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THE HOMO-ISOFLAVONES, A NEW CLASS OF NATURAL PRODUCT. ISOLATION AND STRUCTURE OF EUCOMIN AND EUCOMOL.

P. Böhler and Ch. Tamm
Institut für Organische Chemie der
Universität Basel, Switzerland.

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Eucomin and Eucomol are two new compounds which we have isolated from the bulbs of Eucomis bicolor BAK. (Liliaceae). They belong to a new class of natural products which we name homo-isoflavones. Structure 1 is assigned to Eucomin and structure 5 to Eucomol on the basis of the following evidence.

Eucomin, $C_{17}H_{14}O_5$*, crystallizes in yellow needles of m.p. 194-196°; $[\alpha]_D^{25} \pm 0°$ (dioxan). Its UV-spectrum exhibits a broad absorption maximum at 365 nm (log ε = 3.33) with shoulders at 194 (3.38) and 214 nm (3.31). The IR-spectrum (KBr) shows frequences at 3320 (OH); 1645 (C=C); 1630 (C=O); 1600, 1590, 1550, 1450 and 830 (p-subst. benzene ring); 810 (CH=C-); 1270 (C_6H_5-O-C) cm^{-1}. The NMR-spectrum at 100 MHz** (d-DMSO) reveals the presence of 1 methoxyl group (singlet at 3.76 ppm), 2 hydroxyl groups (singlets at 10.60 and 12.70 ppm) and 6 aromatic protons. Two of these, appearing at 5.83 (1H) and 5.88 ppm (1H) with a meta-coupling of 2 cps, are attached to C-6 and C-8. The other 4 protons form

* 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.

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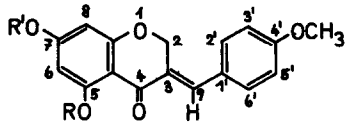
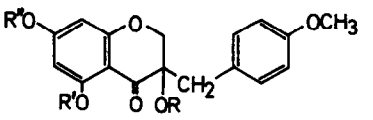
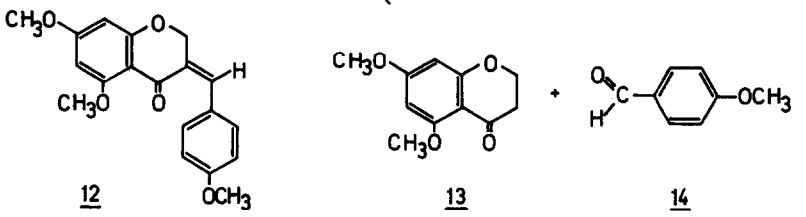


1 R = R' = H: Eucomin
2 R = H; R' = Ac
3 R = H; R' = CH_3
4 R = R' = CH_3



5 R = R' = R" = H: Eucomol
6 R = R' = R" = Ac
7 R = R" = Ac; R' = H
8 R = H; R' = R" = CH_3
9 R = R' = H; R" = CH_3
10 R = R' = Ac; R" = CH_3
11 R = Ac; R' = R" = CH_3



12 13 14

a perturbed AA'BB' (or AA'XX')-system centered at ca. 6.98 (2H; J ~ 9 cps) and ca. 7.34 ppm (2H; J ~ 9 cps) which is consistent with a para-substituted benzene ring. A further proton at 7.64-7.66 ppm is split into a triplet by coupling with the two aliphatic protons at C-2 which appear as a doublet at 5.30 ppm (J = 2 cps). The latter is transformed to a sharp singlet when the C-9-proton is irradiated. Upon irradiation of the C-2-protons the vinylic C-9-proton is decoupled and appears as a singlet at 7.66 ppm. The exocyclic position and the trans geometry of the double bond is indicated by the chemical shift of the C-2- and C-9-protons and by the position of the UV-absorption maximum. The mass spectrum of Eucomin (1) shows peaks at m/e 298 (M^+), 283 (M-15) and 3 peaks at m/e 153, 152 and 146 indicating a type D-fragmentation[1]. Treatment of Eucomin (1) with acetic anhydride at 140° leads to mono-O-

-acetyl-eucomin (2) ($C_{19}H_{16}O_6$; m.p. 146-147°) with $(CH_3O)_2SO_2$-NaOH to the monomethyl derivative 3 ($C_{18}H_{16}O_5$; m.p. 145-149°) and with CH_3I-Ag_2O in DMF[2] to the dimethyl derivative 4 ($C_{19}H_{18}O_5$; m.p. 141-144°). A further proof of structure 1 for Eucomin was provided by the total synthesis of its dimethyl derivative 4 from 5,7-dimethoxy-chroman-4-one (13)[3] and anisaldehyde (14) using dry HCl and acetic acid as condensing agent.

