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THE HOMO-ISOFLAVONES II[1]. ISOLATION AND STRUCTURE OF 4'-O-METHYL-PUNCTATIN, AUTUMNALIN AND 3,9-DIHYDRO-AUTUMNALIN

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In an earlier communication[1] the isolation and structure of Eucomin and Eucomol which belong to a new class of natural products, the homo-isoflavones, was described. Similar studies on the bulbs of *Eucomis autumnalis* GRAEB (Liliaceae) have resulted in the isolation of three new members of this class in addition to the previously described eucomin.

4'-O-Methyl-punctatin (1), $C_{18}H_{16}O_6$ *, yellow needles or rods, m.p. 213.5-214.5°; $[\alpha]_D^{27} = \pm 0°$ (dioxan). The IR-spectrum (KBr) showed frequencies at 3380; 1637; 1600, 1560, 1507, 1490 and 820 cm^{-1} (p-subst. benzene ring), 805 (CH=C) and 1255 (aryl ether) cm^{-1}. The UV-spectrum (EtOH) exhibited a main broad absorption at 360 nm (log ε = 4.51) with shoulders at 310 (4.17) and 227 (4.29) and rising absorption about 200 (4.55) nm (log ε). Addition of anhydrous Na-acetate and of $AlCl_3$ caused red shifts of the long wavelength band of 38 nm and 26.5 nm respectively which is characteristic of hydroxyl groups in the 7 and 5 positions[2,3]. The n.m.r. spectrum at 100 MHz** (d_6-DMSO) reveals the presence of two methoxyl groups (singlets at 3.63 and 3.81 ppm), two hydroxyl groups, singlets at 10.55 (C-7) and 12.49 (hydrogen bonded C-5) ppm and of five aromatic protons. One of these occurs as a sharp singlet at 5.93 ppm which is assigned to the C-6 proton and the other four form a perturbed AA'BB' system at ca. 6.97 (2H; $J \sim 9$ Hz) and ca. 7.35 ppm (2H; $J \sim 9$ Hz) which is consistent with a para-substituted benzene ring. A further proton at 7.64-7.68 ppm is split into a triplet by coupling with the two aliphatic protons at C-2 which appear as a doublet at 5.34 ppm ($J \sim 2$ Hz). This relationship was shown by double resonance studies wherein the latter was transformed into a singlet when the vinylic

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* Derived from the elemental analysis and the mass spectrum. We are indebted to Dr. W. Vetter, F. Hoffmann-La Roche & Co. A.G., Basel, for the measurement of the mass spectra and the accurate masses.

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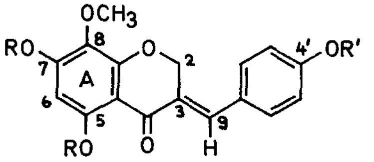
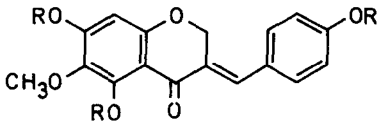
C-9 proton was irradiated and similarly the C-9 proton collapsed to a singlet when the C-2 protons were irradiated. The exocyclic nature and trans geometry of the double bond is indicated by the position of the UV-absorption and the chemical shift of the C-2 and C-9 protons. The mass spectrum showed the molecular ion as base peak, m/e 328.0946 (100 %, M^+, $C_{18}H_{16}O_6$), m/e 313 (38 %, M-CH_3) and peaks at m/e 183 (22 %), 182 (21 %), 168 (10 %, 183-CH_3), 166.9981 (66 %, 182-CH_3, $C_7H_3O_5$) and 146.0729 (60 %, $C_{10}H_{10}O$) indicating a type D fragmentation[4a] and confirming the presence of one of the methoxyl groups in the 4'-position. Treatment of 4'-O-methyl-punctatin (1) with acetic anhydride and pyridine leads to di-O-acetyl-4'-O-methyl-punctatin (2) ($C_{22}H_{20}O_8$, amorphous) and with dimethyl sulphate/K_2CO_3 in acetone to the dimethyl derivative 3 ($C_{20}H_{20}O_6$, M^+ 356.1257, m.p. 145-149.5°). The positions of the four methoxyl groups in the n.m.r. spectrum ($CDCl_3$) were 3.77, 3.83 and 3.92 (2) ppm which were shifted to 3.23, 3.30, 3.51 and 3.75 ppm when benzene was used as the solvent which is consistent with a 5,7,8-oxygenation pattern in ring A[5]. Comparison of 3 with synthetic 4',5,7,8-tetra-methoxy-homo-isoflavone[6] showed them to be identical.

