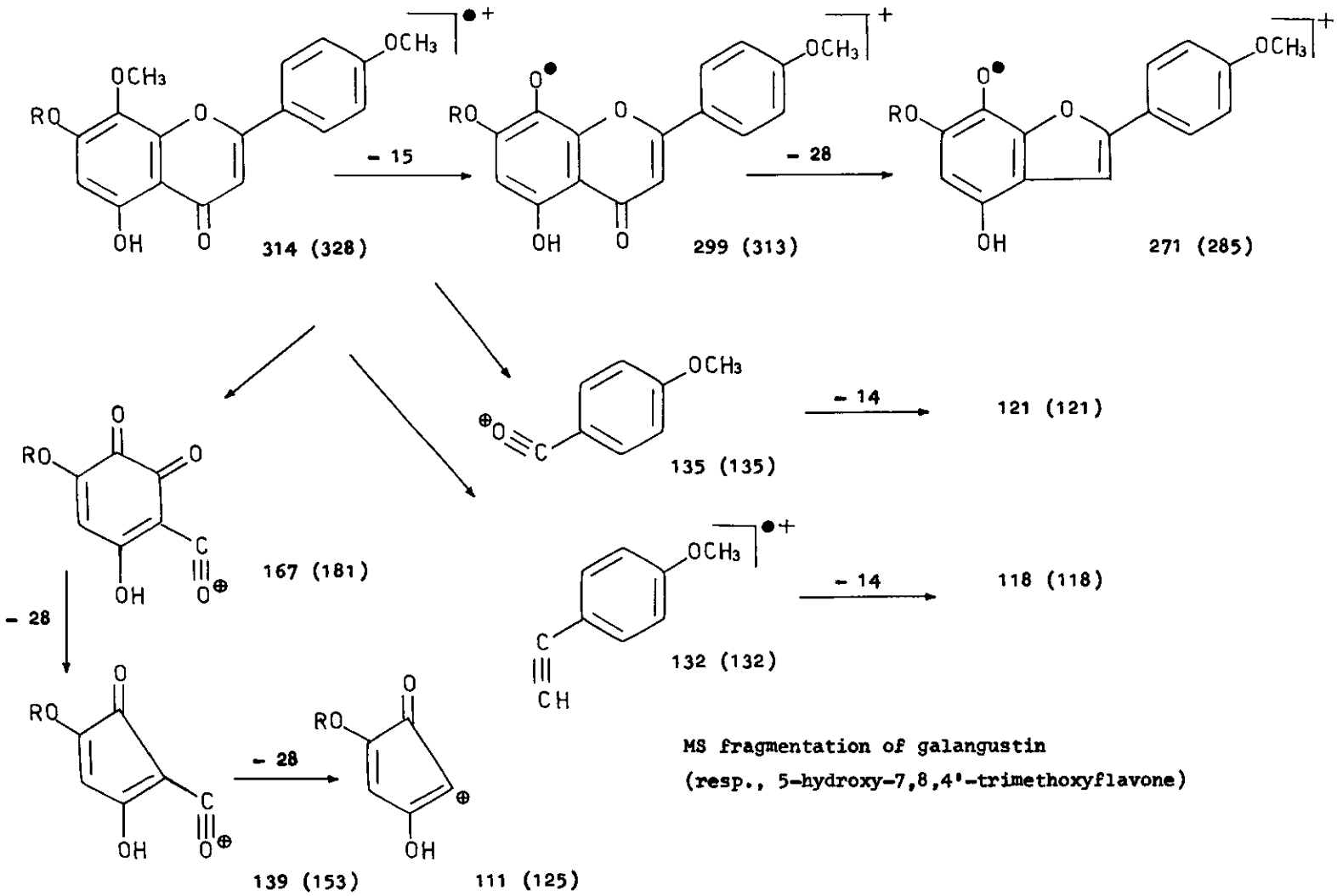
on ring B.

Acetylation of galangustin with Ac_2O-pyridine yields a diacetate $C_{21}H_{18}O_8$ (MS, M^+ 398), m.p. 217°C (from EtOAc). Its MS has peaks at m/z 398, 356, 314, 299, 285, 271, 234, 167, 153, 139, 135, 133, 132. The NMR spectrum (60 MHz, $CDCl_3$) shows signals at δ 2.28 and 2.33 (s, 2 $OCOCH_3$), 3.81 and 3.97 (s, 2 OCH_3), 6.56 (s, 1 H), 6.76 (s, 1 H), 7.00 and 7.84 (A_2B_2 quartet J 9 Hz, 4 H).

Methylation of galangustin with ethereal diazomethane gives a $C_{18}H_{16}O_6$ derivative (MS, M^+ 328), m.p. 223-224°C, identified (m.p., MS, NMR, UV) as 5-hydroxy-7,8,4'-trimethoxyflavone [I], already known as both a synthetic[5] and a natural[6] product. MS: peaks at m/z 328 (36%), 313 (100), 285 (12), 181 (23), 153 (87), 135 (19), 133 (32), 132 (19), 125 (48), 121 (5), 118 (15). NMR (60 MHz, $CDCl_3$): δ 3.83 (s, 1 OCH_3), 3.86 (s, 2 OCH_3), 6.38 (s, H-6), 6.56 (s, H-3), 7.01 and 7.93 (A_2B_2 quartet, J 9 Hz, 2',3',5',6'-H), 12.65 (s, chelated phenolic OH).

The identification of [I] thus proves that position 6 is not substituted in galangustin; positions 7,8 and 4' must be therefore the sites of two methoxy and one hydroxy groups. In theory, galangustin could have the structures [II] or [III] or [IV]. But its mass spectrum, when compared with the spectrum of [I], proves beyond any doubt that the hydroxy group rests on ring A at positions 7 or 8. So structure [IV] can be ruled out definitively; moreover, the flavone [IV] had been described previously[6] as a natural and synthetic product, and its physical and spectroscopic data are quite different from those of galangustin. Also the flavone [III] had been synthesized[5,7] and its data are not in agreement with those of our product.

Only the structure [II] can account for the evidence given here. Therefore, galangustin is 5,7-dihydroxy-8,4'-dimethoxyflavone. The behaviour of the UV spectrum is consistent[3,4,8,9] with structure [II]. The fragmentations in the mass spectra of galangustin and [I], as depicted in the schema, are in agreement with previous reports[10,11,12].



MS fragmentation of galangustin
(resp., 5-hydroxy-7,8,4'-trimethoxyflavone)

It can be remarked that a product, named cirsitakaogenin, was reported recently[13] as an extractive from Cirsium japonicum D.C. var. takaoense Kitamura (family Compositae) and claimed to have structure [II]. However, the physical and spectroscopic data quoted in the above paper[13] do not agree at all[14] with those found on our product. Therefore we believe that the two products are clearly different; cirsitakaogenin has not structure [II] but an isomeric one, and it is worthy of further investigation.

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14. Reported[13] cirsitakaogenin, m.p. 259-260°C; diacetate, m.p. 186-187°C.

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