Irradiation of 4 with a high pressure Hg-lamp at 300-400 nm leads to the cis-isomer 12 in whose NMR-spectrum the vinylic proton at C-9 is shifted from 7.69 to 6.69 ppm (triplet) and the methylene protons at C-2 from 5.22 ppm (doublet, J = 1.75 cps) to 4.84 ppm (doublet, J = 1.25 cps)[4]. The AA'BB'-system (4H) is centered at 6.81 and 7.84 ppm, while that of 4 is located at 6.86 and 7.18 ppm. These observations confirm the trans-configuration of the double bond in Eucomin (1).

Eucomol, $C_{17}H_{16}O_6$*, crystallized in colourless hexagonal plates of m.p. 134.5 - 135°; $[\alpha]_D^{25}$ - 32° (chloroform). The UV-spectrum (ethanol) shows maxima at 195 (3.84), 214 (3.49), 293 (3.29) and a shoulder at 326 (2.97) nm (log ε). Addition of Na-acetate shifts the main peak from 293 nm to 330 nm and of $AlCl_3$ to 315 nm. These spectroscopic properties are characteristic for the presence of 2 hydroxyls at C-5 and C-7[5,6]. The IR-spectrum (KBr) is characterized by bands at 3450 and 3380-3305 (OH); 1635 (C=O); 1610, 1585, 1510, 1446 and 838 (p-subst. benzene ring); 1245 (C_6H_5-O-C)cm^{-1}. The NMR-spectrum of Eucomol (5) at 100 MHz ($CDCl_3$) shows 1 methoxyl group at 3.73 ppm and 3 hydroxyl groups at 3.32, 6.02-6.04 and 11.20 ppm. In d-DMSO a singlet appears at 5.86 instead of 3.32 ppm indicating the presence of a tertiary hydroxyl. The doublets at 5.94 and 5.98 ppm (J = 2 cps) are assigned to aromatic protons in meta positions (C-6, C-8) and the remaining 4 aromatic protons (AA'BB' or AA'XX'-system at 6.80 ppm; J ~ 8 cps and 7.08 ppm; J ~ 8 cps) to a para-substituted benzene ring. The two protons at C-2 appear at 4.02 and 4.16 ppm (AB-system; J = 11 cps). The signal at 2.90 ppm (2H) is characteristic

for the methylene portion of a benzyl group (C-9). These assignments are confirmed by spin-spin decoupling experiments in which irradiation at C-9 produces a symmetric AA'BB'-system with a change of the intensities. The mass spectrum of Eucomol (5) shows peaks at m/e 316 (M^+), 195 (trihydroxy-chroman-4--one ion) and 121 (p-methoxy-benzylium or -tropylium ion) according to a type A_4-fragmentation[1]. Acetylation of Eucomol (5) leads to the triacetate 6 ($C_{23}H_{22}O_9$, amorphous, $[\alpha]_D^{25}$ - 38° (chloroform) and diacetate 7 ($C_{21}H_{20}O_8$; amorphous). Treatment of Eucomol (5) with CH_2N_2 in methanol or ether gives the trimethylether 8 ($C_{19}H_{20}O_6$, m.p. 120-121°, $[\alpha]_D^{25}$ - 71° (chloroform) as main product and the dimethylether 9 ($C_{18}H_{18}O_6$, amorphous, $[\alpha]_D^{25}$ - 31° (chloroform) as secondary product. The ratio of these products is reversed when ether is used as solvent. Acetylation of compounds 8 and 9 leads to the corresponding acetyl derivatives 10 ($C_{22}H_{22}O_8$, amorphous, $[\alpha]_D^{25}$ - 44°, chloroform) and 11 ($C_{21}H_{22}O_7$, amorphous, $[\alpha]_D^{25}$ - 101°, chloroform). The spectroscopic properties of all derivatives are in excellent agreement with the proposed structures.

The structures of Eucomin and Eucomol differ from those of the classical isoflavones by the insertion of a carbon atom into the skeleton, a situation which is of considerable biogenetic interest.

The details of this investigation are to be published in Helv. Chim. Acta.

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