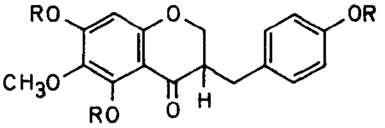
Autumnalin (4), $C_{17}H_{14}O_6$[*], yellow rods, m.p. 244.5-247.5°; $[\alpha]_D^{24} = \pm 0°$ (dioxan). The IR-spectrum (KBr) showed frequencies at 3420; 1650; 1600, 1580, 1510, 1470 and 825 (p. subst. benzene ring) 817 (CH=C) and 1227 (aryl ether) cm^{-1}. The UV-spectrum (EtOH) displayed a main broad absorption at 363 nm (log ε = 4.53) with shoulders at 236 (4.17) and 209 (4.46) and a short wavelength maximum at 200.5 (4.51) nm (log ε). Addition of anhydrous Na-acetate and of $AlCl_3$ caused a red shift of the long wavelength band of 34 and 26 nm respectively whilst NaOH caused a red shift of 74 nm with an increase in intensity (log ε = 4.68) of this band, these properties being characteristic of hydroxyl groups at 7,5 and 4' positions[2]. The n.m.r. spectrum at 100 MHz (d_6-DMSO) showed the presence of one methoxyl group (singlet, 3.72 ppm), the strongly hydrogen bonded 5-hydroxyl proton (singlet, 12.89 ppm) and a broad absorption ca. 3.40 ppm of the 7 and 4' hydroxyl protons which were exchanging due to a trace of water in the solvent. A sharp singlet at 5.96 ppm was assigned to the C-8 proton and a perturbed AA'BB' system centred at ca. 6.90 (2H; J∼9 Hz) and ca. 7.34 ppm (2H; J∼9 Hz) to a para-substituted benzene ring. A triplet at 7.66-7.72 ppm (C-9 proton) was shown to be coupled with the two aliphatic protons at C-2 (5.34 ppm, J∼2 Hz) by spin-spin-decoupling. Again the exocyclic nature and trans geometry of the double bond is indicated by the chemical shift of the C-2 and C-9 protons and the position of the UV-absorption. The mass spectrum of 4 showed the molecular ion m/e 314.0793 (92 %, M^+, $C_{17}H_{14}O_6$), m/e 299 (35 %, M-CH_3), and peaks at m/e 183.0291 (17 %, $C_8H_7O_5$), 182 (7.9 %), 168 (13 %, 183-CH_3), 166.9980 (86 %, 182-CH_3, $C_7H_3O_5$), 132 (22 %)and 133.0649 (43.5 %, 132 + H, C_9H_9O) which indicates a type D fragmentation 4a) and confirms the location of the methoxyl group in ring A. Methylation of 4 with dimethyl sulphate/K_2CO_3 in acetone produces tri-O-methyl-autumnalin (5), $C_{20}H_{20}O_6$, M^+ 356.1259, m.p. 115-117.5°. The positions of the four methoxyl groups in the n.m.r. spectrum ($CDCl_3$) were: 3.87, 3.88, 3.92 and 4.02 ppm, which changed to 3.20, 3.28, 3.79 and 4.17 ppm when deuterobenzene was used as the solvent. These solvent shifts are consistent with a 5,6,7-oxygenation pattern in ring A 5), thus indicating structure 4 for Autumnalin.





1 R=H, R' = CH_3 4'-O-methyl-punctatin
2 R= R' = Ac
3 R= R' = CH_3

4 R=H Autumnalin
5 R=CH_3



6 R=H 3,9-Dihydro-autumnalin
7 R=Ac
8 R=CH_3

3,9-Dihydro-autumnalin (6), $C_{17}H_{16}O_6$*, pale yellow cubes, m.p. 207-209°; $[\alpha]_D^{24}$= -10° (dioxan). The IR-spectrum (KBr) showed bands at 3360; 1650; 1605, 1587, 1510, 1470, 1447 and 827 (p. subst. benzene ring) and 1267 (aryl ether) cm^{-1}. The UV-spectrum (EtOH) had absorptions at 336 (3.94), 292 (4.61) and 210 (4.72) with an inflection at 235 (4.38) and a shoulder at 220 (4.67) nm (log ε). Addition of anhydrous Na-acetate shifts the main peak at 292 to 333 nm and $AlCl_3$ to 314 nm, these shifts being characteristic of hydroxyl groups an C-7 and C-5 2) 3). The n.m.r. spectrum at 100 MHz (d_6-DMSO) shows the presence of one methoxyl group (singlet, 3.60 ppm) and three hydroxyl groups at 9.16, 10.48 and 12.14 (hydrogen bonded C-5) ppm. A singlet at 5.87 ppm is assigned to the isolated C-8 proton whilst the remaining four aromatic protons form a perturbed AA'BB' system centred at ca. 6.62 (2H; J∼8 Hz) and ca.

6.96 (2H; $J \sim 8$ Hz) indicating a para-substituted benzene ring. A multiplet ca. 2.90 ppm is assigned to the benzylic C-9 protons and another ca. 4.10 ppm to the aliphatic C-2 protons. The mass spectrum of 6 showed the molecular ion m/e 316.0948 (73 %, M^+, $C_{17}H_{16}O_6$), m/e 301 (4.4 %, M-CH_3), and peaks at m/e 210.0527 (51 %, $C_{10}H_{10}O_5$), 195.0293 (41.5 %, 210-CH_3, $C_9H_7O_5$) and 107 (100 %, p-hydroxybenzylium or tropylium ion) according to a type A_4 fragmentation[4b] and indicating that the methoxyl group is in ring A. Ions also occur at m/e 183 (9.5 %), 182 (6.5 %) and 166.9981 (14.2 %, $C_7H_3O_5$) which represents the retro-Diels-Alder type fragmentation which is less prolific in the saturated series. Acetylation of 6 with acetic anhydride/pyridine or refluxing acetic anhydride leads to the tri-O-acetyl-derivative 7, $C_{23}H_{22}O_9$, amorphous, $[\alpha]_D^{24}$= -5° ($CHCl_3$) and methylation with dimethyl sulphate/K_2CO_3 in acetone yields the tri-O-methyl-derivative 8, $C_{20}H_{22}O_6$, M^+ 358.1417, $[\alpha]_D^{29}$= -3° ($CHCl_3$), m.p. 75.0-76.5°. The positions of the four methoxyl groups in the n.m.r.spectrum ($CDCl_3$) of 8 are 3.81, 3.83, 3.90 and 3.96 ppm which are shifted to 3.21, 3.35, 3.76 and 4.05 ppm when benzene is used as the solvent thus indicating a 5,6,7-oxygenation pattern[5] in ring A. The non-identity of 8 with the hydrogenation product of synthetic tri-O-methyl-punctatin thus confirms the structure of 3,9-dihydro-autumnalin as 6.

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